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ENVIRONMENTAL HEALTH

RESEARCH Open Access

Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure

Robin Mesnage[1], Matthew Arno[2], Manuela Costanzo[3], Manuela Malatesta[3], Gilles-Eric Séralini[4] and Michael N. Antoniou[1*]

Abstract

Background: Glyphosate-based herbicides (GBH) are the major pesticides used worldwide. Converging evidence suggests that GBH, such as Roundup, pose a particular health risk to liver and kidneys although low environmentally relevant doses have not been examined. To address this issue, a 2-year study in rats administering 0.1 ppb Roundup (50 ng/L glyphosate equivalent) via drinking water (giving a daily intake of 4 ng/kg bw/day of glyphosate) was conducted. A marked increased incidence of anatomorphological and blood/urine biochemical changes was indicative of liver and kidney structure and functional pathology. In order to confirm these findings we have conducted a transcriptome microarray analysis of the liver and kidneys from these same animals.

Results: The expression of 4224 and 4447 transcript clusters (a group of probes corresponding to a known or putative gene) were found to be altered respectively in liver and kidney ($p < 0.01$, $q < 0.08$). Changes in gene expression varied from −3.5 to 3.7 fold in liver and from −4.3 to 5.3 in kidneys. Among the 1319 transcript clusters whose expression was altered in both tissues, ontological enrichment in 3 functional categories among 868 genes were found. First, genes involved in mRNA splicing and small nucleolar RNA were mostly upregulated, suggesting disruption of normal spliceosome activity. Electron microscopic analysis of hepatocytes confirmed nucleolar structural disruption. Second, genes controlling chromatin structure (especially histone-lysine N-methyltransferases) were mostly upregulated. Third, genes related to respiratory chain complex I and the tricarboxylic acid cycle were mostly downregulated. Pathway analysis suggests a modulation of the mTOR and phosphatidylinositol signalling pathways. Gene disturbances associated with the chronic administration of ultra-low dose Roundup reflect a liver and kidney lipotoxic condition and increased cellular growth that may be linked with regeneration in response to toxic effects causing damage to tissues. Observed alterations in gene expression were consistent with fibrosis, necrosis, phospholipidosis, mitochondrial membrane dysfunction and ischemia, which correlate with and thus confirm observations of pathology made at an anatomical, histological and biochemical level.

Conclusion: Our results suggest that chronic exposure to a GBH in an established laboratory animal toxicity model system at an ultra-low, environmental dose can result in liver and kidney damage with potential significant health implications for animal and human populations.

Keywords: Pesticides, Glyphosate, Transcriptome, Chronic toxicity, Liver, Kidney

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Cardiotoxic Electrophysiological Effects of the Herbicide Roundup® in Rat and Rabbit Ventricular Myocardium In Vitro

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Abstract Roundup (R), a glyphosate (G)-based herbicide (GBH), containing unknown adjuvants is widely dispersed around the world. Used principally by farmers, intoxications have increasingly been reported. We have studied R effects (containing 36 % of G) on right ventricular tissues (male Sprague–Dawley rats, up to 20,000 ppm and female New Zealand rabbits, at 25 and 50 ppm), to investigate R cardiac electrophysiological actions in vitro. We tested the reduced Ca^{++} intracellular uptake mechanism as one potential cause of the electrical abnormalities after GBH superfusion, using the Na^{+}/K^{+}-ATPase inhibitor ouabain or the 1,4-dihydropyridine L-type calcium channel agonist BAY K 8644 which increases I_{Ca}. R concentrations were selected based on human blood ranges found after acute intoxication. The study showed dose-dependent V_{max}, APD_{50} and APD_{90} variations during 45 min of R superfusion. At the highest concentrations tested, there was a high incidence of conduction blocks, and 30-min washout with normal Tyrode solution did not restore excitability. We also observed an increased incidence of arrhythmias at different doses of R. Ouabain and BAY K 8644 prevented V_{max} decrease, APD_{90} increase and the cardiac inexcitability induced by R 50 ppm. Glyphosate alone (18 and 180 ppm) had no significant electrophysiological effects. Thus, the action potential prolonging effect of R pointing to I_{Ca} interference might explain both conduction blocks and proarrhythmia in vitro. These mechanisms may well be causative of QT prolongation, atrioventricular conduction blocks and arrhythmias in man after GBH acute intoxications as reported in retrospective hospital records.

Keywords Roundup · Glyphosate · Action potential duration · Conduction blocks · Pro-arrhythmia · Calcium

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Introduction

Exposure of human and mammalian populations to environmental and industrial contaminants represents a growing concern due to the impact of these pollutants on human health [1]. Roundup (R), a glyphosate (G)-based herbicide (GBH), containing adjuvants such as polyoxy ethyl amine (POEA) is the most used in the world. Although several commercial formulations exist, only a few specifically declare their adjuvant contents [2]. R residues are found in tap water, food or feed as adjuvants or other active ingredients are found in ground water, to

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RESEARCH ARTICLE Open Access

Simultaneous exposure to multiple heavy metals and glyphosate may contribute to Sri Lankan agricultural nephropathy

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Abstract

Background: Sri Lankan Agricultural Nephropathy (SAN), a new form of chronic kidney disease among paddy farmers was first reported in 1994. It has now become the most debilitating public health issue in the dry zone of Sri Lanka. Previous studies showed SAN is a tubulo-interstitial type nephropathy and exposure to arsenic and cadmium may play a role in pathogenesis of the disease.

Methods: Urine samples of patients with SAN ($N = 10$) from Padavi-Sripura, a disease endemic area, and from two sets of controls, one from healthy participants ($N = 10$) from the same endemic area and the other from a non-endemic area ($N = 10$; Colombo district) were analyzed for 19 heavy metals and for the presence of the pesticide- glyphosate.

Results: In both cases and the controls who live in the endemic region, median concentrations of urinary Sb, As, Cd, Co, Pb, Mn, Ni, Ti and V exceed the reference range. With the exception of Mo in patients and Al, Cu, Mo, Se, Ti and Zn in endemic controls, creatinine adjusted values of urinary heavy metals and glyphosate were significantly higher when compared to non-endemic controls. Creatinine unadjusted values were significant higher for 14 of the 20 chemicals studied in endemic controls and 7 in patients, compared to non-endemic controls. The highest urinary glyphosate concentration was recorded in SAN patients (range 61.0-195.1 μg/g creatinine).

Conclusions: People in disease endemic area exposed to multiple heavy metals and glyphosate. Results are supportive of toxicological origin of SAN that is confined to specific geographical areas. Although we could not localize a single nephrotoxin as the culprit for SAN, multiple heavy metals and glyphosates may play a role in the pathogenesis. Heavy metals excessively present in the urine samples of patients with SAN are capable of causing damage to kidneys. Synergistic effects of multiple heavy metals and agrochemicals may be nephrotoxic.

Keywords: Chronic kidney disease, Heavy metals, Pesticides, Sri Lanka, Synergistic effect

Background

Heavy metals are natural components of the earth's crust. These elements are the oldest toxins known to humans, having been used for thousands of years. Potential sources of heavy metal exposure include natural sources, industrial processes, commercial products, folk remedies, contaminated food and herbal products [1]. Different definitions for heavy metals have been proposed based on density, atomic number or atomic weight, chemical properties and toxicity. In general, heavy metals comprise elements that exhibit metallic properties and mainly include the transition metals, metalloids, lanthanides and actinides. One definition entails that heavy metals are inorganic elements which have five times the specific gravity of water [2]. Usually heavy metals have an atomic number of 21 or higher and a specific gravity greater than 3.5 [1]. All heavy metals demonstrate toxic effects on living organisms via the interference of the metabolic pathways [1, 3]. Some heavy metals are essential micronutrients. However, depending on the route of ingestion, dose, valence state, mode of exposure (acute versus chronic), and the age of the individual the heavy metals can cause varying degree of toxicity. The most commonly affected organ systems include gastrointestinal, cardiovascular, hematopoietic, renal, and central

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Glyphosate-based herbicides reduce the activity and reproduction of earthworms and lead to increased soil nutrient concentrations

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Herbicide use is increasing worldwide both in agriculture and private gardens. However, our knowledge of potential side-effects on non-target soil organisms, even on such eminent ones as earthworms, is still very scarce. In a greenhouse experiment, we assessed the impact of the most widely used glyphosate-based herbicide Roundup on two earthworm species with different feeding strategies. We demonstrate, that the surface casting activity of vertically burrowing earthworms (*Lumbricus terrestris*) almost ceased three weeks after herbicide application, while the activity of soil dwelling earthworms (*Aporrectodea caliginosa*) was not affected. Reproduction of the soil dwellers was reduced by 56% within three months after herbicide application. Herbicide application led to increased soil concentrations of nitrate by 1592% and phosphate by 127%, pointing to potential risks for nutrient leaching into streams, lakes, or groundwater aquifers. These sizeable herbicide-induced impacts on agroecosystems are particularly worrisome because these herbicides have been globally used for decades.

During the past 50 years the human population has more than doubled, while the productive arable area has increased only by 10%[1,2]. As a consequence, the intensity of agricultural production has increased dramatically including the use of pesticides. Among pesticides, glyphosate-based herbicides are most widely used - hardly available data state a global usage of about 650,000 tons[3] at sales worth about 6.5 billion US $ in 2010[4]. Glyphosate-based herbicides have been so widely used because they are very effective, acting non-selectively on plants by inhibiting the shikimic acid metabolic pathway found exclusively in plants and some microorganisms[5]. Hence, animals should theoretically not be affected by the application of glyphosate. Moreover, glyphosate is considered environmentally friendly due to its fast degradation[5] and strong adsorption to soil particles that should reduce leaching losses from the soil profile[6]. Nevertheless, evidence that glyphosate-based herbicides can harm non-target organisms, particularly amphibians[7,8], symbiotic mycorrhizal fungi or earthworms continues to mount[9,10].

Earthworms constitute a majority of soil faunal biomass in many temperate agroecosystems, with up to 1000 individuals and 300 g of biomass in each square meter of land[11]. They act as ecosystem engineers[12] by physically shredding plant litter, mineralizing it in their guts (along with soil organic matter), and enhancing soil nutrient availability through the production of up to 40 tons of casts per hectare annually[13] that can promote plant productivity[14–16]. Earthworm burrowing also enhances soil

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Glyphosate Commercial Formulation Causes Cytotoxicity, Oxidative Effects, and Apoptosis on Human Cells: Differences With its Active Ingredient

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Abstract

In the present study, the effects on oxidative balance and cellular end points of glyphosate, aminomethylphosphonic acid (AMPA), and a glyphosate formulation (G formulation) were examined in HepG2 cell line, at dilution levels far below agricultural recommendations. Our results show that G formulation had toxic effects while no effects were found with acid glyphosate and AMPA treatments. Glyphosate formulation exposure produced an increase in reactive oxygen species, nitrotyrosine formation, superoxide dismutase activity, and glutathione (GSH) levels, while no effects were observed for catalase and GSH-S-transferase activities. Also, G formulation triggered caspase 3/7 activation and hence induced apoptosis pathway in this cell line. Aminomethylphosphonic acid exposure produced an increase in GSH levels while no differences were observed in other antioxidant parameters. No effects were observed when the cells were exposed to acid glyphosate. These results confirm that G formulations have adjuvants working together with the active ingredient and causing toxic effects that are not seen with acid glyphosate.

Keywords

apoptosis, cytotoxicity, glyphosate, *in vtro*, oxidative stress

Introduction

Glyphosate is a nonselective postemergent herbicide that inhibits 5-enolpyruvylshikimate-3-phosphate synthase, a key enzyme of the aromatic amino acid biosynthetic pathway in plants.[1] The main breakdown product of glyphosate in soil is aminomethylphosphonic acid (AMPA), which is broken down further by soil microorganisms.[2]

Half-lives of glyphosate and AMPA in soil range from 2 to 197 days and 76 to 240 days, respectively.[3] They can persist in the environment as residues in soils and crops for up to 3 years.[4] Although humans are not a direct target, they could be in contact with glyphosate due to occupational exposure[5,6] and/or through dietary exposure.[7,8]

Pesticides as active ingredients are combined with other ingredients to create the commercial formulas on the market. Other ingredients include a wide array of compounds; information regarding some of these is considered confidential business information and they are not of public-free access. The toxic effects may be a consequence of the active or other ingredients in the formulation or both.[9,10] The herbicide glyphosate is sold worldwide under a variety of commercial names. Since glyphosate is not applied in the field as a pure active ingredient the toxicity of commercial form should be assayed.[11] Previous studies exposing human cells to glyphosate revealed that glyphosate formulation (G formulation) is more toxic than the active component itself, supporting the idea that additives in commercial formulations play a role in herbicide's toxicity.[12-15]

It has been reported that many pesticides (including herbicides) generate intracellular reactive oxygen species (ROS).[11,16-18] We have demonstrated that an increase in ROS levels triggers oxidative damage to proteins, nucleic acids, and lipids as well as the increase in activity of different antioxidant enzymes.[19,20] Environmental stressors that are well known to induce oxidative stress and alterations to the cellular redox balance have been widely shown as apoptosis regulators. Despite evidence that glyphosate induces cytotoxicity, oxidative damage, and apoptosis in several models,[21-25] the molecular mechanisms and the effects on humans remain largely unknown.

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The Influence of Glyphosate on the Microbiota and Production of Botulinum Neurotoxin During Ruminal Fermentation

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Abstract The aim of the present study is to investigate the impact of glyphosate on the microbiota and on the botulinum neurotoxin (BoNT) expression during in vitro ruminal fermentation. This study was conducted using two DAISY^{II}-incubators with four ventilated incubation vessels filled with rumen fluid of a 4-year-old non-lactating Holstein–Friesian cow. Two hundred milliliter rumen fluid and 800 ml buffer solution were used with six filter bags containing 500 mg concentrated feed or crude fiber-enriched diet. Final concentrations of 0, 1, 10, and 100 µg/ml of glyphosate in the diluted rumen fluids were added and incubated under CO_2-aerated conditions for 48 h. The protozoal population was analyzed microscopically and the ruminal flora was characterized using the fluorescence in situ hybridization technique. *Clostridium botulinum* and BoNT were quantified using most probable number and ELISA, respectively. Results showed that glyphosate had an inhibitory effect on select groups of the ruminal microbiota, but increased the population of pathogenic species. The BoNT was produced during incubation when inoculum was treated with high doses of glyphosate. In conclusion, glyphosate causes dysbiosis which favors the production of BoNT in the rumen. The global regulations restrictions for the use of glyphosate should be re-evaluated.

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Introduction

An increasing number of nonspecific diseases in dairy farms have been described in Germany and other countries in recent years. The observed symptoms in general were indigestion (constipation alternating with diarrhea), non-infectious chronic laminitis, engorged veins, oedemas, retracted abdomen, cachexia, and apathy. Most of the cases occurred during the peripartal period and often resulted in sudden death [7]. Böhnel et al. [7] assumed that the botulinum neurotoxin (BoNT) produced by *Clostridium* (*C.*) *botulinum* in the intestines was responsible for the symptoms described as a disease complex named 'visceral botulism.' *C. botulinum* is ubiquitous in the environment and, although it is not a member of the normal gastrointestinal flora of ruminants, the bacterium can occur sporadically or through the oral intake of contaminated silage [15, 25, 27, 28]. The ingestion of *C. botulinum* or BoNT does not automatically lead to intoxication since small amounts of BoNT in the gastrointestinal tract of ruminants can be degraded by proteolytic bacteria [3].

Bacteriocines produced by lactic acid bacteria can degrade *C. botulinum* bacteria. *Enterococcus* spp. in particular have an inhibitory effect on the growth of *C. botulinum* and inhibit the production of BoNT [26, 36]; however, changes in composition of the gastrointestinal microbiota could favor the establishment of *C. botulinum* and the production of BoNT. An important factor possibly affecting the gastrointestinal microbiota in ruminants is the broad-spectrum herbicide glyphosate.

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RESEARCH ARTICLE

Effects of sublethal doses of glyphosate on honeybee navigation

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ABSTRACT

Glyphosate (GLY) is a herbicide that is widely used in agriculture for weed control. Although reports about the impact of GLY in snails, crustaceans and amphibians exist, few studies have investigated its sublethal effects in non-target organisms such as the honeybee *Apis mellifera*, the main pollen vector in commercial crops. Here, we tested whether exposure to three sublethal concentrations of GLY (2.5, 5 and 10 mg l^{-1}: corresponding to 0.125, 0.250 and 0.500 μg per animal) affects the homeward flight path of honeybees in an open field. We performed an experiment in which forager honeybees were trained to an artificial feeder, and then captured, fed with sugar solution containing traces of GLY and released from a novel site either once or twice. Their homeward trajectories were tracked using harmonic radar technology. We found that honeybees that had been fed with solution containing 10 mg l^{-1} GLY spent more time performing homeward flights than control bees or bees treated with lower concentrations. They also performed more indirect homing flights. Moreover, the proportion of direct homeward flights performed after a second release from the same site increased in control bees but not in treated bees. These results suggest that, in honeybees, exposure to levels of GLY commonly found in agricultural settings impairs the cognitive capacities needed to retrieve and integrate spatial information for a successful return to the hive. Therefore, honeybee navigation is affected by ingesting traces of the most widely used herbicide worldwide, with potential long-term negative consequences for colony foraging success.

KEY WORDS: *Apis mellifera*, Glyphosate, Sublethal effects, Navigation, Harmonic radar tracking

INTRODUCTION

Honeybees (*Apis mellifera*) are the main pollinators in agricultural settings (Aizen et al., 2009) and as such are highly exposed to any perturbation occurring in the surroundings of crop fields. Consequently, this eusocial insect can serve as a biosensor to accurately determine environmental pollutants (Devillers and Pham-Delègue, 2002). Any foreign substance present in gathered resources (i.e. pollen and nectar) may also be stored and accumulated inside the nest for long periods, potentially affecting nest mates of all stages (Devillers and Pham-Delègue, 2002). This applies in particular to highly water-soluble agrochemicals such as the herbicide glyphosate *N*-(phosphonomethyl) glycine, which may remain on crops after application for long periods (Zhang et al., 2011). Any subsequent accumulation of agrochemicals inside the hive could have negative effects which are often inconspicuous in the short term (Giesy et al., 2000), but which could impair individual behaviors and social organization in the long term (Kirchner, 1999).

The use of glyphosate (GLY) as a broad-spectrum post-emergent herbicide for weed control has spread rapidly in the last few decades (Goldsborough and Brown, 1988) to become one of the most commonly used agrochemicals worldwide (Zhang et al., 2011). The typical methods of administration involve spraying it directly onto foliage and aerial application (Giesy et al., 2000). As a consequence, traces of the herbicide can also be found in the surroundings of fields cultivated with the target crop. GLY deters plant growth by inhibiting an aromatic amino acid pathway that is apparently present only in plants, microorganisms and fungi, not animals (Amrhein et al., 1980; Carlisle and Trevors, 1988; Duke et al., 1989; Franz et al., 1997).

Several studies have reported negative effects of this herbicide on vertebrates and invertebrates. GLY doses between 0.1 and 10 mg acid equivalent l^{-1} have been found to reduce growth in the earthworm *Aporrectoden caliginom* (Springett and Gray, 1992) and affect reproduction and development in the freshwater snail *Pseudosuccinea columella* (Tate et al., 1997). A negative effect has also been reported in amphibians after chronic exposure to different concentrations of glyphosate (3.8–18 mg l^{-1}; Howe et al., 2004; Relyea, 2005a,b). Despite these findings and others that report negative and lethal effects on invertebrates such as amphipods (Dutra et al., 2011), the sublethal impacts of GLY on non-target organisms such as insect pollinators have so far been poorly evaluated (Herbert et al., 2014; Thompson et al., 2014). In this study, we used sublethal concentrations of GLY ranging from 2.5 to 10 mg l^{-1}.

Honeybees show a behavioral repertoire that allows the evaluation of perturbations in well-known stereotypical responses. The behavior in which bees protrude their probosces after being stimulated by applying sucrose solution to their antennae is one of these responses, and it can be used to test the effects of environmental pollutants on appetitive behavior (Devillers and Pham-Delègue, 2002). A recent study found that a concentration of glyphosate (2.5 mg l^{-1}), within the recommended range for aquatic and terrestrial weed control (Giesy et al., 2000), affects gustatory responsiveness and learning performance in harnessed bees [tested with proboscis extension response (PER) assays]. However, no effect was observed on locomotive activity when foragers collected sucrose solution contaminated with the herbicide at an artificial feeder, suggesting that GLY may accumulate inside the hive (Herbert et al., 2014). Also, Herbert and co-workers (2014) found that an acute exposure to sublethal GLY concentrations offered during olfactory PER conditioning decreased short-term memory and impaired more complex forms of associative learning in foragers.

Studies have already shown that other agrochemical compounds used for pest control, such as neonicotinoids, negatively affect honeybee gustatory sensitivity and even their dance maneuvers (Eiri and Nieh, 2012). Non-lethal doses of imidacloprid (75–

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GLYPHOSATE AND ITS DEGRADATION PRODUCT AMPA OCCUR FREQUENTLY AND WIDELY IN U.S. SOILS, SURFACE WATER, GROUNDWATER, AND PRECIPITATION[1]

W.A. Battaglin, M.T. Meyer, K.M. Kuivila, and J.E. Dietze[2]

ABSTRACT: Glyphosate use in the United States increased from less than 5,000 to more than 80,000 metric tons/yr between 1987 and 2007. Glyphosate is popular due to its ease of use on soybean, cotton, and corn crops that are genetically modified to tolerate it, utility in no-till farming practices, utility in urban areas, and the perception that it has low toxicity and little mobility in the environment. This compilation is the largest and most comprehensive assessment of the environmental occurrence of glyphosate and aminomethylphosphonic acid (AMPA) in the United States conducted to date, summarizing the results of 3,732 water and sediment and 1,018 quality assurance samples collected between 2001 and 2010 from 38 states. Results indicate that glyphosate and AMPA are usually detected together, mobile, and occur widely in the environment. Glyphosate was detected without AMPA in only 2.3% of samples, whereas AMPA was detected without glyphosate in 17.9% of samples. Glyphosate and AMPA were detected frequently in soils and sediment, ditches and drains, precipitation, rivers, and streams; and less frequently in lakes, ponds, and wetlands; soil water; and groundwater. Concentrations of glyphosate were below the levels of concern for humans or wildlife; however, pesticides are often detected in mixtures. Ecosystem effects of chronic low-level exposures to pesticide mixtures are uncertain. The environmental health risk of low-level detections of glyphosate, AMPA, and associated adjuvants and mixtures remain to be determined.

(KEY TERMS: glyphosate; AMPA; water quality; surface water; groundwater; precipitation.)

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INTRODUCTION

Problem

Commercial glyphosate [*N*-(phosphonomethyl) glycine] formulations have been used worldwide for decades, but glyphosate is seldom included in environmental monitoring programs (Gilliom *et al.*, 2006; Loos *et al.*, 2010; U.S. Department of Agriculture, 2011), due in part to difficulties in quantifying this polar and water-soluble compound at environmentally relevant concentrations (Skark *et al.*, 1998; Sanchis *et al.*, 2011). In the early 2000s, scientists at the U.S. Geological Survey (USGS) began developing analytical methods (Lee *et al.*, 2002) and conducting reconnaissance studies (Scribner *et al.*, 2003; Battaglin *et al.*, 2005) for the occurrence of glyphosate and aminomethylphosphonic acid (AMPA) in anticipation of growing gaps in scientific understanding due to (1)

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Glyphosate-Residues in Roundup-Ready Soybean Impair *Daphnia magna* Life-Cycle

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Abstract

Herbicide tolerant plants such as Roundup-Ready soybean contain residues of glyphosate herbicide. These residues are considered safe and previous animal-feeding-studies have failed to find negative effects related to such chemical residues. The present study tests 8 experimental soy-meal diets as feed in groups (each containing 20 individuals) of test-animals (*D. magna*). The diets have different levels of glyphosate residues and we show that animal growth, reproductive maturity and number of offspring are correlated with these chemicals. The tested soybeans are from ordinary agriculture in Iowa USA and the residues are below the regulatory limits. Despite this, clear negative effects are seen in *life-long feeding*. The work enhances the need for including analysis of herbicide residues in future assessment of GMO.

Keywords

Transgenic GTS 40-3-2 Roundup-Ready Soybean, Glyphosate Residues, Life-Long Animal Feeding Study, GMO Risk-Assessment, Herbicide-Tolerant Cultivar Quality, Aquatic Invertebrate Ecotoxicology

1. Introduction

Transgenic glyphosate-tolerant soy (Roundup-Ready soybean = RR-soybean) is the most commonly cultivated genetically modified crop, contributing approximately 80% of global annual soy production of 283 million metric

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RESEARCH ARTICLE

Toxicity of atrazine, glyphosate, and quinclorac in bullfrog tadpoles exposed to concentrations below legal limits

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Abstract This work sought to ascertain survival and possible changes in levels of glycogen, triglycerides, total lipids, cholesterol, protein, and lipid peroxidation in gills, liver, and muscle of bullfrog tadpoles (*Lithobates catesbeianus*) exposed to low concentrations of atrazine (2.5 μg L^{-1}), glyphosate (18 μg L^{-1}), and quinclorac (0.025 μg L^{-1}) at laboratorial conditions. Tadpoles showed a reduction of glycogen and triglyceride in all organs and an increase in lipid peroxidation (LPO) compared with control animals. Total lipid in gills and muscle increased in exposure to atrazine, and gills alone in exposure to glyphosate, but decreased in gills, liver, and muscle after quinclorac. Cholesterol increased in gills and liver after atrazine, in gills and muscle after glyphosate, and decreased in liver after quinclorac. Total protein in gills decreased after exposure to all herbicides, increased in muscle after atrazine, and in liver and muscle after quinclorac. These findings show that at concentrations of these herbicides tested can lead to an increase in energy expenditure to maintain homeostasis and survival of these animals despite the increase in lipid peroxidation levels in all organs analyzed. Responses observed can be one of the factors responsible for the decline in the number of amphibians around the world.

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Keywords Agrochemicals · Biochemical changes · Bullfrog · Lipid peroxidation (LPO) · *Lithobates catesbeianus* · Tadpoles

Introduction

The way humans use the world's natural resources has led to significant impacts on other species that inhabit the planet. One example of this phenomenon is the decline in the number of amphibians over the last few decades, an extinction that has no precedent in any animal class in this period and which may be the result of an isolated action or interaction of different factors, such as habitat loss, ultraviolet radiation, global warming, diseases, over-harvesting, and/or the introduction of agrochemicals, especially pesticides—even at low levels—into the environment (Allran and Karasov 2000; Blaustein et al. 2003; Boone et al. 2005; David and Kartheek 2015; Davidson 2004; Gascon et al. 2005; Relyea 2003; Sayim 2008).

Approximately 1 % of agrochemicals used in the field reach their specific targets. The remaining 99 % can move through the different environmental compartments and may have an indirect effect on non-target organisms exposed to contaminants (Belluck et al. 1991).

Amphibians are among the animals that may be indirectly exposed to these agrochemicals, and the exposure may account for the great amphibian mortality that has been observed in recent years. Tadpoles appear to be more sensitive than adults, which is consistent with the greater fragility of these animals in the larval stage (Blaustein et al. 2003; David and Kartheek 2015; Johansson et al. 2006; Murphy et al. 2000; Sayim 2008; Wang et al. 2001).

The environmental changes induced by the use of agricultural chemicals can interfere with physiological and

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Oral Application of Charcoal and Humic acids to Dairy Cows Influences *Clostridium botulinum* Blood Serum Antibody Level and Glyphosate Excretion in Urine

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Abstract

The present study was initiated to investigate the influence of oral application of charcoal, sauerkraut juice and humic acids on chronic botulism in dairy cows. A total of 380 Schleswig Holstein cows suffering from chronic botulism were fed daily with 400 g/animal charcoal for 4 weeks (1-4 weeks of study), 200 g/animal charcoal (5-10 weeks of study), 120 g/animal humic acid (11-14s week of study), 200g charcoal and 500 ml Sauerkraut juice/animal (13-16 weeks of study), 200 g charcoal and 100 mL Aquahumin/animal (15-18s week of study), 100 g charcoal and 50 mL Aquahumin (19-22 weeks of study) followed by 4 weeks without any supplementation. Bacteriological and immunological parameters investigated included *C. botulinum* and botulinum neurotoxins (BoNT) in faeces, *C. botulinum* ABE and CD antibodies, positive acute phase proteins (APPs) haptoglobin and LPS-binding protein (LBP) using serum ELISA, negative APP paraoxanase by its enzymatic activity and glyphosate in urine by ELISA. Neither BoNT nor *C. botulinum* was detected in feacal samples. From week six until four weeks before the end of the study, there was a significant reduction in antibody levels. All supplementation, except low doses of charcoal (200g / animal) alone, led to a significant reduction of *C. botulinum* ABE and CD antibody levels. There also was a significant reduction of glyphosate in urine following supplementation with a combination of 200g charcoal plus either 500 mL sauerkraut juice or humic acid. Haptoglobin, paraoxanase and LBP were significantly increased by the 24th week of the study. The positive APPs and *C. botulinum* antibodies were significant negative correlations. In conclusion, a charcoal-sauerkraut juice combination and humic acids could be used to control chronic botulism and glyphosate damage in cattle.

Keywords Humic acids; Peripartual cases; *C. botulinum*

Introduction

In recent years, an increased frequency of a new form of bovine botulism has been observed. This form of botulism differs from regular food-born botulism by its slow and chronic development with various unspecific symptoms. This protracted form may develop when small, sub-lethal amounts of BoNT are taken up and/or absorbed over several days or are generated in the hind gut [1,2]. Clinical symptoms of chronic botulism are most often peripartual cases with indigestion (constipation alternating with diarrhea), non-infectious acute laminitis, ataxia and stiff stilted gait, impossibility to get up (paralysis), apathy, engorged veins, positive venous pulse, edema in legs, udder, and dew-lap, retracted abdomen, forced respiration and unexpected death. The prevalence of C. botulinum in cattle can be determined by detection of botulinum neurotoxins (BoNTs) and/or *C. botulinum* vegetative bacteria or spores in the gastrointestinal tract or organs (liver, kidney, lungs and muscles [1,3,4]. A second way to verify chronic botulism is with specific antibodies for BoNTs [3,5,6] detected natural specific antibodies in wild canine species, horses and dairy cows.

C. botulinum is an ubiquitous Gram-positive, spore forming, obligatory anaerobic bacterium that inhabits soil, dust and organic matter such as feces of animals and man, slaughterhouse wastes, residues of biogas plants, and bio-compost. It generates eight highly toxic neurotoxin isoforms (BoNT A-H) that are the most toxic substances known [7-12]. All isoforms, together with the related tetanus neurotoxin (TeNT) secreted by *C. tetani*, are Zn2+-endoproteases. The immunologically distinct neurotoxins (A-H) of *C. botulinum* are homologous proteins consisting of a heavy and light chain linked by an essential disulfide bridge. The light chain blocks the release of acetylcholine at the neuromuscular junction. Human cases are mostly caused by types A, B, or E, while animal diseases are mostly caused by types C and D [1,13,14]. Several C. botulinum strains produce two neurotoxins [11]. Physiological differences are used to divide *C. botulinum* strains into 4 physiological groups; group I, consisting of *C. botulinum* A and proteolytic strains of *C. botulinum* B and F; group II, consisting of *C. botulinum* E and nonproteolytic strains of *C. botulinum* B and F; group III, consisting of *C. botulinum*

Glyphosate, pathways to modern diseases IV: cancer and related pathologies

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Glyphosate is the active ingredient in the pervasive herbicide, Roundup, and its usage, particularly in the United States, has increased dramatically in the last two decades, in step with the widespread adoption of Roundup®-Ready core crops. The World Health Organization recently labelled glyphosate as "probably carcinogenic." In this paper, we review the research literature, with the goal of evaluating the carcinogenic potential of glyphosate. Glyphosate has a large number of tumorigenic effects on biological systems, including direct damage to DNA in sensitive cells, disruption of glycine homeostasis, succinate dehydrogenase inhibition, chelation of manganese, modification to more carcinogenic molecules such as N-nitrosoglyphosate and glyoxylate, disruption of fructose metabolism, etc. Epidemiological evidence supports strong temporal correlations between glyphosate usage on crops and a multitude of cancers that are reaching epidemic proportions, including breast cancer, pancreatic cancer, kidney cancer, thyroid cancer, liver cancer, bladder cancer and myeloid leukaemia. Here, we support these correlations through an examination of Monsanto's early studies on glyphosate, and explain how the biological effects of glyphosate could induce each of these cancers. We believe that the available evidence warrants a reconsideration of the risk/benefit trade-off with respect to glyphosate usage to control weeds, and we advocate much stricter regulation of glyphosate.

Keywords: cataracts, CYP 450 enzymes, glyphosate, gut microbiome, interstitial disease, kidney cancer, non-Hodgkin's lymphoma, pancreatic cancer

1. INTRODUCTION

Glyphosate is the active ingredient in the pervasive herbicide, Roundup. Its usage on crops to control weeds in the United States and elsewhere has increased dramatically in the past two decades, driven by the increase over the same time period in the use of genetically modified (GM)[1] crops, the widespread emergence of glyphosate-resistant weeds among the GM crops (necessitating ever-higher doses to achieve the same herbicidal effect), as well as the increased adoption of glyphosate as a desiccating agent just before harvest. GM crops include corn, soy, canola (rapeseed) and sugar beet [1]. Crop desiccation by glyphosate includes application to non-GM crops such as dried peas, beans and lentils. It should be noted that the use of glyphosate for pre-harvest staging for perennial weed control is now a major crop management strategy. The increase in glyphosate usage in the United States is extremely well correlated with the concurrent increase in the incidence and/or death rate of multiple diseases, including several cancers [1]. These include thyroid cancer, liver cancer, bladder cancer, pancreatic cancer, kidney cancer and myeloid leukaemia, as shown in Table 1, reproduced from [1]. The World Health Organization (WHO) revised its assessment of glyphosate's carcinogenic potential in March 2015, relabelling it as a "probable carcinogen" [2, 3].

Table 1. Pearson's coefficients between time trends in various cancers and glyphosate applications to corn and soy crops, over the interval from 1990–2010, along with corresponding *P*-values, as determined from hospital discharge data and death data maintained by the US Centers for Disease Control (CDC). Table adapted from Swanson et al. 2014 [1].

Disease	*R*	*P*
Thyroid cancer (incidence)	0.988	$\leq 7.6 \times 10^{-9}$
Liver cancer (incidence)	0.960	$\leq 4.6 \times 10^{-8}$
Bladder cancer (deaths)	0.981	$\leq 4.7 \times 10^{-9}$
Pancreatic cancer (incidence)	0.918	$\leq 4.6 \times 10^{-7}$
Kidney cancer (incidence)	0.973	$\leq 2.0 \times 10^{-8}$
Myeloid leukaemia (deaths)	0.878	$\leq 1.5 \times 10^{-6}$

Sri Lanka's newly elected president, Maithripala Sirisena, banned glyphosate imports as one of his first acts following election. This action was based on studies by Jayasumana et al. that provided compelling evidence that glyphosate was a key factor in the chronic kidney disease that was affecting an alarming number of young

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[1] Usually called genetically engineered (GE) in the USA.

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The herbicide glyphosate causes behavioral changes and alterations in dopaminergic markers in male Sprague-Dawley rat

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ABSTRACT

Glyphosate (Glyph) is the active ingredient of several herbicide formulations. Reports of Glyph exposure in humans and animal models suggest that it may be neurotoxic. To evaluate the effects of Glyph on the nervous system, male Sprague-Dawley rats were given six intraperitoneal injections of 50, 100, or 150 mg Glyph/kg BW over 2 weeks (three injections/week). We assessed dopaminergic markers and their association with locomotor activity. Repeated exposure to Glyph caused hypoactivity immediately after each injection, and it was also apparent 2 days after the last injection in rats exposed to the highest dose. Glyph did not decrease monoamines, tyrosine hydroxylase (TH), or mesencephalic TH+ cells when measured 2 or 16 days after the last Glyph injection. In contrast, Glyph decreased specific binding to D1 dopamine (DA) receptors in the nucleus accumbens (NAcc) when measured 2 days after the last Glyph injection. Microdialysis experiments showed that a systemic injection of 150 mg Glyph/kg BW decreased basal extracellular DA levels and high-potassium-induced DA release in striatum. Glyph did not affect the extracellular concentrations of 3,4-dihydroxyphenylacetic acid or homovanillic acid. These results indicate that repeated Glyph exposure results in hypoactivity accompanied by decreases in specific binding to D1-DA receptors in the NAcc, and that acute exposure to Glyph has evident effects on striatal DA levels. Additional experiments are necessary in order to unveil the specific targets of Glyph on dopaminergic system, and whether Glyph could be affecting other neurotransmitter systems involved in motor control.

1. Introduction

Glyphosate (Glyph) is a phosphonomethyl amino acid derivative used as active ingredient in some herbicides. In recent years, the commercialization of glyphosate herbicides has increased due to development and sowing of glyphosate-resistant seeds, such as corn, soybeans, canola, and cotton (Dill et al., 2008). In plants, glyphosate inhibits the synthesis of aromatic amino acids, a metabolic pathway absent in mammals. Thus, it was considered that glyphosate herbicides were not a risk for the health of mammals including humans (Williams et al., 2000). However, in recent years, reports of human exposure and animal models suggest that both the commercial mixture containing glyphosate and the active ingredient glyphosate could have neurotoxic effects. Regarding human studies, glyphosate has been detected in brain and cerebrospinal fluid after exposure to commercial mixtures, revealing that the active ingredient can cross the blood brain barrier (Menkes et al., 1991; Sato et al., 2011). In addition, structural MRI studies in a subject exposed to the commercial mixture of glyphosate showed modifications in the T2 signal in substantia nigra, periaqueductal gray and globus pallidus, revealing possible bilateral lesions (Barbosa et al., 2001). Abnormal EEG activity and a Parkinsonian syndrome characterized by limb tremor at rest, global akinesia and rigidity have been observed after occupational exposure and accidental ingestion of the commercial mixture of glyphosate (Barbosa et al., 2001; Malhotra et al., 2010; Wang et al., 2011).

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Hypothesis

Glyphosate, Hard Water and Nephrotoxic Metals: Are They the Culprits Behind the Epidemic of Chronic Kidney Disease of Unknown Etiology in Sri Lanka?

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Abstract: The current chronic kidney disease epidemic, the major health issue in the rice paddy farming areas in Sri Lanka has been the subject of many scientific and political debates over the last decade. Although there is no agreement among scientists about the etiology of the disease, a majority of them has concluded that this is a toxic nephropathy. None of the hypotheses put forward so far could explain coherently the totality of clinical, biochemical, histopathological findings, and the unique geographical distribution of the disease and its appearance in the mid-1990s. A strong association between the consumption of hard water and the occurrence of this special kidney disease has been observed, but the relationship has not been explained consistently. Here, we have hypothesized the association of using glyphosate, the most widely used herbicide in the disease endemic area and its unique metal chelating properties. The possible role played by glyphosate-metal complexes in this epidemic has not been given any serious consideration by investigators for the last two decades. Furthermore, it may explain similar kidney disease epidemics observed in Andra Pradesh (India) and Central America. Although glyphosate alone does not cause an epidemic of chronic kidney disease,

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Research Article Open Access

Field Investigations of Glyphosate in Urine of Danish Dairy Cows

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Abstract

In the present study, thirty dairy cows from each of eight Danish dairy farms were investigated for excretion of glyphosate in urine. Blood serum parameters indicative of cytotoxicity as alkaline phosphatase (AP), glutamate dehydrogenase (GLDH), glutamate oxaloacetate transaminase (GOT), creatinine kinase CK), nephrotoxicity, (urea, creatine), cholesterol and the trace elements as manganese (Mn), cobalt (Co), selenium (Se), copper (Cu) and zinc (Zn) were investigated. All cows excreted glyphosate in their urine but in varying concentrations. Increased levels of GLDH, GOT and CK in cows from all farms demonstrate a possible effect of glyphosate on liver and muscle cells. High urea levels in some farms could be due to nephrotoxicity of glyphosate. Also the unexpected very low levels of Mn and Co were observed in all animals which could be explained due to a strong mineral chelating effect of glyphosate. In contrast the mean levels of Cu, Zn and Se were within the normal reference range. In conclusion, this study gives the first documentation to which extent Danish dairy cattle are exposed to Glyphosate and its impact on blood parameters.

Keywords: Glyphosate; Trace elements; Blood parameters; Dairy cattle; Urine

Introduction

Glyphosate (*N*-(phosphonomethyl) glycine) is a highly effective herbicide that inhibits 5-enolpyruvyl shikimate 3-phosphate synthase (EPSPS), an enzyme of the shikimate pathway that is necessary to synthesize aromatic amino acids and other aromatic components in higher plants, algae, bacteria and fungi [1]. The herbicidal action is generated by chelating manganese required in the reduction of the flavin mononucleotide (FMN) co-factor of EPSPS [2]. Glyphosate is the most extensively used herbicide worldwide. The intensive use of glyphosate has led to its wide-spread contamination of different ecosystems where it influences plants, microorganisms, animals and many components of the food chain. Moreover, glyphosate and its primary metabolite aminomethylphosphonate (AMPA) have been detected in immature seed [3], harvested seeds [4] and ground water [5]. There are differing opinions about the safety of this herbicide because long-term toxicology studies have not been conducted and the EPSPS enzyme is absent in humans and animals [6]. However, inhibition of EPSPS is not the only activity of glyphosate in warm blooded animals. Other inhibited pathways are reported such as Cyp450 aromatase inhibition, genotoxic activity [7], teratogenic activity [8] and trace element chelation [9-11]. Also glyphosate could disturb the normal gut bacterial community [12,13]. Some *in vitro* investigations with glyphosate have verified its cytotoxic effects on different cells at very low, sub-agricultural concentrations [14-16]. In a long-term investigation, Seralini and coworkers [17] reported significantly higher mammary tumor rates in female rats drinking glyphosate at 1 ppb, a very low concentration. Marked and severe kidney nephropathies and liver congestion were also reported. In the present study, we investigated 30 cows at each of eight farms to evaluate relationships between regular intake of glyphosate in feed of dairy cows, as measured by excretion in urine, and changes in serum biochemistry, especially enzymes indicative of cytotoxicity such as alkaline phosphatase (AP), creatinine kinase (CK), glutamate dehydrogenase (GLDH), glutamate oxaloacetate transaminase (GOT); parameters demonstrating nephrotoxicity (urea, creatinine); a lipid pathway parameter (cholesterole); as well as the trace elements copper (Cu), cobalt (Co), manganese (Mn), selenium (Se), and zinc (Zn).

Material and Methods

Animals

Thirty cows (15 fresh calving, 15 high yielding cows) at each of eight Danish farms were investigated. More details are shown in Table 1. The age of these animals ranged from 4 to 7 years with an average body weight of 550-600 Kg.

Glyphosate testing of urine

Urine samples were diluted 1:20 with distilled water (aqua distillated, Braun, Germany) and tested for glyphosate by ELISA (Abraxis, USA) according to the manufacturer's instructions. Test validation was done with Gas Chromatography-Mass Spectroscopy (GC-MS) by Medizinische Labor (Bremen, Germany). The correlation coefficient between the two tests was 0.96 (Data not shown).

Farm	Total number of cows	Average milk yields kg/cow
W	150	9.1
K	180	10.3
R	175	10.2
V	200	8.6
S	140	10.7
T	180	11.2
B	400	10.8
E	300	8.8

Table 1: Characterization of Danish dairy farms investigated in this study.

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RESEARCH ARTICLE

Sublethal Exposure to Commercial Formulations of the Herbicides Dicamba, 2,4-Dichlorophenoxyacetic Acid, and Glyphosate Cause Changes in Antibiotic Susceptibility in *Escherichia coli* and *Salmonella enterica* serovar Typhimurium

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ABSTRACT **Biocides, such as herbicides, are routinely tested for toxicity but not for sublethal effects on microbes. Many biocides are known to induce an adaptive multiple-antibiotic resistance phenotype. This can be due to either an increase in the expression of efflux pumps, a reduced synthesis of outer membrane porins, or both. Exposures of *Escherichia coli* and *Salmonella enterica* serovar Typhimurium to commercial formulations of three herbicides—dicamba (Kamba), 2,4-dichlorophenoxyacetic acid (2,4-D), and glyphosate (Roundup)—were found to induce a changed response to antibiotics. Killing curves in the presence and absence of sublethal herbicide concentrations showed that the directions and the magnitudes of responses varied by herbicide, antibiotic, and species. When induced, MICs of antibiotics of five different classes changed up to 6-fold. In some cases the MIC increased, and in others it decreased. Herbicide concentrations needed to invoke the maximal response were above current food maximum residue levels but within application levels for all herbicides. Compounds that could cause induction had additive effects in combination. The role of *soxS*, an inducer of the AcrAB efflux pump, was tested in β-galactosidase assays with *soxS-lacZ* fusion strains of *E. coli*. Dicamba was a moderate inducer of the *sox* regulon. Growth assays with Phe-Arg β-naphtylamide (PAβN), an efflux pump inhibitor, confirmed a significant role of efflux in the increased tolerance of *E. coli* to chloramphenicol in the presence of dicamba and to kanamycin in the presence of glyphosate. Pathways of exposure with relevance to the health of humans, domestic animals, and critical insects are discussed.**

IMPORTANCE **Increasingly common chemicals used in agriculture, domestic gardens, and public places can induce a multiple-antibiotic resistance phenotype in potential pathogens. The effect occurs upon simultaneous exposure to antibiotics and is faster than the lethal effect of antibiotics. The magnitude of the induced response may undermine antibiotic therapy and substantially increase the probability of spontaneous mutation to higher levels of resistance. The combination of high use of both herbicides and antibiotics in proximity to farm animals and important insects, such as honeybees, might also compromise their therapeutic effects and drive greater use of antibiotics. To address the crisis of antibiotic resistance requires broadening our view of environmental contributors to the evolution of resistance.**

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A biocide is a compound that is lethal to an organism. Biocides that are developed specifically to control bacteria include disinfectants, desiccants, and antimicrobial agents (e.g., antibiotics). The end of the antibiotic era has been forecast for decades. In the mid-1990s, two major American magazines, *Time* and *Newsweek*, ran cover stories on the dual threat of antibiotic resistance and new levels of pathogen virulence. In the last year, both the World Health Organization (1) and the U.S. Centers for Disease Control and Prevention (2) issued stern reports on the continuing and growing problem of antibiotic resistance. The latter estimates that in the United States alone, "more than two million people are sickened every year with antibiotic-resistant infections, with at least 23,000 dying as a result. The estimates are based on conservative assumptions and are likely minimum estimates." The emergence of antibiotic resistance in species that cause disease in humans and domestic animals is the result of human use (3). Most antimicrobial agents, including antibiotics, predate by billions of years the extensive application of antibiotics to humans, and the resistance of human pathogens has appeared in force only since the middle of the last century, corresponding to the time of their commercial use in medicine and agriculture.

All pharmacokinetic and pharmacodynamic models that are

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The effect of metabolites and impurities of glyphosate on human erythrocytes (*in vitro*)

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ABSTRACT

The toxicity of herbicides to animals and human is an issue of worldwide concern. The present study was undertaken to evaluate toxic potential of widely used pesticide – glyphosate, its metabolites: aminomethylphosphonic acid (AMPA); methylphosphonic acid and its impurities: *N*-(phosphonomethyl)iminodiacetic acid (PMIDA), *N*-methylglyphosate, hydroxymethylphosphonic acid and bis-(phosphonomethyl)amine.

We evaluated the effect of those compounds on hemolysis, hemoglobin oxidation, reactive oxygen species (ROS) formation and changes in morphology of human erythrocytes. The erythrocytes were exposed to different concentrations of glyphosate and its metabolites and impurities (0.01–5 mM) for 1, 4 and 24 h.

Glyphosate, its metabolites and impurities induced a little hemolysis and hemoglobin oxidation. All changes were very low, even after 24 h incubation. Most of the investigated compounds induced reactive oxygen species formation from 0.25 mM, except the *N*-methylglyphosate which caused an increase in ROS formation from 0.5 mM. Moreover, the investigated xenobiotics did not change the size and shape (except bis-(phosphonomethyl)amine) of the human erythrocytes.

Changes in human erythrocytes were observed only when high concentrations of the compounds were applied. Some investigated metabolites and impurities caused a slight stronger damage to human erythrocytes than a glyphosate.

The results clearly show that the changes induced in the erythrocytes can occur only as a result of poisoning with these compounds.

1. Introduction

Glyphosate-based formulations are used all over the world to protect agricultural and horticultural crops. The European Commission planned to verify the toxicity of glyphosate in 2012, but in the end of 2010 it decided not to perform this verification up to 2015 [1]. Furthermore, due to the Regulation of the European Parliament and Council Regulation 1107/2009/EC on 21st of October 2009 [2], it is necessary to identify metabolites and impurities present in the technical pesticide and undertake toxicological researches concerning these substances. Moreover the analysis of deleterious effects of metabolites and impurities of pesticides seem to be very important to evaluate the toxicological risk that is exerted by these compounds. There is evidence that metabolites and impurities of the pesticides reveal stronger toxicity than their parent compounds [3–6].

We analyzed two metabolites of glyphosate: aminomethylphosphonic acid (AMPA) and methylphosphonic acid [7,8]. AMPA is a primary metabolite of glyphosate that is formed under the action of enzymes [7,9–12].

Glyphosate preparations can also occur many impurities where the number and the type depends on the type of pesticide production technology. These impurities include *N*-(phosphonomethyl)iminodiacetic acid (PMIDA), which is a key substrate in the immediate stage to receive a glyphosate in Monsanto technology [13–17], and therefore is considered as a impurity of a glyphosate.

The second examined product is formed during production of glyphosate (PMIDA oxidation step to glyphosate) and is a

Abbreviations: AChE, acetylcholinesterase; AMPA, aminomethylphosphonic acid; PMIDA, *N*-(phosphonomethyl)iminodiacetic acid; ROS, reactive oxygen species; H_2R123, dihydrorhodamine 123; NAC, *N*-acetylcysteine.

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Occurrence of glyphosate and AMPA in an agricultural watershed from the southeastern region of Argentina

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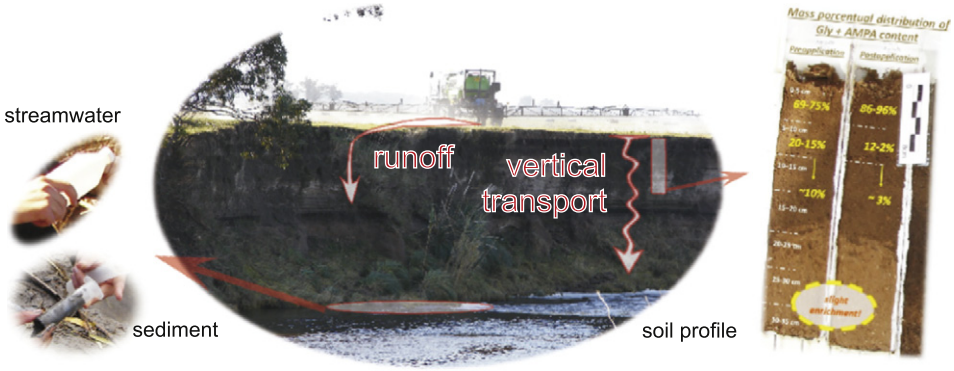
HIGHLIGHTS

- The fate of GLY + AMPA was studied in agricultural soil profiles from soybean fields.
- GLY + AMPA in soil profile were well correlated with organic carbon content and pH.
- GLY was concentrated in the upper soil layer after application.
- GLY and AMPA were detected in stream-water and sediment at lower levels than soils.

GRAPHICAL ABSTRACT



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ABSTRACT

Glyphosate (GLY) and AMPA concentrations were determined in sandy soil profiles, during pre- and post-application events in two agricultural soybean fields (S1 and S2). Streamwater and sediment samples were also analyzed. Post-application sampling was carried out one month later from the event. Concentrations of GLY + AMPA in surface soils (0–5 cm depth) during pre-application period showed values 20-fold higher (0.093–0.163 μg/g d.w.) than control area (0.005 μg/g d.w.). After application event soils showed markedly higher pesticide concentrations. A predominance of AMPA (80%) was observed in S1 (early application), while 34% in S2 for surface soils. GLY + AMPA concentrations decreased with depth and correlated strongly with organic carbon (r between 0.74 and 0.88, $p < 0.05$) and pH (r between −0.81 and −0.76, $p < 0.001$). The slight enrichment of pesticides observed from 25 cm depth to deeper layer, in addition to the alkaline pH along the profile, is of high concern about groundwater contamination. Sediments from pre-application period showed relatively lower pesticide levels (0.0053–0.0263 μg/g d.w.) than surface soil with a predominance of glyphosate, indicating a limited degradation. Levels of contaminants (mainly AMPA) in streamwater (ND-0.5 ng/mL) denote the low persistence of these compounds. However, a direct relationship in AMPA concentration was observed between sediment and streamwater. Despite the known relatively short half-life of glyphosate in soils, GLY + AMPA occurrence is registered in almost all matrices at different sampling times (pre- and post-application events). The

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Alteration in the cytokine levels and histopathological damage in common carp induced by glyphosate

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HIGHLIGHTS

- Glyphosate has low toxicity on common carp.
- Glyphosate-exposure alters the contents of cytokines.
- Glyphosate caused histopathological damage to common carp.
- Glyphosate has immunotoxic effects on common carp.

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ABSTRACT

Glyphosate is one of the most frequently used herbicides, and it has been demonstrated to generate a series of toxicological problems in animals and humans. However, relatively little is known about the effects of glyphosate on the immune system of fish. In the present study, the acute toxicity of glyphosate on common carp was first determined; then, the contents of interferon-γ (IFN-γ), interleukin-1β (IL-1β), and tumor necrosis factor -α (TNF-α) and histopathological alterations in the liver, kidneys, and spleen of common carp exposed to 52.08 or 104.15 mg L^{-1} of glyphosate for 168 h were also determined and evaluated. The results of the acute toxicity tests showed that the 96 h LC_{50} of glyphosate for common carp was 520.77 mg L^{-1}. Moreover, sub-acute exposure of glyphosate altered the contents of IFN-γ, IL-1β, and TNF-α in fish immune organs. For example, there was a remarkable increase in the IFN-γ content in the kidneys, while there was a decrease in the liver and spleen. The IL-1β content increased in liver and kidneys, but it decreased in the spleen, and TNF-α mainly increased in the fish liver, kidneys, and spleen. In addition, glyphosate-exposure also caused remarkable histopathological damage in the fish liver, kidneys, and spleen. These results suggest that glyphosate-caused cytokine alterations may result in an immune suppression or excessive activation in the treated common carp as well as may cause immune dysfunction or reduced immunity. In conclusion, glyphosate has immunotoxic effects on common carp.

1. Introduction

Glyphosate (N-[phosphonomethyl] glycine, $C_3H_8NO_5P$) is a broad-spectrum, nonselective, and nonsystemic herbicide that is frequently used in agricultural and non-agricultural systems (Baylis, 2000). Glyphosate and its putative metabolite aminomethylphosphonic acid (AMPA) have been found in urban streams, and the half-life of glyphosate in aquatic environments is normally in the range of 7–14 days (Gholami-Seyedkolaei et al., 2013). In recent years, the adverse effect of glyphosate on fish has received substantial attention (Glusczak et al., 2007; Lushchak et al., 2009) although it has been considered to have relatively low toxicity for aquatic organisms, including fish (Solomon and Thompson, 2003). There have been many few reports about the toxicity of glyphosate in fish, such as liver histological alterations induced by sublethal glyphosate exposures in common carp (Neskovic et al., 1996), Nile tilapia (Jiraungkoorskul et al., 2002), and curimbatá (Langiano and Martinez, 2008); biochemical toxicity on common carp (Gholami-Seyedkolaei et al., 2013); increased level of cortisol, plasma glucose, and catalase activity in silver catfish (Cericato et al., 2008) and curimbatá (Langiano and Martinez, 2008); and a significant reduction in superoxide dismutase, glutathione S-transferase, and glutathione reductase in goldfish (Lushchak et al., 2009). Meanwhile, the low concentrations of glyphosate in rice or soybean fields might cause alterations in the metabolic and enzymatic parameters of silver catfish (Glusczak et al., 2007) and other fish species (Glusczak et al., 2006; Lushchak et al., 2009).

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Review

Potential toxic effects of glyphosate and its commercial formulations below regulatory limits

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ABSTRACT

Glyphosate-based herbicides (GlyBH), including Roundup, are the most widely used pesticides worldwide. Their uses have increased exponentially since their introduction on the market. Residue levels in food or water, as well as human exposures, are escalating. We have reviewed the toxic effects of GlyBH measured below regulatory limits by evaluating the published literature and regulatory reports. We reveal a coherent body of evidence indicating that GlyBH could be toxic below the regulatory lowest observed adverse effect level for chronic toxic effects. It includes teratogenic, tumorigenic and hepatorenal effects. They could be explained by endocrine disruption and oxidative stress, causing metabolic alterations, depending on dose and exposure time. Some effects were detected in the range of the recommended acceptable daily intake. Toxic effects of commercial formulations can also be explained by GlyBH adjuvants, which have their own toxicity, but also enhance glyphosate toxicity. These challenge the assumption of safety of GlyBH at the levels at which they contaminate food and the environment, albeit these levels may fall below regulatory thresholds. Neurodevelopmental, reproductive, and transgenerational effects of GlyBH must be revisited, since a growing body of knowledge suggests the predominance of endocrine disrupting mechanisms caused by environmentally relevant levels of exposure.

Contents

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ENVIRONMENTAL HEALTH

RESEARCH Open Access

Drinking well water and occupational exposure to Herbicides is associated with chronic kidney disease, in Padavi-Sripura, Sri Lanka

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Abstract

Background: The chronic kidney disease of unknown etiology (CKDu) among paddy farmers in was first reported in 1994 and has now become most important public health issue in dry zone of Sri Lanka. The objective was to identify risk factors associated with the epidemic in an area with high prevalence.

Methods: A case control study was carried out in Padavi-Sripura hospital in Trincomalee district. CKDu patients were defined using health ministry criteria. All confirmed cases (N = 125) fulfilling the entry criteria were recruited to the study. Control selection (N = 180) was done from people visiting the hospital for CKDu screening. Socio-demographic and data related to usage of applying pesticides and fertilizers were studied. Drinking water was also analyzed using ICP-MS and ELISA to determine the levels of metals and glyphosate.

Results: Majority of patients were farmers (N = 107, 85.6%) and were educated up to 'Ordinary Level' (N = 92, 73.6%). We specifically analyzed for the effect modification of, farming by sex, which showed a significantly higher risk for male farmers with OR 4.69 (95% CI 1.06-20.69) in comparison to their female counterparts. In the multivariable analysis the highest risk for CKDu was observed among participants who drank well water (OR 2.52, 95% CI 1.12-5.70) and had history of drinking water from an abandoned well (OR 5.43, 95% CI 2.88-10.26) and spray glyphosate (OR 5.12, 95% CI 2.33-11.26) as a pesticide. Water analysis showed significantly higher amount of hardness, electrical conductivity and glyphosate levels in abandoned wells. In addition Ca, Mg, Ba, Sr, Fe, Ti, V and Sr were high in abandoned wells. Surface water from reservoirs in the endemic area also showed contamination with glyphosate but at a much lower level. Glyphosate was not seen in water samples in the Colombo district.

Conclusion: The current study strongly favors the hypothesis that CKDu epidemic among farmers in dry zone of Sri Lanka is associated with, history of drinking water from a well that was abandoned. In addition, it is associated with spraying glyphosate and other pesticides in paddy fields. Farmers do not use personnel protective equipments and wears scanty clothing due to heat when spraying pesticides.

Keywords: Chronic Kidney disease, Tubulointerstitial nephritis, Well water, Herbicides, Glyphosate, Sri Lanka

Background

A chronic kidney disease (CKD) with unusual characteristics was first reported in 1994 among middle-aged paddy farmers in Padaviya farming colony in the north-eastern boarder of the North Central Province (NCP) of Sri Lanka [1]. Some authors used the term CKDu to denote this condition where "u" stands for unknown or uncertain etiology. Twenty years after the first report, this disease is the most important public health issue in NCP with more than 50,000 estimated patients, and spreading on an epidemic scale to other farming areas in the Northern, Eastern, North Western, Central, and Uva provinces of the country [2]. The prevalence of the disease among those aged 15–70 years is estimated at 15.1% in the Anuradhapura district in NCP [3]. The unique feature of this CKD epidemic is that its etiology

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Glyphosate Sublethal Effects on the Population Dynamics of the Earthworm *Eisenia fetida* (Savigny, 1826)

Marina Santadino · Carlos Coviella · Fernando Momo

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Abstract Pesticides' sublethal effects are not regularly taken into account when assessing agrochemical's toxicity. With the objective of detecting chronic, sublethal effects of the widely used herbicide glyphosate, an experiment was performed using the earthworm *Eisenia fetida* as model organism. Earthworm adults were randomly assigned to three glyphosate treatments: control (no glyphosate), regular dose for perennial weeds, and double dose. Six *E. fetida* individuals were placed in each pot. Two random pots were taken weekly from each treatment and the number of adults, individual weight, number of cocoons, and presence and number of young earthworms were recorded. A matrix analysis was performed with the data. The matrix population model built showed that while the control population had a positive growth rate, both glyphosate treatments showed negative growth rates. The results suggest that under these sublethal effects, non-target populations are at risk of local extinction, underscoring the importance of this type of studies in agrochemical environmental risk assessment.

Keywords Ecotoxicology · Chronic effects · Earthworms · Pesticides · Agrochemicals

Capsule Non-target organisms can be at risk of local extinction due to agrochemicals chronic sublethal effects, which are not consistently taken into account in toxicity and risk assessment studies.

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1 Introduction

Since the mid 1990s, the use of genetically modified crops has been rapidly adopted worldwide (Qaim 2005). Argentina is the third producer of transgenic crops in the world, with about 15 % of the global surface dedicated to transgenic crops, only surpassed by the USA and Brazil (James 2011). Out of all the crops, soybean is the one that presents the greatest growth in Argentina. Since the 1970s, the surface has grown steadily. While in 1971, only 37,700 ha were occupied with soybean by 2012, the surface dedicated to this crop was 19.7 million hectares (FAO 2012), reaching almost 66 % of the overall cropping surface in Argentina. The rapid adoption of new technologies (i.e., the use of transgenic soybeans resistant to glyphosate and no tillage) contributed to make the soybean exports and its derivatives one of the main sources of the country's foreign exchange with a contribution of approximately US$**2500** million for 2013. By the 2006 cropping season, almost 100 % of the surface sown with soybean in Argentina was already transgenic (Trigo and Cap 2003). The increase in the use of these

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Research Article Open Access

The High Cost of Pesticides: Human and Animal Diseases

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Abstract

A significant degradation in the health of wild animals in Montana has been recorded over the past two decades. We surmise that the health issues are related to pesticide exposure. We present some of the evidence of the deterioration of the health in wildlife, which we used to inspire investigations on human health in the US population. While the animals' exposure is through food, water and air, we believe that human exposure is predominantly through food, as the majority of the population does not reside near agricultural fields and forests.

We have obtained US government data on pesticide usage and on human disease patterns over time from the 1998-2010 hospital discharge data. Since glyphosate is by far the most widely used herbicide, we believe it to be a major source of contamination for humans. Correlations between glyphosate usage and specific health issues, along with the known toxicology profile of glyphosate obtained from the literature, reflect a plausible causal relationship.

Because much of the wildlife data is from deer fawns, most of the human data presented here involve newborn infants, but we also present some data for children 0-15 years old and for the full population (except newborn). We found many diseases and conditions whose hospital discharge rates match remarkably well with the rate of glyphosate usage on corn, soy, and wheat crops. These include head and face anomalies (R=0.95), newborn eye disorders, newborn blood disorders (R=0.92), newborn skin disorders (R=0.96), lymph disorders in children 0-15 (R=0.86) and in the general population except newborn (R=0.89), congenital heart conditions in newborns (R= 0.98), enlarged right ventricle in all age groups except newborn (R=0.96), newborn lung problems (R=0.95), pulmonary bleeding and edema for all age groups except newborn (R=0.97), liver cancer for all age groups except newborn (R=0.93), newborn metabolic disorders (R=0.95) and newborn genitourinary disorders (R=0.96).

Keywords: Glyphosate; Brachygnathia; Hypothyroidism; Congenital heart defects; Thymus; Lymphedema; Hepatic carcinoma; Hypospadias; Genitourinary disorders

Introduction

One of the promises assured with genetically engineered (GE) herbicide-resistant crops was that they would require many fewer pesticides, providing a more sustainable agricultural option. Several GE crops, including cotton, canola, corn, soy, sugar beets and alfalfa, are engineered to withstand direct application of glyphosate, the active ingredient in the pervasive herbicide, Roundup. As a result of the widespread acceptance of GE crops, the increasing practice of using glyphosate for pre-harvest dry-down in grains and legumes, along with the emergence of glyphosate-resistant weeds, the use of glyphosate has skyrocketed since 1996 [1-3].

With the exception of glyphosate, pesticide use on crops was indeed reduced for the first 5 or 6 years after the introduction of these GE crops. Then something happened after about 2002, resulting in a steep increase in glyphosate and 2,4-D applications on corn, soy and potato, along with an increase in dicamba on wheat. This coincides with a steep increase in the number of confirmed cases of glyphosate-resistant weeds [1] as shown in Figure 1.

The active ingredient in the pesticides is usually an acid. To make the pesticides more water soluble and therefore easier to package and distribute, they are chemically altered into a salt or ester formulation. Various salt formulations include isopropylamine, diammonium, monoammonium, or potassium as the cation. Adjuvants are increasingly added to enhance the efficacy of the herbicides, particularly with the advent of the glyphosate-resistant weeds. One adjuvant is oxalic acid or an oxalate salt (potassium oxalate, e.g.) added to the stable salt formulations. For example, a 2006 patent by Xu et al. [4] discloses pesticide compositions, especially storage-stable herbicidal concentrates, containing oxalic acid and glyphosate that allegedly exhibit enhanced efficacy due to the addition of oxalic

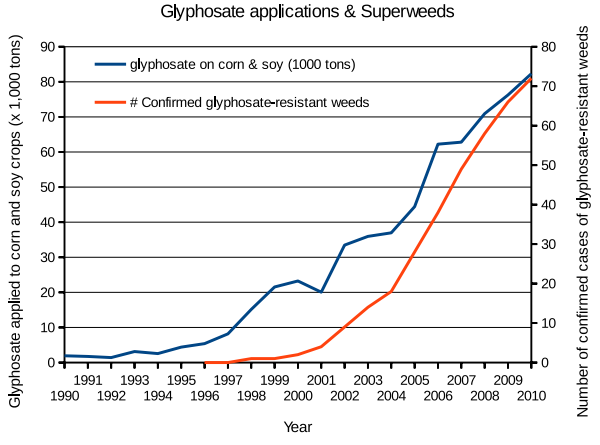

Figure 1: Glyphosate applications to corn, soy and cotton along with the advent of glyphosate-resistant weeds.

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BMC Genomics

RESEARCH ARTICLE Open Access

Global transcriptomic profiling demonstrates induction of oxidative stress and of compensatory cellular stress responses in brown trout exposed to glyphosate and Roundup

Tamsyn M Uren Webster* and Eduarda M Santos*

Abstract

Background: Glyphosate, the active ingredient in Roundup formulations, is the most widely used herbicide worldwide, and as a result contaminates surface waters and has been detected in food residues, drinking water and human urine, raising concerns for potential environmental and human health impacts. Research has shown that glyphosate and Roundup can induce a broad range of biological effects in exposed organisms, particularly via generation of oxidative stress. However, there has been no comprehensive investigation of the global molecular mechanisms of toxicity of glyphosate and Roundup for any species. We aimed to characterise and compare the global mechanisms of toxicity of glyphosate and Roundup in the liver of brown trout (*Salmo trutta*), an ecologically and economically important vertebrate species, using RNA-seq on an Illumina HiSeq 2500 platform. To do this, we exposed juvenile female brown trout to 0, 0.01, 0.5 and 10 mg/L of glyphosate and Roundup (glyphosate acid equivalent) for 14 days, and sequenced 6 replicate liver samples from each treatment.

Results: We assembled the brown trout transcriptome using an optimised *de novo* approach, and subsequent differential expression analysis identified a total of 1020 differentially-regulated transcripts across all treatments. These included transcripts encoding components of the antioxidant system, a number of stress-response proteins and pro-apoptotic signalling molecules. Functional analysis also revealed over-representation of pathways involved in regulating of cell-proliferation and turnover, and up-regulation of energy metabolism and other metabolic processes.

Conclusions: These transcriptional changes are consistent with generation of oxidative stress and the widespread induction of compensatory cellular stress response pathways. The mechanisms of toxicity identified were similar across both glyphosate and Roundup treatments, including for environmentally relevant concentrations. The significant alterations in transcript expression observed at the lowest concentrations tested raises concerns for the potential toxicity of this herbicide to fish populations inhabiting contaminated rivers.

Keywords: RNA-seq, Transcriptome, Herbicide, Salmonids, Toxicogenomics

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www.sbg.org.br

Short Communication

Evaluation of DNA damage in an Ecuadorian population exposed to glyphosate

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Abstract

We analyzed the consequences of aerial spraying with glyphosate added to a surfactant solution in the northern part of Ecuador. A total of 24 exposed and 21 unexposed control individuals were investigated using the comet assay. The results showed a higher degree of DNA damage in the exposed group (comet length = 35.5 μm) compared to the control group (comet length = 25.94 μm). These results suggest that in the formulation used during aerial spraying glyphosate had a genotoxic effect on the exposed individuals.

Key words: comet assay, DNA damage, Ecuador, genotoxicity, glyphosate.

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Glyphosate is a non-selective herbicide which is the main chemical component in many systemic herbicides used to control most annual and perennial plants. It controls weeds by inhibiting the synthesis of aromatic amino acids necessary for protein formation, which link primary and secondary metabolism in susceptible plants (Carlisle and Trevors, 1988; U.S. Forest Service, 1997).

According to some reports glyphosate shows no adverse effects on soil microorganisms, it is relatively non-toxic to fish (U.S. Forest Service, 1997) and is of relatively low toxicity to birds and mammals, including humans (Batt *et al.*, 1980; Evans and Batty, Williams *et al.*, 2000; Goldstein *et al.*, 2002). However, Lioi *et al.*, (1998) reported de induction of oxidative stress and mutagenic effects for some pesticides, including glyphosate, in bovines and Paz-y-Miño *et al.*, (2002a) reported that some pesticides were associated with genetic damage in human populations subjected to high pesticide exposure levels due intensive use, misuse or failure of control measures.

Since January 2001, the northern area of Ecuador (mainly Sucumbíos district) has been subjected to aerial spraying by the Colombian Government with Roundup-Ultra, a herbicide formulation containing glyphosate, polyethoxylated tallowamine surfactant (POEA) and the adjuvant Cosmoflux 411F which is a propriety Colombian component probably included to aid the adherence or absorption of the herbicide (Ministerio de Relaciones Exteriores, Ecuador (MREE), 2003). According to the National Narcotic Council for air spraying of illicit cultures the load of the airplane was 1137 to 1705 liters and the effective unloading with Roundup Ultra (43.9% of glyphosate) was 23.4 liters ha^{-1} equivalent to 10.3 L ha^{-1} of glyphosate (Acción Ecológica, 2003, Nivia, 2001). The main purpose of spraying glyphosate in this formulation is to eradicate illicit crops grown in this area, and several research projects have been carried out to investigate the consequences of the use of this formulation in Ecuador (MRE, Ecuador, 2003; Acción Ecológica, 2003).

The comet assay can be used to evaluate DNA damage and provides a useful tool for estimating the genetic risk from exposure to complex mixtures of chemicals (Paz-y-Miño *et al.*, 2002b), this assay having been widely applied in genotoxicity studies of factors such as X-rays and pesticides (Singh *et al.*, 1988; Tice *et al.*, 1990; Scarpato *et al.*, 1996; Slamenová *et al.*, 1999; Blasiak *et al*; 1999; Garaj-Vrhovac and Zeljezic, 2000; Paz-y-Miño *et al.*, 2002a; Paz-y-Miño *et al.*, 2002b; Acción Ecológica, 2003).

The aim of the study described in this paper was to determine the possible influence of the formulation of

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Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease

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Abstract

Many neurological diseases, including autism, depression, dementia, anxiety disorder and Parkinson's disease, are associated with abnormal sleep patterns, which are directly linked to pineal gland dysfunction. The pineal gland is highly susceptible to environmental toxicants. Two pervasive substances in modern industrialized nations are aluminum and glyphosate, the active ingredient in the herbicide, Roundup ®. In this paper, we show how these two toxicants work synergistically to induce neurological damage. Glyphosate disrupts gut bacteria, leading to an overgrowth of Clostridium difficile. Its toxic product, p-cresol, is linked to autism in both human and mouse models. p-Cresol enhances uptake of aluminum via transferrin. Anemia, a result of both aluminum disruption of heme and impaired heme synthesis by glyphosate, leads to hypoxia, which induces increased pineal gland transferrin synthesis. Premature birth is associated with hypoxic stress and with substantial increased risk to the subsequent development of autism, linking hypoxia to autism. Glyphosate chelates aluminum, allowing ingested aluminum to bypass the gut barrier. This leads to anemia-induced hypoxia, promoting neurotoxicity and damaging the pineal gland. Both glyphosate and aluminum disrupt cytochrome P450 enzymes, which are involved in melatonin metabolism. Furthermore, melatonin is derived from tryptophan, whose synthesis in plants and microbes is blocked by glyphosate. We also demonstrate a plausible role for vitamin D3 dysbiosis in impaired gut function and impaired serotonin synthesis. This paper proposes that impaired sulfate supply to the brain mediates the damage induced by the synergistic action of aluminum and glyphosate on the pineal gland and related midbrain nuclei.

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Compositional differences in soybeans on the market: Glyphosate accumulates in Roundup Ready GM soybeans

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Highlights
- Glyphosate tolerant GM soybeans contain high residues of glyphosate and AMPA.
- Soybeans from different agricultural practices differ in nutritional quality.
- Organic soybeans showed a more healthy nutritional profile than other soybeans.
- Organic soy contained more sugars, protein and zinc, but less fibre and omega-6.
- This study rejects that GM soy is "substantially equivalent" to non-GM soybeans.

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ABSTRACT

This article describes the nutrient and elemental composition, including residues of herbicides and pesticides, of 31 soybean batches from Iowa, USA. The soy samples were grouped into three different categories: (i) genetically modified, glyphosate-tolerant soy (GM-soy); (ii) unmodified soy cultivated using a conventional "chemical" cultivation regime; and (iii) unmodified soy cultivated using an organic cultivation regime. Organic soybeans showed the healthiest nutritional profile with more sugars, such as glucose, fructose, sucrose and maltose, significantly more total protein, zinc and less fibre than both conventional and GM-soy. Organic soybeans also contained less total saturated fat and total omega-6 fatty acids than both conventional and GM-soy. GM-soy contained high residues of glyphosate and AMPA (mean 3.3 and 5.7 mg/kg, respectively). Conventional and organic soybean batches contained none of these agrochemicals. Using 35 different nutritional and elemental variables to characterise each soy sample, we were able to discriminate GM, conventional and organic soybeans without exception, demonstrating "substantial non-equivalence" in compositional characteristics for 'ready-to-market' soybeans.

1. Introduction

Food and food quality is crucial. Given its significance for human and animal health, we investigate whether plant products from a defined geographical region, produced under different agricultural practices are substantially equivalent or not, in terms of quality indicators like nutritional content, elemental characteristics and herbicide/pesticide residues.

By comparing herbicide tolerant ("Roundup Ready") GM soybeans directly from farmers' fields, with extended references to both conventional, i.e., non-GM soybeans cultivated under a conventional "chemical" cultivation regime (pre-plant herbicides and pesticides used), and organic, i.e., non-GM soybeans cultivated under a "no chemical" cultivation regime (no herbicides or pesticides used), a test of real-life samples 'ready-to-market' can be performed.

Globally, glyphosate-tolerant GM soy is the number one GM crop plant. The herbicide glyphosate is the most widely used herbicide globally, with a production of 620,000 tons in 2008. The world soybean production in 2011 was 251.5 million Metric tons, with the United States (33%), Brazil (29%), Argentina (19%), China (5%) and India (4%) as the main producing countries.

In 2011–2012, soybeans were planted on about 30 million hectares in the USA, with Roundup Ready GM soy contributing 93–94% of the production. Also in the other leading producing countries, this same GM soy dominates the market accounting for 83% and 100% of production, respectively in Brazil and Argentina. Globally, Roundup Ready GM soybeans contributed to 75% of the total soy production in 2011. astonishing corporate-controlled monoculture = international risk to food supply

The first-generation glyphosate-tolerant GM-soy plant (event 40-3-2), produced and patented by Monsanto Company, has been genetically modified to tolerate exposure to glyphosate-based herbicides during the entire growth season. For herbicide-tolerant GM plants, herbicide co-technology is an integral part of the production system and will always be used by the farmer. However, in early studies of the composition of Roundup-Ready GM soy, the researchers did not spray the tested plants with the recommended herbicide (Millstone, Brunner, & Mayer, 1999). This shortcoming was quickly corrected, and also sprayed GM soybeans were claimed to be substantially equivalent to non-GM soybeans (Harrigan et al., 2007). Still, and surprisingly, even in these studies, the residues of herbicides were not measured.

The concept of 'substantial equivalence' (i.e., close nutritional and elemental similarity between a genetically modified (GM) crop and a non-GM traditional counterpart) has been used to claim that GM crops are substantially equivalent to, and therefore as safe and

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Research Article Open Access

Detection of Glyphosate Residues in Animals and Humans

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Abstract

In the present study glyphosate residues were tested in urine and different organs of dairy cows as well as in urine of hares, rabbits and humans using ELISA and Gas Chromatography-Mass Spectroscopy (GC-MS). The correlation coefficients between ELISA and GC-MS were 0.96, 0.87, 0.97and 0.96 for cattle, human, and rabbit urine and organs, respectively. The recovery rate of glyphosate in spiked meat using ELISA was 91%. Glyphosate excretion in German dairy cows was significantly lower than Danish cows. Cows kept in genetically modified free area had significantly lower glyphosate concentrations in urine than conventional husbandry cows. Also glyphosate was detected in different organs of slaughtered cows as intestine, liver, muscles, spleen and kidney. Fattening rabbits showed significantly higher glyphosate residues in urine than hares. Moreover, glyphosate was significantly higher in urine of humans with conventional feeding. Furthermore, chronically ill humans showed significantly higher glyphosate residues in urine than healthy population. The presence of glyphosate residues in both humans and animals could haul the entire population towards numerous health hazards, studying the impact of glyphosate residues on health is warranted and the global regulations for the use of glyphosate may have to be re-evaluated.

Keywords: Glyphosate; Animals; Husbandry cows; Health hazards; Gas Chromatography Mass Spectroscopy (GC-MS); ELISA

Introduction

Glyphosate (N-phosphonomethyl glycine) is registered as herbicide for many food and non-food crops as well as non-crop areas where total vegetation control is desired. The predominating uses of glyphosate, in descending order, are stubble management, pre-sowing application and pre-harvest application (desiccation). Glyphosate is also used to prevent weeds in fields with glyphosate resistant genetically modified (GM) crops like soybean, rapeseed, corn, etc. Since 1996 the amount and the number of genetically engineered crops dramatically increased worldwide. It is estimated that 90% of the transgenic crops grown worldwide are glyphosate resistant [1]. The rapidly growing problem of glyphosate-resistant weeds is reflected in steady increases in the use of glyphosate on crops. Steams, leaves and beans of glyphosate resistant soy are contaminated with glyphosate. Moreover, due to the intensive use of glyphosate it was frequently detected in water, rain and air. Chang and coworkers [2] detected glyphosate concentrations in air and rain up to 2.5 µg/L in agricultural areas in Mississippi and Iowa. In Europe GM soybean for food and feed was admitted in 1996. All animals and humans eating this soy chronically incorporate unknown amounts of this herbicide. Residues of glyphosate in tissues and organs of food animals fed with GM feed (soybean, corn, etc.) are not considered or neglected in legislation. The influence of glyphosate residues on the quality of animal Products intended for human food is almost unknown. The incorporation of GM soybean meal in broiler feed significantly affects the color parameter for breast muscles [3]. In contrast Erickson and coworkers [4] did not find any effects on the performance and carcass characteristics of feedlot steers. Furthermore, glyphosate is a potent chelator fixing trace and macro elements [5-7].

The mode of action of glyphosate is through specific inhibition of 5-enolpyruvyl shikimate 3-phosphate synthase (EPSPS), an enzyme of the shikimate pathway that governs the synthesis of aromatic amino compounds in higher plants, algae, bacteria and fungi [8]. As this enzyme is absent in mammals it is often assumed that glyphosate is not harmful for mammalians. Even so, there is an ongoing debate about the safety of this herbicide. Firstly, long-term toxicology of the low glyphosate residues has not been investigated in vertebrates. Secondly although EPSPS is absent, glyphosate has been reported to inhibit other enzymes, e.g., enzymes of the cytochrome P450 (Cyp450) family [8]. Other inhibition pathways are reported. Richard et al. [9] reported that such as glyphosate inhibits Cyp450 aromatase inhibition, indicated crucial for sex steroid hormone synthesis. inhibits inhibition?

Glyphosate also interferes with cytochrome P450 enzymes which include numerous proteins able to metabolize xenobiotics [10]. This may also act synergistically with disruption of the biosynthesis of aromatic amino acids by gut bacteria, as well as impairment in serum sulfate transport. Recently, it was suggested that gastrointestinal disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and Alzheimer's disease are associated with Western diet [11]. Furthermore, genotoxic activity [12], teratogenic activity [13], and disturbance of the normal gut bacterial community [14,15] due to glyphosate are reported. Glyphosate showed cytotoxic effects on different cells *in vitro* [16-18], and Barbosa et al. [19], proposed that glyphosate may have contributed to the Parkinsonism due to its chemical similarity with glycine, a co-factor required for activation of the N-methyl-d-aspartase (NMDA) receptor, which controls excitatory actions in the central nervous system and is also involved in memory and learning. However, in clinical studies has not shown NMDA activity in relation to glyphosate poisoning [20].

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Short Communication Open Access

Detection of Glyphosate in Malformed Piglets

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Summary

Glyphosate residues in different organs and tissues as lungs, liver, kidney, brain, gut wall and heart of malformed euthanized one-day-old Danish piglets (N= 38) were tested using ELISA. All organs or tissues had glyphosate in different concentrations. The highest concentrations were seen in the lungs (Range 0.4-80 µg/ml) and hearts (Range 0.15-80 µg/ml). The lowest concentrations were detected in muscles (4.4-6.4 µg/g). The detection of such glyphosate concentrations in these malformed piglets could be an allusion to the cause of these congenital anomalies. Further investigations are urgently needed to prove or exclude the role of glyphosate in malformations in piglets and other animals.

Introduction

In spring of last year a Danish pig farmer brought 38 live borne but malformed one-day-old piglets into our laboratory because of extraordinary high percentages of malformations in piglets. It was reported an assumption about the possible causes of this incident. It was noticed that the rate of malformations increased to one out of 260 born piglets if sow feeds contain 0.87-1.13 ppm glyphosate (N-phosphonomethylglycine) in the first 40 days of pregnancy. In case of 0.25 ppm glyphosate in sow feeds one of 1432 piglets was malformed. These piglets showed different abnormalities as ear atrophy,spinal and cranial deformations, cranium hole in head and leg atrophy; in one piglet one eye was not developed, it had only a large one. Piglets without trunk, with elephant tongue, and female piglet with testes were also present. One malformed piglet showed a swollen belly and fore gut and hind gut were not connected (Figure 1). Different organs and tissues as lungs, liver, kidney, brain, gut wall and heart of malformed euthanized one-day-old Danish piglets were tested for glyphosate using ELISA [1]. Briefly, tissue samples were minced to small pieces (~0.25 cm). In relation to the ability to retain water, samples were diluted with distilled water (Braun, Germany). The specimens were heated at 100°C for 10 min, homogenized and frozen at -80°C for 8 h. Samples were carefully thawed at 40°C and centrifuged at 10.000 x g for 10 min. The supernatant was filtered with an ultra-centrifugal filter with a cut off of 3000 Da to remove proteins and peptides. Filtrates were centrifuged (10.000 x g) again at 20°C for 10 min and the supernatant was tested for glyphosate using ELISA kits (Abraxis, USA) according to the manufacturer´s protocol.

Glyphosate residues were detected in the above mentioned tissues and organs of these piglets in different concentrations (Table 1). All organs or tissues had no significant differences in glyphosate concentration. The highest concentrations were seen in the lung (Range 0.4-80 µg/ml) and hearts (Range 0.15-80 µg/ml). The lowest concentrations were detected in muscles (4.4-6.4 µg/ml). It is postulated that glyphosate reaches the piglets through the placenta of their dams.

The predominant uses of glyphosate are for stubble management, pre-sowing weed control and pre-harvest application (desiccation) [2]. Glyphosate is also used for weed control in fields of genetically modified (GM) crops like soybean, rapeseed, corn, cotton, sugar beets, alfalfa, etc, where it is directly applied to the plants [3]. The rapidly growing problem of glyphosate-resistant weeds is reflected in a steady increase in the rate of glyphosate used on crops. Stems, leaves and beans of glyphosate resistant soy are contaminated with glyphosate. Moreover, because of the extensive use of glyphosate, it is frequently detected in water, rain and air [4,5]. Recently, glyphosate residues were tested in urine and different organs of dairy cows as well as in urine of hares, rabbits and humans in different concentrations [6]. Glyphosate and its commercial herbicides severely affect embryonic and placental cells, producing mitochondrial damage, necrosis and programmed cell death with doses far below the used agricultural concentrations. Paganelli et al. [7] found congenital malformations in chicken embryos with glyphosate at a concentration of 8-12 µM glyphosate in the injected side. The molecular phenotypes were correlated with a disruption of developmental mechanisms involving the neural crest, embryotic midline formation and cephalic patterning induced by the active principal of glyphosate not by the adjuvants due to impairment of retinoid signaling. The authors gave an overview of reports of malformations in children of families living few meters from where this herbicide was sprayed. The risk of malformation in human embryos is very high when their mothers are contaminated at 2 to 8 weeks of pregnancy. The detected glyphosate concentrations in organs, gut walls and meat of these piglets suspect correlation to glyphosate. Daruich and co-workers [8] concluded that glyphosate causes various disorders both in the parent female and in the progeny. Paternal exposure to glyphosate is recognized to be a cause of birth defects by pesticide mediated alterations of germ cells [9,10].

In conclusion, glyphosate could reach the animals through food

	Minimum	Maximum	Mean ±SD
Lung (N=38)	0.15	80	7.7 ± 18
Liver (N=38)	0	29.25	2.1 ± 2.2
Kidney (N=38)	0.1	38	3.2 ± 1.8
Muscles (N=38)	4.4	6.4	4.9 ± 1.8
Brain (N=38)	0.4	19.7	3.1 ± 4.1
Intestin (N=12)	0.7	7.7	2.4 ± 19
Heart (N=8)	0.4	80	12.9 ± 29.8

[1]Glyphosate was detected using ELISA [1] and data are expressed as µg/g.

Table 1: Glyphosate residues in different organs of malformed piglets[1].

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Journal of Organic Systems, 9(2), 2014 ORIGINAL PAPER

Genetically engineered crops, glyphosate and the deterioration of health in the United States of America

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Abstract

A huge increase in the incidence and prevalence of chronic diseases has been reported in the United States (US) over the last 20 years. Similar increases have been seen globally. The herbicide glyphosate was introduced in 1974 and its use is accelerating with the advent of herbicide-tolerant genetically engineered (GE) crops. Evidence is mounting that glyphosate interferes with many metabolic processes in plants and animals and glyphosate residues have been detected in both. Glyphosate disrupts the endocrine system and the balance of gut bacteria, it damages DNA and is a driver of mutations that lead to cancer.

In the present study, US government databases were searched for GE crop data, glyphosate application data and disease epidemiological data. Correlation analyses were then performed on a total of 22 diseases in these time-series data sets. The Pearson correlation coefficients are highly significant ($< 10^{-5}$) between glyphosate applications and hypertension (R = 0.923), stroke (R = 0.925), diabetes prevalence (R = 0.971), diabetes incidence (R = 0.935), obesity (R = 0.962), lipoprotein metabolism disorder (R = 0.973), Alzheimer's (R = 0.917), senile dementia (R = 0.994), Parkinson's (R = 0.875), multiple sclerosis (R = 0.828), autism (R = 0.989), inflammatory bowel disease (R = 0.938), intestinal infections (R = 0.974), end stage renal disease (R = 0.975), acute kidney failure (R = 0.978), cancers of the thyroid (R = 0.988), liver (R = 0.960), bladder (R = 0.981), pancreas (R = 0.918), kidney (R = 0.973) and myeloid leukaemia (R = 0.878).

The Pearson correlation coefficients are highly significant ($< 10^{-4}$) between the percentage of GE corn and soy planted in the US and hypertension (R = 0.961), stroke (R = 0.983), diabetes prevalence (R = 0.983), diabetes incidence (R = 0.955), obesity (R = 0.962), lipoprotein metabolism disorder (R = 0.955), Alzheimer's (R = 0.937), Parkinson's (R = 0.952), multiple sclerosis (R = 0.876), hepatitis C (R = 0.946), end stage renal disease (R = 0.958), acute kidney failure (R = 0.967), cancers of the thyroid (R = 0.938), liver (R = 0.911), bladder (R = 0.945), pancreas (R = 0.841), kidney (R = 0.940) and myeloid leukaemia (R = 0.889). The significance and strength of the correlations show that the effects of glyphosate and GE crops on human health should be further investigated.

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Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, andglyphosate.

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Glyphosate has been detected in the blood and urine of agricultural workers, indicating absorption. Soil microbes degrade glyphosate to aminomethylphosphoric acid (AMPA). Blood AMPA detection after poisonings suggests intestinal microbial metabolism in humans. Glyphosate and glyphosate formulations induced DNA and chromosomal damage in mammals, and in human and animal cells in vitro. One study reported increases in blood markers of chromosomal damage (micronuclei) in residents of several communities after spraying of glyphosate formulations.[16] Bacterial mutagenesis tests were negative. Glyphosate, glyphosate formulations, and AMPA induced oxidative stress in rodents and in vitro. The Working Group classified glyphosate as "probably carcinogenic to humans" (Group 2A).

We declare no competing interests.

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Article 1

Chemical Taking: Glyphosate and the Eradication of Due Process in Colombia

David A. Wilhite

CHEMICAL TAKING:

GLYPHOSATE AND THE ERADICATION OF DUE PROCESS IN COLOMBIA

*by David A. Wilhite**

INTRODUCTION

Cocaine politics continues to take a toll on Colombian social, political, economic, and legal stability. Coca[1] is indigenous to the Andean Mountains and for hundreds of years, native populations and immigrants to the region have consumed its leaves for both medicinal and customary purposes.[2] The United States consumes cocaine at a rate of over 300 metric tons per year.[3] Each year approximately 6,548,000 North Americans consume cocaine, annually spending $43.6 billion.[4] In an effort to curb this consumption, and because coca is the base of cocaine, the American and Colombian governments have combined forces using pesticide in an attempt to eradicate the problem at its perceived source, the coca plant.[5]

The legal, social, and political effects of spraying Glyphosate on coca plants demonstrate flaws in the policy of relying on a chemical to perform a government function. Glyphosate is a legal chemical, most famously the base of Monsanto's Round-Up. The chemical is produced in the United States, mixed in Colombia,[6] and sprayed by American planes on the Colombian countryside.[7] Despite this lawful chain, images, accounts, and notions of stripped tropical forest as well as bereft local farmers and indigenous communities raise questions as to the legality of spraying Glyphosate.[8] This article explores the effect of the spraying of Glyphosate with special attention to the issue of property rights. Through an analysis of Colombian expropriation laws, this article will argue that government reliance on aerial spraying of coca crops results in an illegal chemical expropriation.

> *[S]praying is for a public purpose, the resulting temporary disruption in productivity may constitute an illegal temporary taking. . .*

THE USE OF GLYPHOSATE: A CHEMICAL EXPROPRIATION?

Part of Plan Colombia and the Andean Counterdrug Initiative ("CEI") involves the aerial spraying of illegal coca cultivations with Glyphosate.[9] The Colombian Government is currently spraying a Glyphosate cocktail on coca crops throughout its territory, from the Amazon River Basin to the Northern Caribbean coast.[10] This program is meant to eliminate the cultivation of coca by killing the plant before it can be converted to cocaine, illegally transported, and consumed in the lucrative American market.[11]

For decades in Colombia, three extra-military armed groups have battled with drug lords, the State, each other, and the civilian population, resulting in as many as 30,000 deaths in some years [12] and 2.5 million displaced persons (second only to Sudan in number of displaced persons).[13] These violent groups as well as political and diplomatic wrangling fuel a devastating guerilla conflict.[14] Armed groups and drug lords rely in large part on capital from the illegal drug trade,[15] as well as extortion, kidnappings, and forced displacement.[16] To dam the flow of illegal capital, the Colombian government cooperates with the United States in an attempt to eradicate the illegal cultivation of the coca plant.[17]

Dusting planes, Blackhawk helicopters, American military agents, and U.S. Department of Defense contractors work in unison with Colombian forces and under U.S. Congressionally mandated guidelines[18] to apply Glyphosate to coca cultivations using aerial spraying.[19] The aerial eradication program in Colombia sprayed a record 136,551 hectares of coca and over 3,000 hectares (7,000 acres) of opium poppy in 2004.[20] In 2005, Colombia cultivated 80,000 of the 158,000 hectares cultivated in Colombia, Bolivia, and Peru.[21]

Though scientists from the U.S. Environmental Protection Agency and Organization of American States have found Glysophate's negative environmental and human consequences to be negligible, controversy persists.[22] A sprayed field takes approximately six to eight months to recover productive crops.[23] The use of a second chemical in the Glyphosate cocktail, Cosmoflux, allows the Glysophate to penetrate the waxy leaves of tropical plants.[24]

Spray pilots apply the herbicide at altitudes of less than one hundred feet,[25] and "while every effort is made to minimize human and mechanical mistakes, occasional errors are unavoidable."[26] As such, many neighboring cultivations, both illicit and licit, have been destroyed. Glysophate spraying has allegedly resulted in harm to "food plots, including bananas, beans, plan-

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Toxicology

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Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: Involvement of glutamate excitotoxicity

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Kinase pathways

ABSTRACT

Previous studies demonstrate that glyphosate exposure is associated with oxidative damage and neurotoxicity. Therefore, the mechanism of glyphosate-induced neurotoxic effects needs to be determined. The aim of this study was to investigate whether Roundup® (a glyphosate-based herbicide) leads to neurotoxicity in hippocampus of immature rats following acute (30 min) and chronic (pregnancy and lactation) pesticide exposure. Maternal exposure to pesticide was undertaken by treating dams orally with 1% Roundup® (0.38% glyphosate) during pregnancy and lactation (till 15-day-old). Hippocampal slices from 15 day old rats were acutely exposed to Roundup® (0.00005–0.1%) during 30 min and experiments were carried out to determine whether glyphosate affects $^{45}Ca^{2+}$ influx and cell viability. Moreover, we investigated the pesticide effects on oxidative stress parameters, ^{14}C-α-methyl-amino-isobutyric acid (^{14}C-MeAIB) accumulation, as well as glutamate uptake, release and metabolism. Results showed that acute exposure to Roundup® (30 min) increases $^{45}Ca^{2+}$ influx by activating NMDA receptors and voltage-dependent Ca^{2+} channels, leading to oxidative stress and neural cell death. The mechanisms underlying Roundup®-induced neurotoxicity also involve the activation of CaMKII and ERK. Moreover, acute exposure to Roundup® increased ^{3}H-glutamate released into the synaptic cleft, decreased GSH content and increased the lipoperoxidation, characterizing excitotoxicity and oxidative damage. We also observed that both acute and chronic exposure to Roundup® decreased ^{3}H-glutamate uptake and metabolism, while induced $^{45}Ca^{2+}$ uptake and ^{14}C-MeAIB accumulation in immature rat hippocampus. Taken together, these results demonstrated that Roundup® might lead to excessive extracellular glutamate levels and consequently to glutamate excitotoxicity and oxidative stress in rat hippocampus.

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Roundup® exposure promotes gills and liver impairments, DNA damage and inhibition of brain cholinergic activity in the Amazon teleost fish *Colossoma macropomum*

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HIGHLIGHTS

- RD caused histopathology, increased hematological indexes and reduction of GST.
- RD increased hepatic levels of EROD and antioxidant defenses (GPx).
- RD caused DNA damage and inhibition of AChE activity.
- Alterations were dose-dependent.

ARTICLE INFO

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Aquaculture

ABSTRACT

Roundup Original® (RD) is a glyphosate-based herbicide used to control weeds in agriculture. Contamination of Amazon waters has increased as a consequence of anthropogenic pressure, including the use of herbicides as RD. The central goal of this study was to evaluate the toxic effects of RD on juveniles of tambaqui (*Colossoma macropomum*). Our findings show that biomarkers in tambaqui are organ specific and dependent on RD concentration. Alterations in gills structural and respiratory epithelium were followed by changes in hematological parameters such as concentration of hemoglobin, particularly in fish exposed to the higher concentration tested (75% of RD LC_{50} 96 h). In addition, both RD concentrations affected the biotransformation process in gills of tambaqui negatively. Instead, liver responses suggest that a production of reactive oxygen species (ROS) occurred in fish exposed to RD, particularly in the animals exposed to 75% RD, as seen by imbalances in biotransformation and antioxidant systems. The increased DNA damage observed in red blood cells of tambaqui exposed to RD is in agreement with this hypothesis. Finally, both tested sub-lethal concentrations of RD markedly inhibited the cholinesterase activity in fish brain. Thus, we can suggest that RD is potentially toxic to tambaqui and possibly to other tropical fish species.

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human reproduction

ORIGINAL ARTICLE *Infertility*

Fruit and vegetable intake and their pesticide residues in relation to semen quality among men from a fertility clinic

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STUDY QUESTION: Is consumption of fruits and vegetables with high levels of pesticide residues associated with lower semen quality?

SUMMARY ANSWER: Consumption of fruits and vegetables with high levels of pesticide residues was associated with a lower total sperm count and a lower percentage of morphologically normal sperm among men presenting to a fertility clinic.

WHAT IS KNOWN ALREADY: Occupational and environmental exposure to pesticides is associated with lower semen quality. Whether the same is true for exposure through diet is unknown.

STUDY DESIGN, SIZE, DURATION: Men enrolled in the Environment and Reproductive Health (EARTH) Study, an ongoing prospective cohort at an academic medical fertility center. Male partners ($n = 155$) in subfertile couples provided 338 semen samples during 2007–2012.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Semen samples were collected over an 18-month period following diet assessment. Sperm concentration and motility were evaluated by computer-aided semen analysis (CASA). Fruits and vegetables were categorized as containing high or low-to-moderate pesticide residues based on data from the annual United States Department of Agriculture Pesticide Data Program. Linear mixed models were used to analyze the association of fruit and vegetable intake with sperm parameters accounting for within-person correlations across repeat samples while adjusting for potential confounders.

MAIN RESULTS AND THE ROLE OF CHANCE: Total fruit and vegetable intake was unrelated to semen quality parameters. High pesticide residue fruit and vegetable intake, however, was associated with poorer semen quality. On average, men in highest quartile of high pesticide residue fruit and vegetable intake (≥1.5 servings/day) had 49% (95% confidence interval (CI): 31%, 63%) lower total sperm count and 32% (95% CI: 7%, 58%) lower percentage of morphologically normal sperm than men in the lowest quartile of intake (<0.5 servings/day) (P, trend = 0.003 and 0.02, respectively). Low-to-moderate pesticide residue fruit and vegetable intake was associated with a higher percentage of morphologically normal sperm (P, trend = 0.04).

LIMITATIONS, REASONS FOR CAUTION: Surveillance data, rather than individual pesticide assessment, was used to assess the pesticide residue status of fruits and vegetables. CASA is a useful method for clinical evaluation but may be considered less favorable for accurate semen analysis in the research setting. Owing to the observational nature of the study, confirmation is required by interventional studies as well.

WIDER IMPLICATIONS OF THE FINDINGS: To our knowledge, this is the first report on the consumption of fruits and vegetables with high levels of pesticide residue in relation to semen quality. Further confirmation of these findings is warranted.

STUDY FUNDING/COMPETING INTEREST(S): Supported by National Institutes of Health grants ES009718, ES022955, ES000002, P30 DK046200 and Ruth L. Kirschstein National Research Service Award T32 DK007703-16. None of the authors has any conflicts of interest to declare.

Key words: fruits and vegetables / pesticide / semen quality

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Genetic damage in soybean workers exposed to pesticides: Evaluation with the comet and buccal micronucleus cytome assays

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Soybean farm workers
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Buccal micronucleus cytome assay

ABSTRACT

Soybean cultivation is widespread in the State of Rio Grande do Sul (RS, Brazil), especially in the city of Espumoso. Soybean workers in this region are increasingly exposed to a wide combination of chemical agents present in formulations of fungicides, herbicides, and insecticides. In the present study, the comet assay in peripheral leukocytes and the buccal micronucleus (MN) cytome assay (BMCyt) in exfoliated buccal cells were used to assess the effects of exposures to pesticides in soybean farm workers from Espumoso. A total of 127 individuals, 81 exposed and 46 non-exposed controls, were evaluated. Comet assay and BMCyt (micronuclei and nuclear buds) data revealed DNA damage in soybean workers. Cell death was also observed (condensed chromatin, karyorhectic, and karyolitic cells). Inhibition of non-specific choline esterase (BchE) was not observed in the workers. The trace element contents of buccal samples were analyzed by Particle-Induced X-ray Emission (PIXE). Higher concentrations of Mg, Al, Si, P, S, and Cl were observed in cells from workers. No associations with use of personal protective equipment, gender, or mode of application of pesticides were observed. Our findings indicate the advisability of monitoring genetic toxicity in soybean farm workers exposed to pesticides.

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Alteration in the cytokine levels and histopathological damage in common carp induced by glyphosate

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HIGHLIGHTS

- Glyphosate has low toxicity on common carp.
- Glyphosate-exposure alters the contents of cytokines.
- Glyphosate caused histopathological damage to common carp.
- Glyphosate has immunotoxic effects on common carp.

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Glyphosate
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Histopathology

ABSTRACT

Glyphosate is one of the most frequently used herbicides, and it has been demonstrated to generate a series of toxicological problems in animals and humans. However, relatively little is known about the effects of glyphosate on the immune system of fish. In the present study, the acute toxicity of glyphosate on common carp was first determined; then, the contents of interferon-γ (IFN-γ), interleukin-1β (IL-1β), and tumor necrosis factor -α (TNF-α) and histopathological alterations in the liver, kidneys, and spleen of common carp exposed to 52.08 or 104.15 mg L^{-1} of glyphosate for 168 h were also determined and evaluated. The results of the acute toxicity tests showed that the 96 h LC_{50} of glyphosate for common carp was 520.77 mg L^{-1}. Moreover, sub-acute exposure of glyphosate altered the contents of IFN-γ, IL-1β, and TNF-α in fish immune organs. For example, there was a remarkable increase in the IFN-γ content in the kidneys, while there was a decrease in the liver and spleen. The IL-1β content increased in liver and kidneys, but it decreased in the spleen, and TNF-α mainly increased in the fish liver, kidneys, and spleen. In addition, glyphosate-exposure also caused remarkable histopathological damage in the fish liver, kidneys, and spleen. These results suggest that glyphosate-caused cytokine alterations may result in an immune suppression or excessive activation in the treated common carp as well as may cause immune dysfunction or reduced immunity. In conclusion, glyphosate has immunotoxic effects on common carp.

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Glyphosate persistence in seawater

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Seawater
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Microbial

ABSTRACT

Glyphosate is one of the most widely applied herbicides globally but its persistence in seawater has not been reported. Here we quantify the biodegradation of glyphosate using standard "simulation" flask tests with native bacterial populations and coastal seawater from the Great Barrier Reef. The half-life for glyphosate at 25 °C in low-light was 47 days, extending to 267 days in the dark at 25 °C and 315 days in the dark at 31 °C, which is the longest persistence reported for this herbicide. AMPA, the microbial transformation product of glyphosate, was detected under all conditions, confirming that degradation was mediated by the native microbial community. This study demonstrates glyphosate is moderately persistent in the marine water under low light conditions and is highly persistent in the dark. Little degradation would be expected during flood plumes in the tropics, which could potentially deliver dissolved and sediment-bound glyphosate far from shore.

Surg Neurol Int. 2015 Mar 24;6:45. doi: 10.4103/2152-7806.153876. eCollection 2015.

Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies.

Samsel A[1], Seneff S[2].
Author information

Abstract

Manganese (Mn) is an often overlooked but important nutrient, required in small amounts for multiple essential functions in the body. A recent study on cows fed genetically modified Roundup(®)-Ready feed revealed a severe depletion of serum Mn. Glyphosate, the active ingredient in Roundup(®), has also been shown to severely deplete Mn levels in plants. Here, we investigate the impact of Mn on physiology, and its association with gut dysbiosis as well as neuropathologies such as autism, Alzheimer's disease (AD), depression, anxiety syndrome, Parkinson's disease (PD), and prion diseases. Glutamate overexpression in the brain in association with autism, AD, and other neurological diseases can be explained by Mn deficiency. Mn superoxide dismutase protects mitochondria from oxidative damage, and mitochondrial dysfunction is a key feature of autism and Alzheimer's. Chondroitin sulfate synthesis depends on Mn, and its deficiency leads to osteoporosis and osteomalacia. Lactobacillus, depleted in autism, depend critically on Mn for antioxidant protection. Lactobacillus probiotics can treat anxiety, which is a comorbidity of autism and chronic fatigue syndrome. Reduced gut Lactobacillus leads to overgrowth of the pathogen, Salmonella, which is resistant toglyphosate toxicity, and Mn plays a role here as well. Sperm motility depends on Mn, and this may partially explain increased rates of infertility and birth defects. We further reason that, under conditions of adequate Mn in the diet, glyphosate, through its disruption of bile acid homeostasis, ironically promotes toxic accumulation of Mn in the brainstem, leading to conditions such as PD and prion diseases.

Pest Manag Sci. 2015 Mar 17. doi: 10.1002/ps.4005. [Epub ahead of print]

Glyphosate resistance in Echinochloa colona: phenotypic characterisation and quantification of selection intensity.

Goh SS[1], Vila-Aiub MM, Busi R, Powles SB.

Author information

Abstract

BACKGROUND:

A population of Echinochloa colona infesting agricultural fields in the northern region of Western Australia evolved glyphosate resistance after 10 years of glyphosate selection. This study identified two phenotypic (susceptible S versus resistant R) lines from within a segregating glyphosate-resistant population. Estimation of survival, growth and reproductive rates of the phenotypes in response to glyphosateselection helped to characterise the level of resistance, fitness and the selection intensity for glyphosate in this species.

RESULTS:

Estimations of LD_{50} (lethal dose) and GR_{50} (growth rate) showed an eightfold glyphosateresistance in this population. The resistant index based on the estimation of seed number ($SY_{n\ 50}$) showed a 13-fold resistance. As a result of linear combination of plant survival and fecundity rates, plant fitness values of 0.2 and 0.8 were estimated for the S and R phenotypes when exposed to the low dose of 270 g glyphosateha^{-1}. At the recommended dose of 540 g glyphosate ha^{-1}, fitness significantly decreased (fivefold) in S plants but remained markedly similar (0.7) in plants of the R phenotype. Thus, the calculated selection intensity (SI) at 540 g glyphosate ha^{-1} was much greater (SI = 17) than at 270 g glyphosate ha^{-1} (SI = 4).

CONCLUSIONS:

The assessment of plant survival and fecundity in response to glyphosate selection in the S and R phenotypes allowed a greater accuracy in the estimation of population fitness of both phenotypes and thus of glyphosate selection intensity in E. colona. The estimation of seed number or mass of phenotypes under herbicide selection is a true ecological measure of resistance with implications for herbicide resistance evolution. © 2015 Society of Chemical Industry.

Water Environ Res. 2014 Dec;86(12):2294-300.

The impact of Eskoba, a glyphosate formulation, on the freshwater plankton community.

Reno U, Gutierrez MF, Regaldo L, Gagneten AM.

Abstract

This study analyzed the acute effects of a glyphosate-based herbicide (Eskoba) on the microalgae Chlorella vulgaris, the cladoceran Simocephalus vetulus, and the copepod Notodiaptomus conifer, and evaluated the recovery ability of the surviving micro-crustaceans. Survival, age of first reproduction, and fecundity were used as endpoints for S. vetulus, while survival and time to reach the adult stage were used as endpoints for N. conifer. The registered order of sensitivity was S. vetulus (48-hour effective concentration [EC50]: 21 mg/L) > C. vulgaris (72-hour EC50: 58.59 mg/ L) > N. conifer (48-hour EC50: 95 mg/L). Despite the growth of C. vulgaris stimulated after 24 hours of exposure to the commercial formulation of glyphosate Eskoba, it was inhibited after 48 hours by all the concentrations tested. In postexposure experiments, microcrustaceans reduced their life expectancy, S. vetulus decreased its fertility, and N. conifer inhibited its sexual maturity. In summary, it was demonstrated that these species lost their recovery ability.

Cardiovasc Toxicol. 2014 Dec 2. [Epub ahead of print]

Cardiotoxic Electrophysiological Effects of the Herbicide Roundup® in Rat and Rabbit Ventricular Myocardium In Vitro.

Gress S[1], Lemoine S, Puddu PE, Séralini GE, Rouet R.

Author information

Abstract

Roundup (R), a glyphosate (G)-based herbicide (GBH), containing unknown adjuvants is widely dispersed around the world. Used principally by farmers, intoxications have increasingly been reported. We have studied R effects (containing 36 % of G) on right ventricular tissues (male Sprague-Dawley rats, up to 20,000 ppm and female New Zealand rabbits, at 25 and 50 ppm), to investigate R cardiac electrophysiological actions in vitro. We tested the reduced Ca^{++} intracellular uptake mechanism as one potential cause of the electrical abnormalities after GBH superfusion, using the Na^{+}/K^{+}-ATPase inhibitor ouabain or the 1,4-dihydropyridine L-type calcium channel agonist BAY K 8644 which increases I_{Ca}. R concentrations were selected based on human blood ranges found after acute intoxication. The study showed dose-dependent V_{max}, APD_{50} and APD_{90} variations during 45 min of R superfusion. At the highest concentrations tested, there was a high incidence of conduction blocks, and 30-min washout with normal Tyrode solution did not restore excitability. We also observed an increased incidence of arrhythmias at different doses of R. Ouabain and BAY K 8644 prevented V_{max} decrease, APD_{90} increase and the cardiac inexcitability induced by R 50 ppm. Glyphosatealone (18 and 180 ppm) had no significant electrophysiological effects. Thus, the action potential prolonging effect of R pointing to I_{Ca} interference might explain both conduction blocks and proarrhythmia in vitro. These mechanisms may well be causative of QT prolongation, atrioventricular conduction blocks and arrhythmias in man after GBH acute intoxications as reported in retrospective hospital records.

Toxicol Mech Methods. 2015 Jan;25(1):70-80. doi: 10.3109/15376516.2014.989349.

Combined effects of repeated administration of Bretmont Wipeout (glyphosate) and Ultrazin (atrazine) on testosterone, oxidative stress and sperm quality of Wistar rats.

Abarikwu SO[1], Akiri OF, Durojaiye MA, Adenike A.

Author information

Abstract

BACKGROUND:

The potential toxicity resulting from the possible interactions of the herbicides, Ultrazin (atrazine, ATZ) and Bretmont Wipeout (glyphosate, GLY) (as commercialized in Nigeria), is not completely known. We therefore evaluated reproductive- and hepato-toxicity in rats co-exposed to ATZ and GLY.

METHODS:

Six weeks old male rats were exposed by gavage three times per week to ATZ (12.5 mg/kg) or GLY (5 mg/kg) alone or in combination (12.5 mg/kg ATZ + 5 mg/kg GLY) or vehicle (corn oil), for 52 days.

RESULTS:

ATZ and GLY impaired sperm quality but GLY has more adverse effect on sperm quality than ATZ. Testosterone level, sperm motility, sperm counts, live/dead ratio and the weight of the epididymis were lower in the GLY group compared to the ATZ group by 57%, 33%, 20%, 22% and 41% and higher by 109%, 76.7%, 39.6%, 32.3% and 100% respectively in the combine-exposure group (ATZ + GLY) compared to the GLY group. Oxidative stress and histopathological changes were also noticeable in the liver but not in the testis of GLY-treated animals, and the observed effects were more remarkable in the GLY group than the ATZ or the combined-exposure group. The combined effects of the active ingredients on testosterone level, sperm count and hepatic malondialdehyde (MDA) levels were also similar as when the commercial formulations were used.

CONCLUSION:

There are therefore antagonistic interactions between the two toxicants on the toxicity endpoints investigated in this study and these effects are due to the active ingredients of both herbicides in the commercial formulations.

Plant Physiol. 2014 Nov;166(3):1241-54. doi: 10.1104/pp.114.247668. Epub 2014 Sep 10.

De novo genome assembly of the economically important weed horseweed using integrated data from multiple sequencing platforms.

Peng Y[1], Lai Z[1], Lane T[1], Nageswara-Rao M[1], Okada M[1], Jasieniuk M[1], O'Geen H[1], Kim RW[1], Sammons RD[1], Rieseberg LH[1], Stewart CN Jr[2].
Author information

Erratum in

- Plant Physiol. 2014 Dec;166(4):2218.

Abstract

Horseweed (Conyza canadensis), a member of the Compositae (Asteraceae) family, was the first broadleaf weed to evolve resistance to glyphosate. Horseweed, one of the most problematic weeds in the world, is a true diploid (2n = 2x = 18), with the smallest genome of any known agricultural weed (335 Mb). Thus, it is an appropriate candidate to help us understand the genetic and genomic bases of weediness. We undertook a draft de novo genome assembly of horseweed by combining data from multiple sequencing platforms (454 GS-FLX, Illumina HiSeq 2000, and PacBio RS) using various libraries with different insertion sizes (approximately 350 bp, 600 bp, 3 kb, and 10 kb) of a Tennessee-accessed, glyphosate-resistant horseweed biotype. From 116.3 Gb (approximately 350× coverage) of data, the genome was assembled into 13,966 scaffolds with 50% of the assembly = 33,561 bp. The assembly covered 92.3% of the genome, including the complete chloroplast genome (approximately 153 kb) and a nearly complete mitochondrial genome (approximately 450 kb in 120 scaffolds). The nuclear genome is composed of 44,592 protein-coding genes. Genome resequencing of seven additional horseweed biotypes was performed. These sequence data were assembled and used to analyze genome variation. Simple sequence repeat and single-nucleotide polymorphisms were surveyed. Genomic patterns were detected that associated with glyphosate-resistant or -susceptible biotypes. The draft genome will be useful to better understand weediness and the evolution of herbicide resistance and to devise new management strategies. The genome will also be useful as another reference genome in the Compositae. To our knowledge, this article represents the first published draft genome of an agricultural weed.

Free PMC Article

Related citations

Comp Biochem Physiol C Toxicol Pharmacol. 2014 Nov;166:126-33. doi: 10.1016/j.cbpc.2014.07.009. Epub 2014 Aug 9.

Progression of DNA damage induced by a glyphosate-based herbicide in fish (Anguilla anguilla) upon exposure and post-exposure periods--insights into the mechanisms of genotoxicity and DNA repair.

Marques A[1], Guilherme S[2], Gaivão I[3], Santos MA[2], Pacheco M[2].

Author information

Abstract

Roundup® is a glyphosate-based herbicide widely used with both agricultural and non-agricultural purposes, which has been demonstrated to represent a risk to non-target aquatic organisms, namely fish. Among the described effects to fish, genotoxicity has been pointed out as one of the most hazardous. However, thegenotoxic mechanisms of Roundup® as well as the involvement of the oxidative DNA damage repair system are not entirely understood. Hence, this work aimed to improve the knowledge on the progression of DNA damage upon short-term exposure (3 days) and post-exposure (1-14 days) periods in association with DNA repair processes in Anguilla anguilla exposed to Roundup® (58 and 116 μg L(-1)). DNA damage in hepatic cells was evaluated by the comet assay improved with the DNA-lesion specific endonucleases FPG and EndoIII. In order to evaluate the oxidative DNA damage repair ability, an in vitro base excision repair (BER) assay was performed, testing hepatic subcellular extracts. Besides the confirmation of the genotoxic potential of this herbicide, oxidative damage was implicit as an important mechanism of genetic damage, which showed to be transient, since DNA integrity returned to the control levels on the first day after cessation of exposure. An increased capacity to repair oxidative DNA damage emerging in the post-exposure period revealed to be a crucial pathway for the A. anguilla recovery; nevertheless, DNA repair machinery showed to be susceptible to inhibitory actions during the exposure period, disclosing another facet of the risk associated with the tested agrochemical.

Aquat Toxicol. 2014 Oct;155:322-6. doi: 10.1016/j.aquatox.2014.07.006. Epub 2014 Jul 12.

Effect of glyphosate on the sperm quality of zebrafish Danio rerio.

Lopes FM[1], Varela Junior AS[2], Corcini CD[3], da Silva AC[4], Guazzelli VG[5], Tavares G[6], da Rosa CE[7].
Author information

Abstract

Glyphosate is a systemic, non-selective herbicide widely used in agriculture worldwide. It acts as an inhibitor of the enzyme 5-enolpyruvylshikimate-3-phosphate synthase by interrupting the synthesis of essential aromatic amino acids. This pathway is not present in animals, although some studies have shown that the herbicide glyphosate can affect fish reproduction. In this study, the effect of glyphosate on sperm quality of the fish Danio rerio was investigated after 24 and 96 h of exposure at concentrations of 5mg/L and 10mg/L. The spermatic cell concentration, sperm motility and motility period were measured employing conventional microscopy.
The mitochondrial functionality, membrane integrity and DNA integrity were measured by fluorescence microscopy using specific probes. No significant differences in sperm concentration were observed; however, sperm motility and the motility period were reduced after exposure to both glyphosateconcentrations during both exposure periods. The mitochondrial functionality and membrane and DNA integrity were also reduced at the highest concentration during both exposure periods. The results showed thatglyphosate can induce harmful effects on reproductive parameters in D. rerio and that this change would reduce the fertility rate of these animals.

J Exp Biol. 2014 Oct 1;217(Pt 19):3457-64. doi: 10.1242/jeb.109520. Epub 2014 Jul 25.

Effects of field-realistic doses of glyphosate on honeybee appetitive behaviour.

Herbert LT[1], Vázquez DE[1], Arenas A[1], Farina WM[2].

Author information

Abstract

Glyphosate (GLY) is a broad-spectrum herbicide used for weed control. The sub-lethal impact of GLY on non-target organisms such as insect pollinators has not yet been evaluated. Apis mellifera is the main pollinator in agricultural environments and is a well-known model for behavioural research. Honeybees are also accurate biosensors of environmental pollutants and their appetitive behavioural response is a suitable tool with which to test sub-lethal effects of agrochemicals. We studied the effects of field-realistic doses of GLY on honeybees exposed chronically or acutely to the herbicide. We focused on sucrose sensitivity, elemental and non-elemental associative olfactory conditioning of the proboscis extension response (PER), and foraging-related behaviour. We found a reduced sensitivity to sucrose and learning performance for the groups chronically exposed to GLY concentrations within the range of recommended doses. When olfactory PER conditioning was performed with sucrose reward with the same GLY concentrations (acute exposure), elemental learning and short-term memory retention decreased significantly compared with controls. Non-elemental associative learning was also impaired by an acute exposure to GLY traces. Altogether, these results imply that GLY at concentrations found in agro-ecosystems as a result of standard spraying can reduce sensitivity to nectar reward and impair associative learning in honeybees. However, no effect on foraging-related behaviour was found. Therefore, we speculate that successful forager bees could become a source of constant inflow of nectar with GLY traces that could then be distributed among nestmates, stored in the hive and have long-term negative consequences on colony performance.

Aquat Toxicol. 2014 Oct;155:213-21. doi: 10.1016/j.aquatox.2014.06.007. Epub 2014 Jul 9.

Are DNA-damaging effects induced by herbicide formulations (Roundup® and Garlon®) in fish transient and reversible upon cessation of exposure?

Guilherme S[1], Santos MA[2], Gaivão I[3], Pacheco M[2].

Author information

Abstract

Owing to the seasonality of crop cultivation and subsequent periodic/seasonal application of herbicides, their input to the aquatic systems is typically intermittent. Consequently, exposure of fish to this type of contaminants can be short and followed by a period of permanence in non-contaminated areas. Thus, the assessment of genotoxic endpoints in fish after removal of the contamination source appears as a crucial step to improve the knowledge on the dynamics of herbicide genotoxicity, as well as to determine the actual magnitude of risk posed by these agrochemicals. Therefore, the present study intended to shed light on the ability of fish to recover from the DNA damage induced by short-term exposures to the herbicide formulationsRoundup(®) (glyphosate-based) and Garlon(®) (triclopyr-based) upon the exposure cessation. European eel (Anguilla anguilla) was exposed to the above commercial formulations for 3 days, and allowed to recover for 1, 7 and 14 days (post-exposure period). The comet assay was used to identify the DNA damage in blood cells during both exposure and post-exposure periods. As an attempt to clarify the DNA damaging mechanisms involved, an extra-step including the incubation of the nucleotides with DNA lesion-specific repair enzyme was added to the standard comet.
The genotoxic potential of both herbicides was confirmed, concerning the exposure period. In addition, the involvement of oxidative DNA damage on the action ofRoundup(®) (pointed out as pyrimidine bases oxidation) was demonstrated, while for Garlon(®) this damaging mechanism was less evident. Fish exposed to Garlon(®), though presenting some evidence towards a tendency of recovery, did not achieve a complete restoration of DNA integrity. In what concerns toRoundup(®), a recovery was evident when considering non-specific DNA damage on day 14 post-exposure. In addition, this herbicide was able to induce a late oxidative DNA damage (day 14). Blood cells of A. anguilla exposed to Roundup(®) appeared to be more successful in repairing damage with a non-specific cause than that associated to base oxidation. Overall, the present findings highlighted the genetic hazard to fish associated to the addressed agrochemicals, reinforcing the hypothesis of long-lasting damage.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Occup Environ Med. 2014 Jun;71 Suppl 1:A116. doi: 10.1136/oemed-2014-102362.364.

0409 The North American Pooled Project (NAPP): Pooled analyses of case-control studies of pesticides and agricultural exposures, lymphohematopoietic cancers and sarcoma.

Pahwa M[1], Beane Freeman L[2], Spinelli JJ[3], Blair A[2], Pahwa P[4], Dosman JA[5], McLaughlin JR[6], Demers PA[7], Hoar Zahm S[2], Cantor KP[2], Weisenburger DD[8], Harris SA[1].

Author information

Abstract

OBJECTIVES:

Previous studies have noted associations between specific pesticides and multiple cancer types. However, assessments for many pesticides have been limited by small numbers of exposed cases. To address this, we established the North American Pooled Project (NAPP), a collaborative effort to evaluate the relationship of pesticide and agricultural exposures to risks of lymphohematopoietic cancers and sarcoma.

METHOD:

We harmonised previously collected data from three population-based case-control studies conducted in four American states with a similar Canada-wide study conducted in six provinces. Descriptive analyses of pesticide exposures, personal protective equipment (PPE) use, and demographic data were completed. The prevalence of self-reported pesticide use among cases and controls was determined for specific agents and chemical classes.

RESULTS:

The NAPP includes 5131 controls and 3274 cases (non-Hodgkin lymphoma [NHL] N=1690; Hodgkin lymphoma [HL] N=507; multiple myeloma [MM] N=587; soft tissue sarcoma N=490). Preliminary descriptive analyses indicate that approximately two-thirds of controls and NHL and MM cases ever lived or worked on a farm or ranch. Nearly half of controls and half of NHL, HL, and MM cases reported using any pesticide. Over 120 different insecticides, herbicides, and fungicides were reported. More than 17% of participants reported using the phenoxy herbicide 2,4-D and over 5% reported DDT, malathion, atrazine, or glyphosate. Around 6% of NHL cases and controls reported ever using PPE.

CONCLUSIONS:

The large number of cases and controls and high frequency of pesticide use in the NAPP will allow us to evaluate less commonly used pesticides, cancer sub-types, and smaller relative risks than previously possible.

Comp Biochem Physiol C Toxicol Pharmacol. 2014 Sep;165:83-90. doi: 10.1016/j.cbpc.2014.06.003. Epub 2014 Jun 20.

Effects of the surfactant polyoxyethylene amine (POEA) on genotoxic, biochemical and physiological parameters of the freshwater teleost Prochilodus lineatus.

Navarro CD[1], Martinez CB[2].

Author information

Abstract

The surfactant polyoxyethylene amine (POEA) is added to several formulations of glyphosate herbicides that are widely used in agriculture and can contaminate aquatic ecosystems. In the present study, an integrated approach examining genotoxic, biochemical and physiological parameters was employed to evaluate acute effects of POEA on the Neotropical fish Prochilodus lineatus. Juvenile fish were exposed to 0.15 mg·L(-1) (POEA 1), 0.75 mg·L(-1) (POEA 2) and 1.5 mg·L(-1) (POEA 3) of POEA or only water (CTR), and after 24h exposure samples of blood and liver were taken. Compared with CTR, liver of fish exposed to POEA 2 and POEA 3 showed increased activity of 7 ethoxyresorufin-O-deethylase and increased content of glutathione, whereas the activity of glutathione-S-transferase was diminished. On the other hand, fish of the group POEA 1 showed an increase in the activity of superoxide dismutase and in the occurrence of lipid peroxidation. Fish exposed to POEA 3 presented increased hepatic activity of glutathione peroxidase and reduced plasma cortisol. The exposure to POEA at all concentrations tested caused an increase in plasma lactate and a decrease in the hepatic activity of catalase, in the number of red blood cells and in hemoglobin content. The comet assay used for analyzing DNA damage in blood cells indicated the genotoxicity of the surfactant at all concentrations tested. Taken together these results show that POEA can cause effects at various levels, such as hemolysis, DNA damage and lipid peroxidation, which are directly related to an imbalance in the redox state of the fish.

Chemosphere. 2014 Aug;108:93-100. doi: 10.1016/j.chemosphere.2014.02.079. Epub 2014 Apr 12.

Genotoxicity of mixtures of glyphosate and atrazine and their environmental transformation products before and after photoactivation.

Roustan A[1], Aye M[2], De Meo M[3], Di Giorgio C[4].
Author information

Abstract

The photo-inducible cytogenetic toxicity of glyphosate, atrazine, aminomethyl phosphoric acid (AMPA), desethyl-atrazine (DEA), and their various mixtures was assessed by the in vitro micronucleus assay on CHO-K1 cells. Results demonstrated that the cytogenetic potentials of pesticides greatly depended on their physico-chemical environment. The mixture made with the four pesticides exhibited the most potent cytogenetic toxicity, which was 20-fold higher than those of the most active compound AMPA, and 100-fold increased after light-irradiation. Intracellular ROS assessment suggested the involvement of oxidative stress in the genotoxic impact of pesticides and pesticide mixtures. This study established that enhanced cytogenetic activities could be observed in pesticide mixtures containing glyphosate, atrazine, and their degradation products AMPA and DEA. It highlighted the importance of cocktail effects in environmental matrices, and pointed out the limits of usual testing strategies based on individual molecules, to efficiently estimate environmental risks.

MeSH Terms, Substances

Environ Toxicol Chem. 2014 Aug;33(8):1879-84. doi: 10.1002/etc.2635. Epub 2014 Jun 30.

Effects of glyphosate on egg incubation, larvae hatching, and ovarian rematuration in the estuarine crab Neohelice granulata.

Avigliano L[1], Alvarez N, Loughlin CM, Rodríguez EM.

Author information

Abstract

Ovigerous females of the estuarine crab (Neohelice granulate) were exposed to both pure glyphosate (2.5 mg/L and 5 mg/L) and a glyphosate formulation (Roundup Ultramax, containing glyphosate at 2.5 mg/L acid equivalent). At the end of the egg incubation period, a significant reduction in the number of hatched larvae was seen as a result of Roundup exposure. Additionally, several larvae abnormalities were seen in both pureglyphosate (2.5 mg/L) and Roundup treatments, such as hydropsy and hypopigmented eyes, and atrophied eyes were observed in the Roundup treatment. To evaluate the effect of the herbicide on ovarian rematuration, females remained exposed for 32 d. Pure glyphosate at 2.5 mg/L stimulated ovarian maturation over control levels, mainly in terms of a higher gonadosomatic index and a higher percentage of vitellogenic oocytes. A plausible hypothesis to be tested in further experiments is that exposure to glyphosate disrupts the hormonal system controlling reproduction.

Int J Environ Res Public Health. 2014 Apr 23;11(4):4449-527. doi: 10.3390/ijerph110404449.

Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: a systematic review and meta-analysis.

Schinasi L[1], Leon ME[2].

Author information

Abstract

This paper describes results from a systematic review and a series of meta-analyses of nearly three decades worth of epidemiologic research on the relationship between non-Hodgkin lymphoma (NHL) and occupational exposure to agricultural pesticide active ingredients and chemical groups. Estimates of associations of NHL with 21 pesticide chemical groups and 80 active ingredients were extracted from 44 papers, all of which reported results from analyses of studies conducted in high-income countries. Random effects meta-analyses showed that phenoxy herbicides, carbamate insecticides, organophosphorus insecticides and the active ingredient lindane, an organochlorine insecticide, were positively associated with NHL. In a handful of papers, associations between pesticides and NHL subtypes were reported; B cell lymphoma was positively associated with phenoxy herbicides and the organophosphorus herbicide glyphosate. Diffuse large B-cell lymphoma was positively associated with phenoxy herbicide exposure. Despite compelling evidence that NHL is associated with certain chemicals, this review indicates the need for investigations of a larger variety of pesticides in more geographic areas, especially in low- and middle-income countries, which, despite producing a large portion of the world's agriculture, were missing in the literature that were reviewed.

Environ Sci Pollut Res Int. 2014 Apr 15. [Epub ahead of print]

Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (Apis mellifera).

Helmer SH[1], Kerbaol A, Aras P, Jumarie C, Boily M.

Author information

Abstract

The decline in the population of pollinators is a worrying phenomenon worldwide. In North America, the extensive use of herbicides in maize and soya crops may affect the health of nontarget organisms like the honey bee. In this study, caged honey bees were exposed to realistic doses of atrazine, metolachlor, andglyphosate for 10 days via contaminated syrup. Peroxidation of lipids was evaluated using the thiobarbituric acid reactive substance (TBARS) test, and diet-derived antioxidants-carotenoids, all-trans-retinol (at-ROH) and α-tocopherol-were detected and quantified using reversed-phase HPLC techniques. Significant increases in syrup consumption were observed in honey bees exposed to metolachlor, and a lower TBARS value was recorded for the highest dose. No relationship was observed between the peroxidation of lipids and the levels of antioxidants. However, β-carotene, which was found to be the most abundant carotenoid, and at-ROH (derived from β-carotene) both decreased with increasing doses of atrazine and glyphosate. In contrast, metolachlor increased levels of at-ROH without any effects on β-carotene. These results show that the honey bee carotenoid-retinoid system may be altered by sublethal field-realistic doses of herbicides.

Biomed Res Int. 2014;2014:179691. doi: 10.1155/2014/179691. Epub 2014 Feb 26.

Major pesticides are more toxic to human cells than their declared active principles.

Mesnage R[1], Defarge N[1], Spiroux de Vendômois J[2], Séralini GE[1].

Author information

Abstract

Pesticides are used throughout the world as mixtures called formulations. They contain adjuvants, which are often kept confidential and are called inerts by the manufacturing companies, plus a declared active principle, which is usually tested alone. We tested the toxicity of 9 pesticides, comparing active principles and their formulations, on three human cell lines (HepG2, HEK293, and JEG3). Glyphosate, isoproturon, fluroxypyr, pirimicarb, imidacloprid, acetamiprid, tebuconazole, epoxiconazole, and prochloraz constitute, respectively, the active principles of 3 major herbicides, 3 insecticides, and 3 fungicides. We measured mitochondrialactivities, membrane degradations, and caspases 3/7 activities. Fungicides were the most toxic from concentrations 300-600 times lower than agricultural dilutions, followed by herbicides and then insecticides, with very similar profiles in all cell types. Despite its relatively benign reputation, Roundup was among the most toxic herbicides and insecticides tested. Most importantly, 8 formulations out of 9 were up to one thousand times more toxic than their active principles. Our results challenge the relevance of the acceptable daily intake for pesticides because this norm is calculated from the toxicity of the active principle alone. Chronic tests on pesticides may not reflect relevant environmental exposures if only one ingredient of these mixtures is tested alone.

Environ Sci Pollut Res Int. 2014 Jul;21(14):8730-9. doi: 10.1007/s11356-014-2803-1. Epub 2014 Apr 4.

DNA and chromosomal damage induced in fish (Anguilla anguilla L.) by aminomethylphosphonic acid (AMPA)--the major environmental breakdown product of glyphosate.

Guilherme S[1], Santos MA, Gaivão I, Pacheco M.

Author information

Abstract

The assessment of the direct impact of breakdown products of pesticide components on aquatic wildlife is ecotoxicologically relevant, but frequently disregarded. In this context, the evaluation of the genotoxic hazard posed by aminomethylphosphonic acid (AMPA--the major natural degradation product of glyphosate) to fish emerges as a critical but unexplored issue. Hence, the main goal of the present research was to assess the AMPA genotoxic potential to fish following short-term exposures (1 and 3 days) to environmentally realistic concentrations (11.8 and 23.6 μg L(-1)), using the comet and erythrocytic nuclear abnormalities (ENA) assays, as reflecting different levels of damage, i.e. DNA and chromosomal damage, respectively. Overall, the present findings pointed out the genotoxic hazard of AMPA to fish and, subsequently, the importance of including it in future studies concerning the risk assessment of glyphosate-based herbicides in the water systems.

Genet Mol Biol. 2014 Mar;37(1):105-10. Epub 2013 Feb 28.

Comparison of the in vivo and in vitro genotoxicity of glyphosate isopropylamine salt in three different organisms.

Alvarez-Moya C[1], Silva MR[1], Ramírez CV[1], Gallardo DG[1], Sánchez RL[2], Aguirre AC[3], Velasco AF[4].
Author information

Abstract

There is considerable controversy with regard to the genotoxicity of glyphosate, with some reports stating that this compound is non-toxic for fish, birds and mammals. In this work, we used the comet assay to examine the genotoxicity of glyphosate isopropylamine (0.7, 7, 70 and 700 μM) in human lymphocytes, erythrocytes of Oreochromis niloticus and staminal nuclei of Tradescantia (4430) in vitro and in vivo. Cells, nuclei and fish that had and had not been exposed to 5 mM N-nitrosodiethylamine (NDEA) were used as positive and negative controls, respectively. Significant ($p < 0.01$) genetic damage was observed in vivo and in vitro in all cell types and organisms tested. Human lymphocytes and Tradescantia hairs showed lower genetic damage in vivo compared to in vitro, possibly because of efficient metabolization of the herbicide. In O. niloticus erythrocytes, significant ($p < 0.001$) genotoxicity was observed at ≥ 7 μM, whereas in vitro, glyphosphate wasgenotoxic in human lymphocytes and Tradescantia hairs at ≥ 0.7 μM. These results indicate that glyphosateis genotoxic in the cells and organisms studied at concentrations of 0.7-7 μM.

Interdiscip Toxicol. 2013 Dec;6(4):159-84. doi: 10.2478/intox-2013-0026.

Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance.

Samsel A[1], Seneff S[2].

Author information

Abstract

Celiac disease, and, more generally, gluten intolerance, is a growing problem worldwide, but especially in North America and Europe, where an estimated 5% of the population now suffers from it. Symptoms include nausea, diarrhea, skin rashes, macrocytic anemia and depression. It is a multifactorial disease associated with numerous nutritional deficiencies as well as reproductive issues and increased risk to thyroid disease, kidney failure and cancer. Here, we propose that glyphosate, the active ingredient in the herbicide,Roundup(®), is the most important causal factor in this epidemic. Fish exposed to glyphosate develop digestive problems that are reminiscent of celiac disease. Celiac disease is associated with imbalances in gut bacteria that can be fully explained by the known effects of glyphosate on gut bacteria. Characteristics of celiac disease point to impairment in many cytochrome P450 enzymes, which are involved with detoxifying environmental toxins, activating vitamin D3, catabolizing vitamin A, and maintaining bile acid production and sulfate supplies to the gut. Glyphosate is known to inhibit cytochrome P450 enzymes. Deficiencies in iron, cobalt, molybdenum, copper and other rare metals associated with celiac disease can be attributed toglyphosate's strong ability to chelate these elements. Deficiencies in tryptophan, tyrosine, methionine and selenomethionine associated with celiac disease match glyphosate's known depletion of these amino acids. Celiac disease patients have an increased risk to non-Hodgkin's lymphoma, which has also been implicated inglyphosate exposure. Reproductive issues associated with celiac disease, such as infertility, miscarriages, and birth defects, can also be explained by glyphosate. Glyphosate residues in wheat and other crops are likely increasing recently due to the growing practice of crop desiccation just prior to the harvest. We argue that the practice of "ripening" sugar cane with glyphosate may explain the recent surge in kidney failure among agricultural workers in Central America. We conclude with a plea to governments to reconsider policies regarding the safety of glyphosate residues in foods.

BMC Plant Biol. 2014 Mar 21;14:70. doi: 10.1186/1471-2229-14-70.

Sub-lethal glyphosate exposure alters flowering phenology and causes transient male-sterility in Brassica spp.

Londo JP[1], McKinney J, Schwartz M, Bollman M, Sagers C, Watrud L.

Author information

Abstract

BACKGROUND:

Herbicide resistance in weedy plant populations can develop through different mechanisms such as gene flow of herbicide resistance transgenes from crop species into compatible weedy species or by natural evolution of herbicide resistance or tolerance following selection pressure. Results from our previous studies suggest that sub-lethal levels of the herbicide glyphosate can alter the pattern of gene flow betweenglyphosate resistant Canola®, Brassica napus, and glyphosate sensitive varieties of B. napus and B. rapa. The objectives of this study were to examine the phenological and developmental changes that occur in Brassica crop and weed species following sub-lethal doses of the herbicides glyphosate and glufosinate. We examined several vegetative and reproductive traits of potted plants under greenhouse conditions, treated with sub-lethal herbicide sprays.

RESULTS:

Our results indicate that exposure of Brassica spp. to a sub-lethal dose of glyphosate results in altering flowering phenology and reproductive function. Flowering of all sensitive species was significantly delayed and reproductive function, specifically male fertility, was suppressed. Higher dosage levels typically contributed to an increase in the magnitude of phenotypic changes.

CONCLUSIONS:

These results demonstrate that Brassica spp. plants that are exposed to sub-lethal doses ofglyphosate could be subject to very different pollination patterns and an altered pattern of gene flow that would result from changes in the overlap of flowering phenology between species. Implications include the potential for increased glyphosate resistance evolution and spread in weedy communities exposed to sub-lethalglyphosate.

J Toxicol Sci. 2014 Apr;39(2):211-5.

Effects of a POEA surfactant system (Genamin T-200(®)) on two life stages of the Pacific oyster, Crassostrea gigas.

Mottier A[1], Pini J, Costil K.

Author information

Abstract

Surfactants used in herbicide formulations are generally considered inert with no toxic effects on animals. Polyethoxylated tallow amines (POEAs) are non-ionic surfactants used in many herbicide formulations to promote the penetration of the active matter into plant cuticles. The present study aimed to assess the toxicity of a POEA surfactant system, the Genamin T-200®, on two larval stages of the Pacific oyster, Crassostrea gigas. The embryotoxicity of Genamin T-200® was quantified after 36 hr of exposure, considering both arrested development and abnormalities in D-shaped larvae. The ability of pediveliger larvae to metamorphose was studied after 24 hr exposure to Genamin T-200®. According to the European toxicity classification, the present results suggest that Genamin T-200® could be considered very toxic to embryo larval development, with an EC_{50} of 262 µg/l, and toxic to metamorphosis processes with an EC_{50} of 3,027 µg/l. The high toxicity of glyphosate-based formulations compared to the active ingredient and its by-product appears to be due primarily to surfactants.

Toxicology. 2014 Jun 5;320:34-45. doi: 10.1016/j.tox.2014.03.001. Epub 2014 Mar 15.

Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity.

Cattani D[1], de Liz Oliveira Cavalli VL[1], Heinz Rieg CE[1], Domingues JT[1], Dal-Cim T[1], Tasca CI[1], Mena Barreto Silva FR[1], Zamoner A[2].

Author information

Abstract

Previous studies demonstrate that glyphosate exposure is associated with oxidative damage and neurotoxicity. Therefore, the mechanism of glyphosate-induced neurotoxic effects needs to be determined. The aim of this study was to investigate whether Roundup(®) (a glyphosate-based herbicide) leads to neurotoxicity in hippocampus of immature rats following acute (30min) and chronic (pregnancy and lactation) pesticide exposure. Maternal exposure to pesticide was undertaken by treating dams orally with 1%Roundup(®) (0.38% glyphosate) during pregnancy and lactation (till 15-day-old). Hippocampal slices from 15 day old rats were acutely exposed to Roundup(®) (0.00005-0.1%) during 30min and experiments were carried out to determine whether glyphosate affects (45)Ca(2+) influx and cell viability. Moreover, we investigated the pesticide effects on oxidative stress parameters, (14)C-α-methyl-amino-isobutyric acid ((14)C-MeAIB) accumulation, as well as glutamate uptake, release and metabolism. Results showed that acute exposure toRoundup(®) (30min) increases (45)Ca(2+) influx by activating NMDA receptors and voltage-dependent Ca(2+) channels, leading to oxidative stress and neural cell death. The mechanisms underlying Roundup(®)-induced neurotoxicity also involve the activation of CaMKII and ERK. Moreover, acute exposure to Roundup(®) increased (3)H-glutamate released into the synaptic cleft, decreased GSH content and increased the lipoperoxidation, characterizing excitotoxicity and oxidative damage. We also observed that both acute and chronic exposure to Roundup(®) decreased (3)H-glutamate uptake and metabolism, while induced (45)Ca(2+) uptake and (14)C-MeAIB accumulation in immature rat hippocampus. Taken together, these results demonstrated that Roundup(®) might lead to excessive extracellular glutamate levels and consequently to glutamate excitotoxicity and oxidative stress in rat hippocampus.

KEYWORDS:

Calcium; Glutamatergic excitotoxicity; Glyphosate; Kinase pathways; Oxidative stress

J Toxicol Environ Health A. 2014;77(7):405-14. doi: 10.1080/15287394.2014.880393.

Changes in ultrastructure and expression of steroidogenic factor-1 in ovaries of zebrafish Danio rerio exposed to glyphosate.

Armiliato N[1], Ammar D, Nezzi L, Straliotto M, Muller YM, Nazari EM.

Author information

Abstract

Glyphosate is a broad-spectrum organophosphate (OP) herbicide, highly soluble in water, and when applied in terrestrial systems it penetrates into soil, eventually reaching the aquatic community and affecting nontarget organisms. The aim of this study was to evaluate the toxicity of glyphosate on ovaries of zebrafish (Danio rerio). Ovaries (n = 18 per triplicate) were exposed to 65 µg/L of glyphosate [N-(phosphonomethyl) glycine] for 15 d. This concentration was determined according to Resolution 357/2005/CONAMA/Brazil, which establishes the permissible concentration of glyphosate in Brazilian inland waters. Nonexposed ovaries (n = 18 per triplicate) were used as control. Subsequently, morphology and expression of steroidogenic factor-1 (SF-1) of exposed and nonexposed ovaries was determined. No apparent changes were noted in general morphology of exposed and nonexposed ovaries. However, a significant increase in diameter of oocytes was observed after exposure to glyphosate. When ovarian ultrastructure was examined the presence of concentric membranes, appearing as myelin-like structures, associated with the external membranes of mitochondriaand with yolk granules was found. After glyphosate exposure, immunohistochemistry and immunoblotting revealed greater expression of SF-1 in the oocytes, which suggests a relationship between oocyte growth and SF-1 expression. These subtle adverse effects of glyphosate on oocytes raised a potential concern for fishreproduction. These results contribute to understanding glyphosate-induced toxicity to nontarget organisms, showing subcellular and molecular impairments that may affect reproduction in +female fish.

Integr Environ Assess Manag. 2014 Jul;10(3):463-70. doi: 10.1002/ieam.1529. Epub 2014 May 19.

Evaluating exposure and potential effects on honeybee brood (Apis mellifera) development using glyphosate as an example.

Thompson HM[1], Levine SL, Doering J, Norman S, Manson P, Sutton P, von Mérey G.

Author information

Abstract

This study aimed to develop an approach to evaluate potential effects of plant protection products on honeybee brood with colonies at realistic worst-case exposure rates. The approach comprised 2 stages. In the first stage, honeybee colonies were exposed to a commercial formulation of glyphosate applied to flowering Phacelia tanacetifolia with glyphosate residues quantified in relevant matrices (pollen and nectar) collected by foraging bees on days 1, 2, 3, 4, and 7 postapplication and glyphosate levels in larvae were measured on days 4 and 7. Glyphosate levels in pollen were approximately 10 times higher than in nectar andglyphosate demonstrated rapid decline in both matrices. Residue data along with foraging rates and food requirements of the colony were then used to set dose rates in the effects study. In the second stage, the toxicity of technical glyphosate to developing honeybee larvae and pupae, and residues in larvae, were then determined by feeding treated sucrose directly to honeybee colonies at dose rates that reflect worst-case exposure scenarios. There were no significant effects from glyphosate observed in brood survival, development, and mean pupal weight. Additionally, there were no biologically significant levels of adult mortality observed in any glyphosate treatment group. Significant effects were observed only in the fenoxycarb toxic reference group and included increased brood mortality and a decline in the numbers of beesand brood. Mean glyphosate residues in larvae were comparable at 4 days after spray application in the exposure study and also following dosing at a level calculated from the mean measured levels in pollen and nectar, showing the applicability and robustness of the approach for dose setting with honeybee brood studies. This study has developed a versatile and predictive approach for use in higher tier honeybee toxicity studies. It can be used to realistically quantify exposure of colonies to pesticides to allow the appropriate dose rates to be determined, based on realistic worst-case residues in pollen and nectar and estimated intake by the colony, as shown by the residue analysis. Previous studies have used the standard methodology developed primarily to identify pesticides with insect-growth disrupting properties of pesticide formulations, which are less reliant on identifying realistic exposure scenarios. However, this adaptation of the method can be used to determine dose-response effects of colony level exposure to pesticides with a wide range of properties. This approach would limit the number of replicated tunnel or field-scale studies that need to be undertaken to assess effects on honeybee brood and may be of particular benefit where residues in pollen and nectar are crop- and/or formulation-specific, such as systemic seed treatments and granular applications.

KEYWORDS:

Med Pr. 2013;64(5):717-29.

[Glyphosate and its formulations--toxicity, occupational and environmental exposure].

[Article in Polish]

Kwiatkowska M[1], Paweł J[2], Bukowska B[2].

Author information

Abstract

Glyphosate (N-(phosphonomethyl)glycine) is an active ingredient of the most widely used herbicide formulations in protecting agricultural and horticultural crops. Numerous results (mostly published in the years 2010-2013) concerning the action of glyphosate and its formulations in the recent decade were analyzed. Initial reports about alleged biodegradability of glyphosate in the environment turned out to be wrong. It has been shown that glyphosate remains in the soil and can reach people by spreading along with groundwater. Recent publications have shown that glyphosate is detected at low concentrations in the human blood. Publications cited in this article, which indicate a possible induction of neoplastic changes by glyphosateformulation, have raised great concern and controversy in the scientific world. Presenting adverse effects Of glyphosate and its formulations we focused on the role of glyphosate formulations in hormonal disorders by impeding the expression of steroidogenic acute regulatory protein and the inhibition of aromatase activity. The impact of glyphosate on oxygen reactive species formation, changes in redox system and the effect on necrosis and apoptosis in various types of cells was shown. We also revealed that glyphosate as a phosphonate herbicide does not inhibit directly the activity of acetylcholinesterase. Based on numerous studies it was noted that commercial formulations of glyphosate exhibit higher toxicity than that of the active substance itself. The discussed problems clearly show the need to evaluate the toxicity of glyphosate and its formulations and related potential threat to humans.

Related citations

Publication Types, MeSH Terms, Substances

Environ Toxicol Pharmacol. 2014 Jan;37(1):448-54. doi: 10.1016/j.etap.2013.12.012. Epub 2013 Dec 31.

Genotoxic effects of the herbicide Roundup Transorb and its active ingredientglyphosate on the fish Prochilodus lineatus.

Moreno NC[1], Sofia SH[2], Martinez CB[3].

Author information

Abstract

Roundup Transorb (RT) is a glyphosate-based herbicide and despite its wide use around the world there are few studies comparing the effects of the active ingredient with the formulated product. In this context the purpose of this study was to compare the genotoxicity of the active ingredient glyphosate with the formulated product RT in order to clarify whether the active ingredient and the surfactant of the RT formula may exert toxic effects on the DNA molecule in juveniles of fish Prochilodus lineatus. Erythrocytes and gill cells of fish exposed to glyphosate and to RT showed DNA damage scores significantly higher than control animals. These results revealed that both glyphosate itself and RT were genotoxic to gill cells and erythrocytes of P. lineatus, suggesting that their use should be carefully monitored considering their potential impact on tropical aquatic biota.

KEYWORDS:

Comet assay; DNA damage; Erythrocytes; Gill cells; Neotropical fish

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Ecotoxicol Environ Saf. 2014 Feb;100:7-14. doi: 10.1016/j.ecoenv.2013.11.014. Epub 2013 Dec 20.

Genotoxic and biochemical effects of atrazine and Roundup(®), alone and in combination, on the Asian clam Corbicula fluminea.

dos Santos KC[1], Martinez CB[2].

Author information

Abstract

The present study aimed to evaluate biochemical and genotoxic effects of the herbicides atrazine (ATZ) andRoundup(®) (RD) separately, as well as their mixture, on the freshwater clam Corbicula fluminea after 96 h exposure. Animals were exposed to 2 and 10 ppb of ATZ (ATZ2 and ATZ10), 2 and 10 ppm of RD (RD2 and RD10) and the following mixtures: 2 ppb ATZ+2ppm RD (AR2) and 10 ppb ATZ+10 ppm RD (AR10). Activities of ethoxyresorufin-O-deethylase (EROD), glutathione-S-transferase (GST), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR), as well as the multixenobiotic resistance mechanism (MXR), reduced glutathione concentrations (GSH) and lipid peroxidation (LPO) were measured in gills and digestive gland. DNA damage was determined in clams hemocytes through the comet assay. The gills were more susceptible to the action of the herbicides and the results showed that ATZ2 and ATZ10 caused a significant reduction in EROD and the mixture leads to a significant decrease in EROD and MXR. No significant change in the biotransformation parameters was observed in the digestive gland. Regarding the primary antioxidant defenses, SOD activity increased in the gills of clams exposed to ATZ10 and RD10 and in the digestive gland of animals exposed to RD2 and RD10, CAT activity was significantly reduced only in digestive gland of clams exposed RD10 while GPX increased in the gills after exposure to ATZ2 and RD10. The exposure to RD10 caused a significant increase in LPO in both gills and digestive gland. While the exposure to ATZ and RD separately did not increase DNA damage, the exposure to AR2 and AR10 caused a significant increase in the occurrence of DNA damage. In conclusion, this study showed that both herbicides applied alone caused effects on C. fluminea; ATZ interfered mostly in biotransformation while RD interfered mainly in antioxidant defenses leading to lipid peroxidation. The herbicides mixture showed antagonistic effects on the gills EROD and on lipid peroxidation in gills and digestive gland and synergistic effects on the gills MXR and on DNA damage in the hemocytes.

KEYWORDS:

Antioxidants; Biotransformation; DNA damage; Herbicides mixture; Lipid peroxidation; MXR mechanism

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Planta. 2014 Apr;239(4):793-801. doi: 10.1007/s00425-013-2022-x. Epub 2014 Jan 3.

No fitness cost of glyphosate resistance endowed by massive EPSPS gene amplification in Amaranthus palmeri.

Vila-Aiub MM[1], Goh SS, Gaines TA, Han H, Busi R, Yu Q, Powles SB.

Author information

Abstract

Amplification of the EPSPS gene has been previously identified as the glyphosate resistance mechanism in many populations of Amaranthus palmeri, a major weed pest in US agriculture. Here, we evaluate the effects of EPSPS gene amplification on both the level of glyphosate resistance and fitness cost of resistance. A. palmeri individuals resistant to glyphosate by expressing a wide range of EPSPS gene copy numbers were evaluated under competitive conditions in the presence or absence of glyphosate. Survival rates toglyphosate and fitness traits of plants under intra-specific competition were assessed. Plants with higher amplification of the EPSPS gene (53-fold) showed high levels of glyphosate resistance, whereas less amplification of the EPSPS gene (21-fold) endowed a lower level of glyphosate resistance. Withoutglyphosate but under competitive conditions, plants exhibiting up to 76-fold EPSPS gene amplification exhibited similar height, and biomass allocation to vegetative and reproductive organs, compared toglyphosate susceptible A. palmeri plants with no amplification of the EPSPS gene. Both the additive effects of EPSPS gene amplification on the level of glyphosate resistance and the lack of associated fitness costs are key factors contributing to EPSPS gene amplification as a widespread and important glyphosateresistance mechanism likely to become much more evident in weed plant species.

Environ Sci Technol. 2014 Jan 21;48(2):1271-9. doi: 10.1021/es404258h. Epub 2014 Jan 9.

Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (Danio rerio).

Uren Webster TM[1], Laing LV, Florance H, Santos EM.

Author information

Abstract

Roundup and its active ingredient glyphosate are among the most widely used herbicides worldwide and may contaminate surface waters. Research suggests both Roundup and glyphosate induce oxidative stress in fish and may also cause reproductive toxicity in mammalian systems. We aimed to investigate the reproductiveeffects of Roundup and glyphosate in fish and the potential associated mechanisms of toxicity. To do this, we conducted a 21-day exposure of breeding zebrafish (Danio rerio) to 0.01, 0.5, and 10 mg/L (glyphosate acid equivalent) Roundup and 10 mg/L glyphosate. 10 mg/L glyphosate reduced egg production but not fertilization rate in breeding colonies. Both 10 mg/L Roundup and glyphosate increased early stage embryo mortalities and premature hatching. However, exposure during embryogenesis alone did not increase embryo mortality, suggesting that this effect was caused primarily by exposure during gametogenesis. Transcript profiling of the gonads revealed 10 mg/L Roundup and glyphosate induced changes in the expression of cyp19a1 and esr1 in the ovary and hsd3b2, cat, and sod1 in the testis. Our results demonstrate that these chemicals cause reproductive toxicity in zebrafish, although only at high concentrations unlikely to occur in the environment, and likely mechanisms of toxicity include disruption of the steroidogenic biosynthesis pathway and oxidative stress.

Drug Chem Toxicol. 2014 Oct;37(4):370-7. doi: 10.3109/01480545.2013.866138. Epub 2013 Dec 11.

Induction of micronuclei and nuclear lesions in Channa punctatus following exposure to carbosulfan, glyphosate and atrazine.

Nwani CD[1], Nagpure NS, Kumar R, Kushwaha B, Kumar P, Lakra WS.

Author information

Abstract

The genotoxic effects of commonly used agricultural pesticides viz., carbosulfan, glyphosate, and atrazine, were evaluated in Channa punctatus (Pisces, Perciformes) using micronucleus (MN) test and induction of nuclear lesions (NL). The 96 h LC50 value were estimated by probit analysis as 0.27, 32.0 and 42.0 mg L(-1), respectively, for carbosulfan, glyphosate, and atrazine using semi-static bioassays. Based on these values, three sublethal test concentrations of carbosulfan (0.07, 0.13, 0.20 mg L(-1)), glyphosate (8.1, 16.3, 24.4 mg L(-1)) and atrazine (10.6, 21.2, 31.8 mg L(-1)) corresponding to ¼, ½ and ¾ of the LC50 of the pesticides respectively, were selected for exposure for 96 h. Peripheral blood samplings were taken at intervals of 24 h for assessment of MN and NL frequencies. Considerably higher genotoxic damage was induced by carbosulfan as compared to glyphosate and atrazine. There were significant effects ($p < 0.01$) of concentrations in all the treated groups. The induction of MN and NL was highest at 96 h pesticide exposure at all test concentrations. The nuclear abnormalities recorded in this study, such as blebbed-, lobed-, notched- and bi-nuclei, other than micronuclei, are indicators of genotoxic damage.

KEYWORDS:

Atrazine; Channa punctatus; carbosulfan; genotoxicity; glyphosate; micronucleus test; nuclear lesions

Planta. 2014 Jan;239(1):199-212. doi: 10.1007/s00425-013-1972-3. Epub 2013 Oct 20.

Involvement of facultative apomixis in inheritance of EPSPS gene amplification inglyphosate-resistant Amaranthus palmeri.

Ribeiro DN[1], Pan Z, Duke SO, Nandula VK, Baldwin BS, Shaw DR, Dayan FE.

Author information

Abstract

The inheritance of glyphosate resistance in two Amaranthus palmeri populations (R1 and R2) was examined in reciprocal crosses (RC) and second reciprocal crosses (2RC) between glyphosate-resistant (R) and -susceptible (S) parents of this dioecious species. R populations and Female-R × Male-S crosses contain higher 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) gene copy numbers than the S population. EPSPS expression, EPSPS enzyme activity, EPSPS protein quantity, and level of resistance to glyphosate correlated positively with genomic EPSPS relative copy number. Transfer of resistance was more influenced by the female than the male parent in spite of the fact that the multiple copies of EPSPS are amplified in the nuclear genome. This led us to hypothesize that this perplexing pattern of inheritance may result from apomictic seed production in A. palmeri. We confirmed that reproductively isolated R and S female plants produced seeds, indicating that A. palmeri can produce seeds both sexually and apomictically (facultative apomixis). This apomictic trait accounts for the low copy number inheritance in the Female-S × Male-R offsprings. Apomixis may also enhance the stability of the glyphosate resistance trait in the R populations in the absence of reproductive partners.

Related citations

SpringerLink FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Ecotoxicol Environ Saf. 2013 Dec;98:152-61. doi: 10.1016/j.ecoenv.2013.09.009. Epub 2013 Oct 2.

Optimization of recovery patterns in common carp exposed to roundup using response surface methodology: evaluation of neurotoxicity and genotoxicityeffects and biochemical parameters.

Gholami-Seyedkolaei SJ[1], Mirvaghefi A, Farahmand H, Kosari AA, Gholami-Seyedkolaei SJ, Gholami-Seyedkolaei SJ.

Author information

Abstract

The present study is the first report on optimization of recovery conditions of fishes exposed to pesticides using response surface methodology-central composite rotatable design (RSM-CCRD). The sub-lethal toxicity bioassay of Roundup® (2 ppm ~10 percent LC_{50}, 96 h) in common carp (1, 4, 9, 16, 25, 35 and 40 day) was investigated. After exposure for 16 days to Roundup®, some the fishes were introduced to herbicide-free water. The effects of four recovery parameters including time (5-25 d), temperature (18-26 °C), water exchange rate (WER, 10-30), and salinity (0-8 ppt) on the levels of biomarkers of genotoxicity (DNA damage), neurotoxicity (acetylcholinesterase activity (AChE)), and the serum alanine (ALT) and aspartate (AST) aminotransferase in plasma were studied. The polynomial equations were significantly fitted for all response variables with high R^2 values (>0.95), which revealed no indication of lack of fit. The optimum conditions for the maximum AChE activity (37.14 nmol/min/mg protein) and the minimum levels of DNA damage (8.00 percent tail DNA), ALT (27.0 IU/L) and AST (91.0 IU/L) were time of 20 d, temperature of 20 °C, WER of 25 and water salinity of 6 ppt. Thus, a promising improvement for the recovery trend of fishes exposed toRoundup® stress was obtained under the optimized conditions using RSM-CCRD.

KEYWORDS:

Comet assay; Cyprinus carpio L; Herbicide; Recovery optimization; Response surface modeling

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

ISRN Dermatol. 2013 Aug 29;2013:825180. doi: 10.1155/2013/825180. eCollection 2013.

Emptying of Intracellular Calcium Pool and Oxidative Stress Imbalance Are Associated with the Glyphosate-Induced Proliferation in Human Skin Keratinocytes HaCaT Cells.

George J[1], Shukla Y.

Author information

Abstract

We demonstrated that glyphosate possesses tumor promoting potential in mouse skin carcinogenesis and SOD 1, calcyclin (S100A6), and calgranulin B (S100A9) have been associated with this potential, although the mechanism is unclear. We aimed to clarify whether imbalance in between [Ca(2+)] i levels and oxidative stress is associated with glyphosate-induced proliferation in human keratinocytes HaCaT cells. The [Ca(2+)] i levels, ROS generation, and expressions of G1/S cyclins, IP3R1, S100A6, S100A9, and SOD 1, and apoptosis-related proteins were investigated upon glyphosate exposure in HaCaT cells. Glyphosate (0.1 mM) significantly induced proliferation, decreases [Ca(2+)] i , and increases ROS generation in HaCaT cells, whereas antioxidant N-acetyl-L-cysteine (NAC) pretreatment reverts these effects which directly indicated that glyphosate induced cell proliferation by lowering [Ca(2+)] i levels via ROS generation. Glyphosate also enhanced the expression of G1/S cyclins associated with a sharp decrease in G0/G1 and a corresponding increase in S-phases. Additionally, glyphosate also triggers S100A6/S100A9 expression and decreases IP3R1 and SOD 1 expressions in HaCaT cells. Notably, Ca(2+) suppression also prevented apoptotic related events including Bax/Bcl-2 ratio and caspases activation. This study highlights that glyphosate promotes proliferation in HaCaT cells probably by disrupting the balance in between [Ca(2+)] i levels and oxidative stress which in turn facilitated the downregulation of mitochondrial apoptotic signaling pathways.

Bull Environ Contam Toxicol. 2013 Nov;91(5):583-7. doi: 10.1007/s00128-013-1103-7. Epub 2013 Sep 17.

Mutagenicity and genotoxicity in gill erythrocyte cells of Poecilia reticulata exposed to a glyphosate formulation.

De Souza Filho J[1], Sousa CC, Da Silva CC, De Sabóia-Morais SM, Grisolia CK.

Author information

Abstract

Poecilia reticulata were exposed to herbicide Roundup Transorb(®) for micronucleus test, nuclear abnormalities and comet assay. The exposure-concentrations were based on CL50-96 h following 0, 1.41, 2.83, 4.24 and 5.65 µL L(-1) for 24 h. Micronucleus and comets were significantly increased in the gill erythrocyte cells after herbicide exposure compared with the non-exposed group. Results showed a gradual increase in the number of damaged cells, indicating a concentration-dependent effect and that this herbicide was mutagenic and genotoxic to P. reticulata and this effect could be attributed to a combination of compounds contained in the formulation with the active ingredient glyphosate.

Aquat Toxicol. 2013 Oct 15;142-143:176-84. doi: 10.1016/j.aquatox.2013.08.006. Epub 2013 Aug 21.

Toxic effects of the herbicide Roundup in the guppy Poecilia vivipara acclimated to fresh water.

Harayashiki CA[1], Varela AS Jr, Machado AA, Cabrera Lda C, Primel EG, Bianchini A, Corcini CD.

Author information

Abstract

Although it is believed that glyphosate-based herbicides are relatively nontoxic to humans, its broad use in agriculture and consequent contamination of aquatic systems is a concern. In the present study, reproductive(sperm quality) and biochemical parameters (acetylcholinesterase and glutathione S-transferase activity, lipoperoxidation, and antioxidant capacity against peroxyl radicals) were evaluated in adult guppies (Poecilia vivipara) acclimated to fresh water and exposed (96 h) to environmentally realistic concentrations ofglyphosate (130 and 700 μg L(-1)) as the commercial formulation Roundup. Male guppies exposed to Roundupshowed a poorer sperm quality, measured as reduced plasmatic membrane integrity, mitochondrialfunctionality, DNA integrity, motility, motility period and concentration of spermatic cells, than those kept under control condition (no Roundup addition to the water). Most of the spermatic parameters analyzed showed strong association to each other, which may help to understand the mechanisms underlying the observed reduction in sperm quality. Exposure to Roundup did not alter the biochemical parameters analyzed, though differences between genders were observed and deserve further investigations. Findings from the present study suggest that exposure to environmentally relevant concentrations of Roundup may negatively affect at long-term the reproduction of P. vivipara, with consequent changes in fish populations inhabiting environments contaminated with the herbicide.

KEYWORDS:

Biomarkers; Glyphosate; Guppy; Herbicide; Roundup

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Ecotoxicol Environ Saf. 2013 Dec;98:368-73. doi: 10.1016/j.ecoenv.2013.08.011. Epub 2013 Sep 5.

Single-cell gel electrophoresis assay in the ten spotted live-bearer fish, Cnesterodon decemmaculatus (Jenyns, 1842), as bioassay for agrochemical-induced genotoxicity.

Vera-Candioti J[1], Soloneski S, Larramendy ML.

Author information

Abstract

The ability of two 48 percent chlorpyrifos-based insecticides (Lorsban* 48E® and CPF Zamba®), two 50 percent pirimicarb-based insecticides (Aficida® and Patton Flow®), and two 48 percent glyphosate-based herbicides (Panzer® and Credit®) to induce DNA single-strand breaks in peripheral blood erythrocytes of Cnesterodon decemmaculatus (Jenyns, 1842) (Pisces, Poeciliidae) exposed under laboratory conditions was evaluated by the single-cell gel electrophoresis (SCGE) assay. In those fish exposed to Lorsban* 48E®, CPF Zamba®, Aficida®, Patton Flow®, Credit®, and Panzer®, a significant increase of the genetic damage was observed for all formulations regardless of the harvesting time. This genotoxic effect was achieved by an enhancement of Type II-IV comets and a concomitant decrease of Type 0-I comets over control values. A regression analysis revealed that the damage varied as a negative function of the exposure time in those Lorsban* 48E®- and Aficida®-treated fish. On the other hand, a positive correlation between damage increase and exposure time was achieved after Patton Flow® and Credit® treatment. Finally, no correlation was observed between increase in the genetic damage and exposure time after treatment with CPF Zamba® or Panzer®. These results highlight that all agrochemicals inflict primary genotoxic damage at the DNA level at sublethal concentrations, regardless of the exposure time of the aquatic organisms under study, at least within a period of 96 h of treatment.

KEYWORDS:

Agrochemical commercial formulations; Chlorpyrifos; Comet assay; Glyphosate; Pirimicarb; Poeciliidae

Related citations

Publication Types, MeSH Terms, Substances

Free Radic Biol Med. 2013 Dec;65:335-46. doi: 10.1016/j.freeradbiomed.2013.06.043. Epub 2013 Jun 29.

Roundup disrupts male reproductive functions by triggering calcium-mediated cell death in rat testis and Sertoli cells.

de Liz Oliveira Cavalli VL[1], Cattani D, Heinz Rieg CE, Pierozan P, Zanatta L, Benedetti Parisotto E, Wilhelm Filho D, Mena Barreto Silva FR, Pessoa-Pureur R, Zamoner A.

Author information

Abstract

Glyphosate is the primary active constituent of the commercial pesticide Roundup. The present results show that acute Roundup exposure at low doses (36 ppm, 0.036 g/L) for 30 min induces oxidative stress and activates multiple stress-response pathways leading to Sertoli cell death in prepubertal rat testis. The pesticide increased intracellular Ca(2+) concentration by opening L-type voltage-dependent Ca(2+) channels as well as endoplasmic reticulum IP3 and ryanodine receptors, leading to Ca(2+) overload within the cells, which set off oxidative stress and necrotic cell death. Similarly, 30 min incubation of testis with glyphosatealone (36 ppm) also increased (45)Ca(2+) uptake. These events were prevented by the antioxidants Trolox and ascorbic acid. Activated protein kinase C, phosphatidylinositol 3-kinase, and the mitogen-activated protein kinases such as ERK1/2 and p38MAPK play a role in eliciting Ca(2+) influx and cell death. Roundup decreased the levels of reduced glutathione (GSH) and increased the amounts of thiobarbituric acid-reactive species (TBARS) and protein carbonyls. Also, exposure to glyphosate-Roundup stimulated the activity of glutathione peroxidase, glutathione reductase, glutathione S-transferase, γ-glutamyltransferase, catalase, superoxide dismutase, and glucose-6-phosphate dehydrogenase, supporting downregulated GSH levels. Glyphosate has been described as an endocrine disruptor affecting the male reproductive system; however, the molecular basis of its toxicity remains to be clarified. We propose that Roundup toxicity, implicated in Ca(2+) overload, cell signaling misregulation, stress response of the endoplasmic reticulum, and/or depleted antioxidant defenses, could contribute to Sertoli cell disruption in spermatogenesis that could have an impact on male fertility.

KEYWORDS:

Calcium homeostasis; Cell death; Cell signaling; Free radicals; Glyphosate; Oxidative stress; Roundup; Sertoli cell

Free full text

Related citations

ELSEVIER OPEN ACCESS

Publication Types

Environ Toxicol Pharmacol. 2013 Sep;36(2):539-47. doi: 10.1016/j.etap.2013.06.001. Epub 2013 Jun 7.

DNA damage and oxidative stress modulatory effects of glyphosate-based herbicide in freshwater fish, Channa punctatus.

Nwani CD[1], Nagpure NS, Kumar R, Kushwaha B, Lakra WS.

Author information

Abstract

The present study was undertaken to evaluate the genotoxic and oxidative stress modulatory effects of commercial formulation of glyphosate-based herbicide (Roundup(®)) in freshwater fish Channa punctatus. Three sublethal test concentrations of the herbicide viz., SL-I (1/10th of LC50=~3.25mgL(-1)), SL-II (1/8th of LC50=~4.07mgL(-1)) and SL-III (1/5th of LC50=~6.51mgL(-1)) were calculated using 96-LC50 value and the test specimens were exposed to these concentrations. Blood and gill cells of the exposed specimens were sampled on day 1, 7, 14, 21, 28 and 35 to examine the DNA damage using comet assay and to assess the alteration in lipid peroxidation and antioxidant enzymes activities. The highest DNA damage was observed on day 14 at all test concentrations followed by gradual non-linear decline. Induction of oxidative stress in the blood and gill cells were evidenced by increased lipid peroxidation level, while antioxidants namely superoxide dismutase, catalase and glutathione reductase responded in a concentration-dependent manner. The results supported the integrated use of comet and antioxidant assays in determining the toxicity of water pollutants which could be used as part of monitoring programs.

KEYWORDS:

Antioxidant enzymes; Channa punctatus; Comet assay; DNA damage; Oxidative stress; Roundup(®)

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Food Chem Toxicol. 2013 Sep;59:129-36. doi: 10.1016/j.fct.2013.05.057. Epub 2013 Jun 10.

Glyphosate induces human breast cancer cells growth via estrogen receptors.

Thongprakaisang S[1], Thiantanawat A, Rangkadilok N, Suriyo T, Satayavivad J.

Author information

Abstract

Glyphosate is an active ingredient of the most widely used herbicide and it is believed to be less toxic than other pesticides. However, several recent studies showed its potential adverse health effects to humans as it may be an endocrine disruptor. This study focuses on the effects of pure glyphosate on estrogen receptors (ERs) mediated transcriptional activity and their expressions. Glyphosate exerted proliferative effects only in human hormone-dependent breast cancer, T47D cells, but not in hormone-independent breast cancer, MDA-MB231 cells, at 10^{-12} to 10^{-6}M in estrogen withdrawal condition. The proliferative concentrations of glyphosatethat induced the activation of estrogen response element (ERE) transcription activity were 5-13 fold of control in T47D-KBluc cells and this activation was inhibited by an estrogen antagonist, ICI 182780, indicating that the estrogenic activity of glyphosate was mediated via ERs. Furthermore, glyphosate also altered both ERα and β expression. These results indicated that low and environmentally relevant concentrations of glyphosatepossessed estrogenic activity. Glyphosate-based herbicides are widely used for soybean cultivation, and our results also found that there was an additive estrogenic effect between glyphosate and genistein, a phytoestrogen in soybeans. However, these additive effects of glyphosate contamination in soybeans need further animal study.

KEYWORDS:

Estrogenic effect; Genistein; Glyphosate; Human breast cancer; T47D; T47D-KBluc

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Environ Mol Mutagen. 2013 Jun;54(5):362-73. doi: 10.1002/em.21775. Epub 2013 Apr 26.

Toxic, cytotoxic, and genotoxic effects of a glyphosate formulation (Roundup®SL-Cosmoflux®411F) in the direct-developing frog Eleutherodactylus johnstonei.

Meza-Joya FL[1], Ramírez-Pinilla MP, Fuentes-Lorenzo JL.

Author information

Abstract

The aerial spraying of glyphosate formulations in Colombia to eradicate illegal crops has generated great concern about its possible impact on nontarget organisms, particularly amphibians. This study evaluated the toxic, cytotoxic, and genotoxic effects of a glyphosate formulation (Roundup®SL-Cosmoflux®411F) in the direct-developing frog Eleutherodactylus johnstonei by estimating the median lethal application rate (LC50), median hemolytic application rate (HD50), and extent of DNA damage using the in vitro and in vivo Comet assays. Toxicity results indicated that the application rate [37.4 µg acid equivalent (a.e.)/cm(2)] equivalent to that used in aerial spraying (3.74 kg a.e./ha) is not lethal in male and female adult frogs, whereas neonates are highly sensitive. Glyphosate formulation at application rates above 5.4 µg a.e./cm(2) (in vivo) and concentrations above 95 µg a.e./mL (in vitro) showed clear evidence of cytotoxicity. In vivo and in vitro exposure of E. johnstonei erythrocytes to the glyphosate formulation induced DNA breaks in a dose-dependent manner with statistically significant values ($P < 0.05$) at all doses tested. DNA damage initially increased with the duration of exposure and then decreased, suggesting that DNA repair events were occurring during in vivo and in vitro exposures. These results are discussed from the perspective of possible ecotoxicological risks to anuran species from exposure to glyphosate formulation.

Related citations

Full Text Online Wiley Online Library

Publication Types, MeSH Terms, Substances

Toxicol Sci. 2013 Jun;133(2):289-97. doi: 10.1093/toxsci/kft076. Epub 2013 Mar 27.

Specific pesticide-dependent increases in α-synuclein levels in human neuroblastoma (SH-SY5Y) and melanoma (SK-MEL-2) cell lines.

Chorfa A[1], Bétemps D, Morignat E, Lazizzera C, Hogeveen K, Andrieu T, Baron T.

Author information

Abstract

Epidemiological studies indicate a role of genetic and environmental factors in Parkinson's disease involving alterations of the neuronal α-synuclein (α-syn) protein. In particular, a relationship between Parkinson's disease and occupational exposure to pesticides has been repeatedly suggested. Our objective was to precisely assess changes in α-syn levels in human neuroblastoma (SH-SY5Y) and melanoma (SK-MEL-2) cell lines following acute exposure to pesticides (rotenone, paraquat, maneb, and glyphosate) using Western blot and flow cytometry. These human cell lines express α-syn endogenously, and overexpression of α-syn (wild type or mutated A53T) can be obtained following recombinant adenoviral transduction. We found that endogenous α-syn levels in the SH-SY5Y neuroblastoma cell line were markedly increased by paraquat, and to a lesser extent by rotenone and maneb, but not by glyphosate. Rotenone also clearly increased endogenous α-syn levels in the SK-MEL-2 melanoma cell line. In the SH-SY5Y cell line, similar differences were observed in the α-syn adenovirus-transduced cells, with a higher increase of the A53T mutated protein. Paraquat markedly increased α-syn in the SK-MEL-2 adenovirus-transduced cell line, similarly for the wild-type or A53T proteins. The observed differences in the propensities of pesticides to increase α-syn levels are in agreement with numerous reports that indicate a potential role of exposure to certain pesticides in the development of Parkinson's disease. Our data support the hypothesis that pesticides can trigger some molecular events involved in this disease and also in malignant melanoma that consistently shows a significant but still unexplained association with Parkinson's disease.

KEYWORDS:

Parkinson’s disease; malignant melanona.; neuroblastoma; pesticides; α-synuclein

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Related citations

Publication Types, MeSH Terms, Substances

Ecotoxicol Environ Saf. 2013 May;91:129-38. doi: 10.1016/j.ecoenv.2013.01.022. Epub 2013 Mar 7.

Pesticide-induced decrease in rat testicular steroidogenesis is differentially prevented by lipoate and tocopherol.

Astiz M[1], Hurtado de Catalfo GE, García MN, Galletti SM, Errecalde AL, de Alaniz MJ, Marra CA.

Author information

Abstract

We have previously demonstrated that the sub-chronic administration of low doses of Toc or α-Toc,glyphosate and zineb to rats (i.p. 1/250 LD50, three times a week for 5 weeks) provoked severe oxidative stress (OS) in testicles. These effects were also reflected in plasma. Lipoic acid (LA) and α-tocopherol are considered as antioxidants due to their ability to neutralize reactive oxygenated species (ROS) and reset endogenous antioxidant levels. To investigate the possible protective effect on reproductive function, LA and Toc (i.p. 25, 50 and 100mg/kg) were administered simultaneously with the pesticide mixture (PM) for 5 weeks. Both drugs prevented OS and the damage to proteins and lipids caused by PM in a dose-dependent manner. The PM-induced increase levels of prostaglandins E2 and F2α was completely restored by LA but not by Toc. Similarly, only LA was able to restore the inhibition of testosterone production, the decrease of 3β- and 17β-hydroxysteroid dehydrogenases activities, and the elevation of gonatropins (FSH and LH) levels produced by PM. Furthermore, LA was more efficient than Toc in normalizing the histological alterations produced by PM administration, suggesting that pesticides act though other mechanisms that generate oxidative stress. In our experimental model LA displayed a higher protective role against pesticide-induced damage than that observed by Toc administration. Our results suggest that LA administration is a promising therapeutic strategy for coping with disorders suspected to be caused by OS generators - such as pesticides - in malereproductive system.

Aquat Toxicol. 2013 May 15;132-133:1-8. doi: 10.1016/j.aquatox.2013.01.016. Epub 2013 Feb 8.

Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (Euflictis cyanophlyctis) in the presence and absence of predator stress.

Yadav SS[1], Giri S, Singha U, Boro F, Giri A.

Author information

Abstract

Glyphosate, a post emergent herbicide, has become the backbone of no-till agriculture and is considered safe for animals. However, the impact of glyphosate on non-target organisms, especially on amphibians, is the subject of major concern and debate in recent times. We examined the toxic and genotoxic effects ofRoundup, a commercial formulation of glyphosate, in the tadpoles of the Indian skittering frog (Euflictis cyanophlyctis). Roundup at different concentrations (0, 1, 2, 3, 4 and 8mg acid equivalent (ae)/L), tested in a 2×6 factorial design in the presence and absence of predator stress, induced concentration-dependent lethality in tadpoles. The 96-h LC50 for Roundup in the absence and presence of predator stress were 3.76mgae/L and 3.39mgae/L, respectively. The 10-day LC50 value for Roundup was significantly lower, 2.12mgae/L and 1.91mgae/L in the absence and presence of predator stress, respectively. Lower concentrations of Roundup (1, 2 and 3mgae/L) induced the formation of micronuclei (MN) in the erythrocytes of tadpoles at 24-h ($F_{3,56}=10.286$, $p<0.001$), 48-h ($F_{3,56}=48.255$, $p<0.001$), 72-h ($F_{3,56}=118.933$, $p<0.001$) and 96-h ($F_{3,56}=85.414$, $p<0.001$) in a concentration-dependent manner. Presence of predator stress apparently increased the toxicity
and genotoxicity of Roundup; but these effects were not statistically significant. These findings suggest that Roundup at environmentally relevant concentrations has lethal andgenotoxic impact on E. cyanophlyctis; which may have long-term fitness consequence to the species.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Environ Sci Pollut Res Int. 2013 Aug;20(8):5603-14. doi: 10.1007/s11356-013-1568-2. Epub 2013 Feb 27.

Acetylcholinesterase in honey bees (Apis mellifera) exposed to neonicotinoids, atrazine and glyphosate: laboratory and field experiments.

Boily M[1], Sarrasin B, Deblois C, Aras P, Chagnon M.

Author information

Abstract

In Québec, as observed globally, abnormally high honey bee mortality rates have been reported recently. Several potential contributing factors have been identified, and exposure to pesticides is of increasing concern. In maize fields, foraging bees are exposed to residual concentrations of insecticides such as neonicotinoids used for seed coating. Highly toxic to bees, neonicotinoids are also reported to increase AChE activity in other invertebrates exposed to sub-lethal doses. The purpose of this study was therefore to test if the honey bee's AChE activity could be altered by neonicotinoid compounds and to explore possible effects of other common products used in maize fields: atrazine and glyphosate. One week prior to pollen shedding, beehives were placed near three different field types: certified organically grown maize, conventionally grown maize or non-cultivated. At the same time, caged bees were exposed to increasing sub-lethal doses of neonicotinoid insecticides (imidacloprid and clothianidin) and herbicides (atrazine and glyphosate) under controlled conditions. While increased AChE activity was found in all fields after 2 weeks of exposure, beesclose to conventional maize crops showed values higher than those in both organic maize fields and non-cultivated areas. In caged bees, AChE activity increased in response to neonicotinoids, and a slight decrease was observed by glyphosate. These results are discussed with regard to AChE activity as a potential biomarker of exposure for neonicotinoids.

Related citations

Publication Types, MeSH Terms, Substances

Arch Environ Contam Toxicol. 2013 Jul;65(1):98-104. doi: 10.1007/s00244-013-9873-9. Epub 2013 Feb 2.

Effects of water contamination on site selection by amphibians: experiences from an arena approach with European frogs and newts.

Wagner N[1], Lötters S.

Author information

Abstract

Pesticide residues in breeding ponds can cause avoidance by at least some amphibian species. So far, outdoor experiments have been performed only with artificial pools in areas where the focus species usually occur and new colonization has been observed. Results of this kind of study are potentially influenced by natural disturbances and therefore are of limited comparability. We used an easily manufactured and standardizable arena approach, in which animals in reproductive condition for some hours had a choice among pools with different concentrations of a contaminant. Because there has been much debate on the potential environmental impacts of glyphosate-based herbicides, we investigated the impact of glyphosateisopropylamine salt (GLY-IS), Roundup LB PLUS (RU-LB-PLUS), and glyphosate's main metabolite aminomethylphosphonic acid (AMPA) on individual residence time in water. The following European amphibian species were tested: Common frog (Rana temporaria), Palmate newt (Lissotriton helveticus), and Alpine newt (Ichthyosaura alpestris). The residence time in water was not significantly affected by concentrations below or slightly above the European Environmental Quality Standards for AMPA or the German "worst-case" expected environmental concentrations for GLY-IS and RU-LB-PLUS. Occasionally, microclimatic cofactors (nightly minimum ground temperature, water temperature) apparently influenced the residence time. The major drawback of such quick behavior studies is that results can only be transferred to perception and avoidance of contaminated water but not easily to site selection by amphibians. For example, testing oviposition site selection requires more natural water bodies and more time. Hence, to develop a standard procedure in risk assessment, an intermediate design between an arena approach, as presented here, and previously performed field studies should be tested.

Related citations

Publication Types, MeSH Terms, Substances

Ecotoxicol Environ Saf. 2013 Mar;89:166-73. doi: 10.1016/j.ecoenv.2012.11.028. Epub 2012 Dec 25.

Evaluation of the genotoxic and cytotoxic effects of glyphosate-based herbicides in the ten spotted live-bearer fish Cnesterodon decemmaculatus (Jenyns, 1842).

Vera-Candioti J[1], Soloneski S, Larramendy ML.

Author information

Abstract

Mortality, genotoxicity, and cytotoxicity of the 48% glyphosate-based formulations Panzer and Credit(®) were evaluated on Cnesterodon decemmaculatus (Jenyns, 1842) (Pisces, Poeciliidae) under laboratory conditions. Induction of micronuclei (MN) and alterations in the erythrocytes:erythroblasts ratio were employed as end points for genotoxicity and cytotoxicity, respectively. For Panzer(®), mean values of 16.70 and 15.68 mg/L were determined for LC(50) at 24 and 96 h, respectively, and these concentrations reached mean values of 98.50 and 91.73 mg/L for Credit(®). LC(50) values decreased as a negative linear function of Panzer(®) exposure time within the 0-96 h period, but not for Credit(®). LC(50) values indicated that the fish were more sensitive to Panzer(®) than to Credit(®). Both 3.9 and 7.8 mg/L of Panzer(®) increased MN frequency at 48 and 96 h of treatment. When fish were exposed to Credit(®), an increased frequency of MN over control values was found after 96 h for all concentrations assayed, but not after 48 h. No cellular cytotoxicity was found after Panzer(®) and Credit(®) treatment, regardless of both the concentration and the sampling time. Furthermore, our results demonstrated that Panzer(®) and Credit(®) should be considered as glyphosate-based commercial formulations with genotoxic but not cytotoxic effect properties.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

PLoS One. 2012;7(12):e50643. doi: 10.1371/journal.pone.0050643. Epub 2012 Dec 4.

Annual glyphosate treatments alter growth of unaffected bentgrass (Agrostis) weeds and plant community composition.

Ahrens CW[1], Auer CA.

Author information

Abstract

Herbicide resistance is becoming more common in weed ecotypes and crop species including turfgrasses, but current gaps in knowledge limit predictive ecological risk assessments and risk management plans. This project examined the effect of annual glyphosate applications on the vegetative growth and reproductivepotential of two weedy bentgrasses, creeping bentgrass (CB) and redtop (RT), where the glyphosateresistance (GR) trait was mimicked by covering the bentgrass plants during glyphosate application. Five field plots were studied in habitats commonly inhabited by weedy bentgrasses including an agricultural hayfield, natural meadow, and wasteland. Results showed that annual glyphosate treatment improved bentgrass survivorship, vegetative growth, and reproductive potential compared with bentgrass in unsprayed subplots. In the second year of growth, RT plants had an 86-fold increase in flower number in glyphosate-treated subplots versus controls, while CB plants had a 20-fold increase. At the end of the three year study, plant community composition had changed in glyphosate-treated subplots in hayfield and meadow plots compared to controls. Soils in subplots receiving glyphosate had higher nitrate concentrations than controls. This is the first study to mimic the GR trait in bentgrass plants with the goal of quantifying bentgrass response to glyphosate selection pressure and understanding the impacts on surrounding plant communities.

Ecotoxicology. 2013 Mar;22(2):251-62. doi: 10.1007/s10646-012-1021-1. Epub 2012 Dec 6.

Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in Daphnia magna.

Cuhra M[1], Traavik T, Bøhn T.

Author information

Abstract

Low levels of glyphosate based herbicide induced significant negative effects on the aquatic invertebrate Daphnia magna. Glyphosate herbicides such as brands of Roundup, are known to be toxic to daphnids. However, published findings on acute toxicity show significant discrepancies and variation across several orders of magnitude. To test the acute effects of both glyphosate and a commercial formulation of Roundup(hereafter Roundup), we conducted a series of exposure experiments with different clones and age-classes of D. magna. The results demonstrated EC(50) (48) values in the low ppm-range for Roundup as well as for the active ingredient (a.i.) isopropylamine salt of glyphosate (glyphosate IPA) alone. Roundup showed slightly lower acute toxicity than glyphosate IPA alone, i.e. EC(50) values of 3.7-10.6 mg a.i./l, as compared to 1.4-7.2 mg a.i./l for glyphosate IPA. However, in chronic toxicity tests spanning the whole life-cycle, Roundupwas more toxic. D. magna was exposed to sublethal nominal concentrations of 0.05, 0.15, 0.45, 1.35 and 4.05 mg a.i./l for 55 days. Significant reduction of juvenile size was observed even in the lowest test concentrations of 0.05 mg a.i./l, for both glyphosate and Roundup. At 0.45 mg a.i./l, growth, fecundity and abortion rate was affected, but only in animals exposed to Roundup. At 1.35 and 4.05 mg a.i./l of bothglyphosate and Roundup, significant negative effects were seen on most tested parameters, including mortality. D. magna was adversely affected by a near 100 % abortion rate of eggs and embryonic stages at 1.35 mg a.i./l of Roundup. The results indicate that aquatic invertebrate ecology can be adversely affected by relevant ambient concentrations of this major herbicide. We conclude that glyphosate and Roundup toxicity to aquatic invertebrates have been underestimated and that current European Commission and US EPA toxicity classification of these chemicals need to be revised.

J Toxicol Environ Health B Crit Rev. 2012;15(7):433-7; author reply 438-40. doi: 10.1080/10937404.2012.736857.

Letter to the editor: developmental and reproductive outcomes of roundup andglyphosate in humans and animals.

Defarge N, Mesnage R, Gress S, Séralini GE.

Comment on

- Developmental and reproductive outcomes in humans and animals after glyphosate exposure: a critical analysis. [J Toxicol Environ Health B Crit Rev. 2012]

Related citations

View full text

Publication Types, MeSH Terms, Substances

Toxicol In Vitro. 2013 Feb;27(1):191-7. doi: 10.1016/j.tiv.2012.09.021. Epub 2012 Oct 23.

Mixtures of glyphosate and surfactant TN20 accelerate cell death via mitochondrialdamage-induced apoptosis and necrosis.

Kim YH[1], Hong JR, Gil HW, Song HY, Hong SY.

Author information

Abstract

Glyphosate, a common herbicide, is not toxic under normal exposure circumstances. However, this chemical, when combined with a surfactant, is cytotoxic. In this study, the mechanism of the additive effect ofglyphosate and TN-20, a common surfactant in glyphosate herbicides, was investigated. After exposure of rat H9c2 cells to glyphosate and TN-20 mixtures, following assays were performed: flow cytometry to determine the proportion of cells that underwent apoptosis and necrosis; western blotting to determine expression ofmitochondrial proteins (Bcl-2 and Bax); immunological methods to evaluate translocation of cytochrome C; luminometric measurements to determine activity of caspases 3/7 and 9; and tetramethyl rhodamine methyl ester assay to measure mitochondrial membrane potentials. Bcl-1 intensity decreased while Bax intensity increased with exposure to increasing TN-20 and/or glyphosate concentrations. Caspase activity increased and mitochondrial membrane potential decreased only when the cells were exposed to a mixture of both TN-20 and glyphosate, but not after exposure to either one of these compounds. The results support the possibility that mixtures of glyphosate and TN-20 aggravate mitochondrial damage and induce apoptosis and necrosis. Throughout this process, TN-20 seems to disrupt the integrity of the cellular barrier to glyphosateuptake, promoting glyphosate-mediated toxicity.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Pol Merkur Lekarski. 2012 Aug;33(194):59-63.

[Genetically modified food--great unknown].

[Article in Polish]

Cichosz G[1], Wiackowski SK.

Author information

Abstract

Genetically modified food (GMF) creates evident threat to consumers' health. In spite of assurances of biotechnologists, DNA of transgenic plants is instable, so, synthesis of foreign, allergenic proteins is possible. Due to high trypsin inhibitor content the GMF is digested much more slowly what, alike Bt toxin presence, increases probability of alimentary canal diseases. Next threats are bound to the presence of fitoestrogens and residues of Roundup pesticide, that can diminish reproductiveness; and even lead to cancerogenic transformation through disturbance of human hormonal metabolism. In spite of food producers and distributors assurances that food made of GMF raw materials is marked, de facto consumers have no choice. Moreover, along the food law products containing less than 0.9% of GMF protein are not included into genetically modified food.

Related citations

Publication Types, MeSH Terms, Substances

Toxicology. 2013 Nov 16;313(2-3):122-8. doi: 10.1016/j.tox.2012.09.006. Epub 2012 Sep 21.

Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity.

Mesnage R[1], Bernay B, Séralini GE.

Author information

Abstract

Pesticides are always used in formulations as mixtures of an active principle with adjuvants. Glyphosate, the active ingredient of the major pesticide in the world, is an herbicide supposed to be specific on plant metabolism. Its adjuvants are generally considered as inert diluents. Since side effects for all these compounds have been claimed, we studied potential active principles for toxicity on human cells for 9glyphosate-based formulations. For this we detailed their compositions and toxicities, and as controls we used a major adjuvant (the polyethoxylated tallowamine POE-15), glyphosate alone, and a total formulation without glyphosate. This was performed after 24h exposures on hepatic (HepG2), embryonic (HEK293) and placental (JEG3) cell lines. We measured mitochondrial activities, membrane degradations, and caspases 3/7 activities. The compositions in adjuvants were analyzed by mass spectrometry. Here we demonstrate that all formulations are more toxic than glyphosate, and we separated experimentally three groups of formulations differentially toxic according to their concentrations in ethoxylated adjuvants. Among them, POE-15 clearly appears to be the most toxic principle against human cells, even if others are not excluded. It begins to be active with negative dose-dependent effects on cellular respiration and membrane integrity between 1 and 3ppm, at environmental/occupational doses. We demonstrate in addition that POE-15 induces necrosis when its first micellization process occurs, by contrast to glyphosate which is known to promote endocrine disrupting effects after entering cells. Altogether, these results challenge the establishment of guidance values such as the acceptable daily intake of glyphosate, when these are mostly based on a long term in vivo test of glyphosate alone. Since pesticides are always used with adjuvants that could change their toxicity, the necessity to assess their whole formulations as mixtures becomes obvious. This challenges the concept of active principle of pesticides for non-target species.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Séralini et al. Environmental Sciences Europe 2014, 26:14
http://www.enveurope.com/content/26/1/14

Environmental Sciences Europe
a SpringerOpen Journal

RESEARCH Open Access

Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize

Gilles-Eric Séralini[1*], Emilie Clair[1], Robin Mesnage[1], Steeve Gress[1], Nicolas Defarge[1], Manuela Malatesta[2], Didier Hennequin[3] and Joël Spiroux de Vendômois[1]

Abstract

Background: The health effects of a Roundup-tolerant NK603 genetically modified (GM) maize (from 11% in the diet), cultivated with or without Roundup application and Roundup alone (from 0.1 ppb of the full pesticide containing glyphosate and adjuvants) in drinking water, were evaluated for 2 years in rats. This study constitutes a follow-up investigation of a 90-day feeding study conducted by Monsanto in order to obtain commercial release of this GMO, employing the same rat strain and analyzing biochemical parameters on the same number of animals per group as our investigation. Our research represents the first chronic study on these substances, in which all observations including tumors are reported chronologically. Thus, it was not designed as a carcinogenicity study. We report the major findings with 34 organs observed and 56 parameters analyzed at 11 time points for most organs.

Results: Biochemical analyses confirmed very significant chronic kidney deficiencies, for all treatments and both sexes; 76% of the altered parameters were kidney-related. In treated males, liver congestions and necrosis were 2.5 to 5.5 times higher. Marked and severe nephropathies were also generally 1.3 to 2.3 times greater. In females, all treatment groups showed a two- to threefold increase in mortality, and deaths were earlier. This difference was also evident in three male groups fed with GM maize. All results were hormone- and sex-dependent, and the pathological profiles were comparable. Females developed large mammary tumors more frequently and before controls; the pituitary was the second most disabled organ; the sex hormonal balance was modified by consumption of GM maize and Roundup treatments. Males presented up to four times more large palpable tumors starting 600 days earlier than in the control group, in which only one tumor was noted. These results may be explained by not only the non-linear endocrine-disrupting effects of Roundup but also by the overexpression of the EPSPS transgene or other mutational effects in the GM maize and their metabolic consequences.

Conclusion: Our findings imply that long-term (2 year) feeding trials need to be conducted to thoroughly evaluate the safety of GM foods and pesticides in their full commercial formulations.

Keywords: Genetically modified; GMO; Roundup; NK603; Rat; Glyphosate-based herbicides; Endocrine disruption

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Environ Monit Assess. 2013 Apr;185(4):3201-7. doi: 10.1007/s10661-012-2783-x. Epub 2012 Jul 22.

Genotoxic effects of the herbicide Roundup(®) in the fish Corydoras paleatus (Jenyns 1842) after short-term, environmentally low concentration exposure.

de Castilhos Ghisi N[1], Cestari MM.

Author information

Abstract

The glyphosate-based herbicide, Roundup(®), is one of the most used pesticides worldwide. In concert with the advent of transgenic crops resistant to glyphosate, the use of this pesticide has led to an increase in agricultural yields. The objective of this study was to evaluate the genotoxic effect that the herbicideRoundup(®) (at a concentration of 6.67 µg/L, corresponding to 3.20 µg/L glyphosate) can have on the fish Corydoras paleatus. Treatment groups were exposed for 3, 6, and 9 days, and effects were analyzed using the piscine micronucleus test (PMT) and comet assay. A group subjected to filtered water only was used as a negative control. The PMT did not show differences between the control and exposed groups for any of the treatment times. In contrast, the comet assay showed a high rate of DNA damage in group exposed toRoundup(®) for all treatment times, both for blood and hepatic cells. We conclude that for the low concentration used in this research, the herbicide shows potential genotoxic effects. Future research will be important in evaluating the effects of this substance, whose presence in the environment is ever-increasing.

Ecotoxicology. 2012 Nov;21(8):2113-22. doi: 10.1007/s10646-012-0963-7. Epub 2012 Jun 19.

Pesticide application to agricultural fields: effects on the reproduction and avoidance behaviour of Folsomia candida and Eisenia andrei.

Santos MJ[1], Ferreira MF, Cachada A, Duarte AC, Sousa JP.

Author information

Abstract

The objective of this work was to assess the impact of pesticide application to non-target soil organisms simulating what happens following pesticide application in agricultural fields and thus obtaining higher realism on results obtained. For that purpose, three commercial formulations containing the insecticides chlorpyrifos and endosulfan and the herbicide glyphosate were applied to a Mediterranean agricultural field. The soil was collected after spraying and dilution series were prepared with untreated soil to determine the impact of the pesticides on the avoidance behaviour and reproduction of the earthworm Eisenia andrei and the collembolan Folsomia candida. A significant avoidance was observed at the recommended field dose in case of endosulfan by earthworms (60 %) and in case of chlorpyrifos by collembolans (64 %). In addition, both insecticides affected the number of juveniles produced by the earthworms (EC(50) were below the recommended field dose). Glyphosate did not seem to affect either earthworms or collembolans in the recommended field dose. Folsomia candida was more sensitive to pesticide application than Eisenia andrei, what was corroborated by the EC(50) and LC(50) values. In conclusion, insecticides may affect the structure of the soil community by reducing the survival of collembolans and the reproductive capacity of collembolans and earthworms.

22711551

Related citations

Publication Types, MeSH Terms, Substances

Environ Toxicol. 2014 Jun;29(6):612-20. doi: 10.1002/tox.21787. Epub 2012 May 30.

Genotoxic effects of glyphosate or paraquat on earthworm coelomocytes.

Muangphra P[1], Kwankua W, Gooneratne R.

Author information

Abstract

The potential genotoxicity (nuclear anomalies, damage to single-strand DNA) and pinocytic adherence activity of two (glyphosate-based and paraquat-based) commercial herbicides to earthworm coelomocytes (immune cells in the coelomic cavity) were assessed. Coelomocytes were extracted from earthworms (Pheretima peguana) exposed to concentrations <LC50 of glyphosate-based or paraquat-based herbicides on filter paper for 48 h. Three assays were performed: Micronucleus (light microscopy count of micronuclei, binuclei, and trinuclei), Comet (epifluorescent microscope and LUCIA image analyzer measure of tail DNA %, tail length, and tail moment), and Neutral Red (to detect phagocytic or pinocytic activity). The LC50 value for paraquat was 65-fold lower than for glyphosate indicating that paraquat was far more acutely toxic to P. peguana. There were significant (P < 0.05) differences from the control group in total coelomocyte micronuclei, binuclei, and trinuclei frequencies of earthworms exposed to glyphosate at 25 × 10(-1) (10(-3) LC50) and paraquat at 39 × 10(-5) (10(-4) LC50) μg cm(-2) filter paper. In earthworms exposed to glyphosate, no differences in tail DNA%, tail length, and tail moment of coelomocytes were detected. In contrast, for paraquat at 10(-1) LC50 concentration, there were significant (P < 0.05) differences between tail DNA % and tail length, and at LC50 concentration, tail moment was also significantly different when compared with controls. A decline in pinocytic adherence activity in coelomocytes occurred on exposure to glyphosate or paraquat at 10(-3) LC50 concentration. This study showed that, at concentrations well below field application rates, paraquat induces both clastogenic and aneugenic effects on earthworm coelomocytes whereas glyphosate causes only aneugenic effects and therefore does not pose a risk of gene mutation in this earthworm.

KEYWORDS:

Related citations

Full Text Online Wiley Online Library

Publication Types, MeSH Terms, Substances

Mol Ecol. 2012 Oct;21(19):4672-80. doi: 10.1111/j.1365-294X.2012.05627.x. Epub 2012 May 24.

Crossing the divide: gene flow produces intergeneric hybrid in feral transgenic creeping bentgrass population.

Zapiola ML[1], Mallory-Smith CA.

Author information

Abstract

Gene flow is the most frequently expressed public concern related to the deregulation of transgenic events (Snow 2002; Ellstrand 2003). However, assessing the potential for transgene escape is complex because it depends on the opportunities for unintended gene flow, and establishment and persistence of the transgene in the environment (Warwick et al. 2008). Creeping bentgrass (Agrostis stolonifera L.), a turfgrass species widely used on golf courses, has been genetically engineered to be resistant to glyphosate, a nonselective herbicide. Outcrossing species, such as creeping bentgrass (CB), which have several compatible species, have greater chances for gene escape and spontaneous hybridization (i.e. natural, unassisted sexual reproduction between taxa in the field), which challenges transgene containment. Several authors have emphasized the need for evidence of spontaneous hybridization to infer the potential for gene flow (Armstrong et al. 2005). Here we report that a transgenic intergeneric hybrid has been produced as result of spontaneous hybridization of a feral-regulated transgenic pollen receptor (CB) and a nontransgenic pollen donor (rabbitfoot grass, RF, Polypogon monspeliensis (L.) Desf.). We identified an off-type transgenic seedling and confirmed it to be CB × RF intergeneric hybrid. This first report of a transgenic intergeneric hybrid produced in situ with a regulated transgenic event demonstrates the importance of considering all possible avenues for transgene spread at the landscape level before planting a regulated transgenic crop in the field. Spontaneous hybridization adds a level of complexity to transgene monitoring, containment, mitigation and remediation programmes.

Comment in

- Illegal gene flow from transgenic creeping bentgrass: the saga continues. [Mol Ecol. 2012]

Related citations

Full Text Online Wiley Online Library

Publication Types, MeSH Terms, Substances, Secondary Source ID

J Toxicol Environ Health B Crit Rev. 2012;15(4):233-5; author reply 236-7. doi: 10.1080/10937404.2012.672149.

Letter to the editor: toxicity of Roundup and glyphosate.

Bellé R, Marc J, Morales J, Cormier P, Mulner-Lorillon O.

Comment on

- Developmental and reproductive outcomes in humans and animals after glyphosate exposure: a critical analysis. [J Toxicol Environ Health B Crit Rev. 2012]

22571219

Related citations

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Publication Types, MeSH Terms, Substances

Ecotoxicology. 2012 Jul;21(5):1381-90. doi: 10.1007/s10646-012-0892-5. Epub 2012 Apr 8.

Differential genotoxicity of Roundup(®) formulation and its constituents in blood cells of fish (Anguilla anguilla): considerations on chemical interactions and DNA damaging mechanisms.

Guilherme S[1], Santos MA, Barroso C, Gaivão I, Pacheco M.

Author information

Abstract

It has been widely recognized that pesticides represent a potential threat in aquatic ecosystems. However, the knowledge on the genotoxicity of pesticides to fish is still limited. Moreover, genotoxic studies have been almost exclusively focused on the active ingredients, whereas the effect of adjuvants is frequently ignored. Hence, the present study addressed the herbicide Roundup®, evaluating the relative contribution of the active ingredient (glyphosate) and the surfactant (polyethoxylated amine; POEA) to the genotoxicity of the commercial formulation on Anguilla anguilla. Fish were exposed to equivalent concentrations of Roundup® (58, 116 μg L^{-1}), glyphosate (17.9, 35.7 μg L^{-1}) and POEA (9.3, 18.6 μg L^{-1}), during 1 and 3 days. The comet assay was applied to blood cells, either as the standard procedure, or with an extra step involving DNA lesion-specific repair enzymes in an attempt to clarify DNA damaging mechanisms. The results confirmed thegenotoxicity of Roundup®, also demonstrating the genotoxic potential of glyphosate and POEA individually. Though both components contributed to the overall genotoxicity of the pesticide formulation, the sum of their individual effects was never observed, pointing out an antagonistic interaction. Although POEA is far from being considered biologically inert, it did not increase the risk associated to glyphosate when the two were combined. The analysis of oxidatively induced breaks suggested that oxidation of DNA bases was not a dominant mechanism of damage. The present findings highlighted the risk posed to fish populations by the assessed chemicals, jointly or individually, emphasizing the need to define regulatory thresholds for all the formulation components and recommending, in particular, the revision of the hazard classification of POEA.

Related citations

SpringerLink FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Environ Toxicol Pharmacol. 2012 Sep;34(2):144-53. doi: 10.1016/j.etap.2012.02.010. Epub 2012 Mar 15.

A step further toward glyphosate-induced epidermal cell death: involvement ofmitochondrial and oxidative mechanisms.

Heu C[1], Elie-Caille C, Mougey V, Launay S, Nicod L.

Author information

Abstract

A deregulation of programmed cell death mechanisms in human epidermis leads to skin pathologies. We previously showed that glyphosate, an extensively used herbicide, provoked cytotoxic effects on cultured human keratinocytes, affecting their antioxidant capacities and impairing morphological and functional cell characteristics. The aim of the present study, carried out on the human epidermal cell line HaCaT, was to examine the part of apoptosis plays in the cytotoxic effects of glyphosate and the intracellular mechanisms involved in the apoptotic events. We have conducted different incubation periods to reveal the specific events in glyphosate-induced cell death. We observed an increase in the number of early apoptotic cells at a low cytotoxicity level (15%), and then, a decrease, in favor of late apoptotic and necrotic cell rates for more severe cytotoxicity conditions. At the same time, we showed that the glyphosate-induced mitochondrialmembrane potential disruption could be a cause of apoptosis in keratinocyte cultures.

Related citations

ELSEVIER FULL-TEXT ARTICLE

MeSH Terms, Substances

Ecotoxicol Environ Saf. 2012 Jun;80:372-80. doi: 10.1016/j.ecoenv.2012.04.006. Epub 2012 Apr 19.

Effects of herbicides and the chytrid fungus Batrachochytrium dendrobatidis on the health of post-metamorphic northern leopard frogs (Lithobates pipiens).

Paetow LJ[1], Daniel McLaughlin J, Cue RI, Pauli BD, Marcogliese DJ.

Author information

Abstract

Effects of exposure to contaminants such as pesticides along with exposure to pathogens have been listed as two major contributors to the global crisis of declining amphibian populations. These two factors have also been linked in explanations of the causes of these population declines. We conducted a combined exposure experiment to test the hypothesis that exposure to two agricultural herbicides would increase the susceptibility of post-metamorphic northern leopard frogs (Lithobates pipiens) to the amphibian fungal pathogen Batrachochytrium dendrobatidis (Bd). We assessed the independent and interactive effects of these exposures on the health and survival of the frogs. Wild-caught frogs underwent a 21-day exposure to a nominal concentration of either 2.1 µg/L atrazine (Aatrex(®) Liquid 480) or 100 µg a.e./L glyphosate(Roundup(®) Original), followed by Bd, and then were observed until 94 days post-initial exposure to the herbicides. Actual levels of atrazine were between 4.28 ± 0.04 µg/L and 1.70 ± 0.26 µg/L while glyphosatedegraded from 100 µg a.e./L to approximately 7 µg a.e./L within 6 days of initial exposure to the herbicides. Compared to controls, the glyphosate formulation reduced the snout-vent length of frogs during the pesticide exposure (at Day 21), and the atrazine formulation reduced gain in mass up to Day 94. No treatment affected survival, splenosomatic or hepatosomatic indices, the densities and sizes of hepatic and splenic melanomacrophage aggregates, the density and size of hepatic granulomas, proportions of circulating leucocytes, the ratio of neutrophils to lymphocytes, or the ratio of leucocytes to erythrocytes. Histological assessment of samples collected at Day 94 revealed no evidence of Bd infection in any Bd-exposed frogs, while real-time PCR detected only one case of light infection in a single atrazine- and Bd-exposed frog. Frogs exposed to Bd shed their skin significantly more frequently than Bd-unexposed frogs, which may have helped them resist or clear infection, and could explain why no interaction between the herbicides and Bd was detected. The results suggest that these frogs were resistant to Bd infection and that pre-exposure to the herbicides did not alter this resistance. The effects seen on the growth following herbicide exposure is a concern, as reduced growth can lower the reproductive success and survival of the amphibians.

Toxicol Sci. 2012 Jun;127(2):391-402. doi: 10.1093/toxsci/kfs121. Epub 2012 Mar 29.

BLTK1 murine Leydig cells: a novel steroidogenic model for evaluating the effects of reproductive and developmental toxicants.

Forgacs AL[1], Ding Q, Jaremba RG, Huhtaniemi IT, Rahman NA, Zacharewski TR.

Author information

Abstract

Leydig cells are the primary site of androgen biosynthesis in males. Several environmental toxicants target steroidogenesis resulting in both developmental and reproductive effects including testicular dysgenesis syndrome. The aim of this study was to evaluate the effect of several structurally diverse endocrine disrupting compounds (EDCs) on steroidogenesis in a novel BLTK1 murine Leydig cell model. We demonstrate that BLTK1 cells possess a fully functional steroidogenic pathway that produces low basal levels of testosterone (T) and express all the necessary steroidogenic enzymes including Star, Cyp11a1, Cyp17a1, Hsd3b1, Hsd17b3, and Srd5a1. Recombinant human chorionic gonadotropin (rhCG) and forskolin (FSK) elicited concentration- and time-dependent induction of 3',5'-cyclic adenosine monophosphate, progesterone (P), and T, as well as the differential expression of Star, Hsd3b6, Hsd17b3, and Srd5a1 messenger RNA levels. The evaluation of several structurally diverse male reproductive toxicants including 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), atrazine, prochloraz, triclosan, monoethylhexyl phthalate (MEHP), glyphosate, and RDX in BLTK1 cells suggests different modes of action perturb steroidogenesis. For example, prochloraz and triclosan antifungals reduced rhCG induction of T, consistent with published in vivo data but did not alter basal T levels. In contrast, atrazine and MEHP elicited modest induction of basal T but antagonized rhCG-mediated induction of T levels, whereas TCDD, glyphosate, and RDX had no effect on basal or rhCG induction of T in BLTK1 cells. These results suggest that BLTK1 cells maintain rhCG-inducible steroidogenesis and are a viable in vitro Leydig cell model to evaluate the effects of EDCs on steroidogenesis. This model can also be used to elucidate the different mechanisms underlying toxicant-mediated disruption of steroidogenesis.

Nat Prod Res. 2013;27(6):574-8. doi: 10.1080/14786419.2012.673607. Epub 2012 Mar 29.

A comparative study of phytochemical composition of genetically and non-genetically modified soybean (Glycine max L.) and evaluation of antitumor activity.

Marrelli M[1], Tudisco R, Mastellone V, Conforti F.

Author information

Abstract

Colon cancer is one of the major causes of cancer mortality worldwide. The analysed feeds, containing non-genetically modified (GM) soybean and Roundup Ready soybean, showed a different polyphenolic content and lipophilic composition. Non-GM soybean extract possessed twice the polyphenolic content of GM soybean and the highest number of sterols. Among them, y-sitosterol was found to be the major constituent. Methanolic extract of non-GM soybean extract was more potent than GM soybean extract against colon carcinoma cell line LoVo using MTT assay, while the second one showed a slightly higher anti-inflammatory activity. The findings add to epidemiological evidence for the therapeutic effects of soy foods in colorectal carcinoma.

Chemosphere. 2012 Jul;88(4):439-44. doi: 10.1016/j.chemosphere.2012.02.062. Epub 2012 Mar 21.

Acute contact toxicity test of insecticides (Cipermetrina 25, Lorsban 48E, Thionex 35) on honeybees in the southwestern zone of Uruguay.

Carrasco-Letelier L[1], Mendoza-Spina Y, Branchiccela MB.

Author information

Abstract

Glyphosate-resistant soybean cultivation is expanding rapidly in Uruguay, with its land area having increased by 95 times during the past 10 years. Because of the region's Neotropical conditions, insecticide use is required to ensure adequate soybean productivity. However, in areas shared by soybean crops and beekeepers - such as the southwestern zone of Uruguay (SWZU) - the use of insecticides can increase the risks of honeybee death and honey contamination. Uruguayan commercial and legal guidelines set out practices and field doses designed to prevent acute intoxication with insecticides. However, honeybees in the SWZU are predominantly a polyhybrid subspecies different from that used to set international reference values, and hence they may have a different acute toxicity response, thus rendering such precautions ineffective. The aim of this work was to assess the acute toxicity response of polyhybrid honeybees in the SWZU to cypermethrin (commercial formulation: Cipermetrina 25 Agrin®), chlorpyrifos (commercial formulation: Lorsban 48E®), and endosulfan (commercial formulation: Thionex 35®). Acute toxicity bioassays were conducted to determine the median lethal dose (LD(50)) of each insecticide for the honeybees. The results indicate that, compared with EU reference values, SWZU honeybees have a higher toxicological sensitivity to chlorpyrifos and endosulfan, and a lower toxicological sensitivity to cypermethrin, based on the commercial formulations tested. However, when these results were adjusted according to their field dose equivalents, only chlorpyrifos emerged as a potential problem for beekeeping, as the maximum recommended field dose of Lorsban 48E® for soybean crops in Uruguay is 23 times the corresponding LD(50) for honeybees in the SWZU.

Publication Types, MeSH Terms, Substances

Bull Environ Contam Toxicol. 2012 May;88(5):659-65. doi: 10.1007/s00128-012-0570-6. Epub 2012 Mar 4.

Glyphosate, alachor and maleic hydrazide have genotoxic effect on Trigonella foenum-graecum L.

Siddiqui S[1], Meghvansi MK, Khan SS.

Author information

Abstract

In the present study effects of herbicides glyphosate (GP), alachlor (AL) and maleic hydrazide (MH) is studied on mitotic cells of Trigonella foenum-graecum L. Seeds of T. foenum-graecum L. treated with a series of concentrations ranging from 0.1%, 0.2%, 0.3%, 0.4% and 0.5% for 1, 2 and 6 h and their effect on mitotic index and chromosomal aberrations was studied. The results indicate that these herbicides reduced mitotic index in dose-dependent manner. In addition, increase in the percentage of abnormal mitotic plates was observed in herbicide treated groups which was both concentration and time dependent. Commonly observed abnormalities were c-mitosis, laggards, bridges, stickiness, c-anaphase, precocious separation, un-equal distribution and fragments. The result of the present investigation indicates that commonly used herbicides GP, AL and MH have significant genotoxic effect on T. foenum-graecum plant.

J Struct Biol. 2012 Apr;178(1):1-7. doi: 10.1016/j.jsb.2012.02.007. Epub 2012 Feb 17.

Glyphosate-induced stiffening of HaCaT keratinocytes, a Peak Force Tapping study on living cells.

Heu C[1], Berquand A, Elie-Caille C, Nicod L.

Author information

Abstract

The skin is the first physiological barrier, with a complex constitution, that provides defensive functions against multiple physical and chemical aggressions. Glyphosate is an extensively used herbicide that has been shown to increase the risk of cancer. Moreover there is increasing evidence suggesting that the mechanical phenotype plays an important role in malignant transformation. Atomic force microscopy (AFM) has emerged within the last decade as a powerful tool for providing a nanometer-scale resolution imaging of biological samples. Peak Force Tapping (PFT) is a newly released AFM-based investigation technique allowing extraction of chemical and mechanical properties from a wide range of samples at a relatively high speed and a high resolution. The present work uses the PFT technology to investigate HaCaT keratinocytes, a human epidermal cell line, and offers an original approach to study chemically-induced changes in the cellular mechanical properties under near-physiological conditions. These experiments indicate glyphosateinduces cell membrane stiffening, and the appearance of cytoskeleton structures at a subcellular level, for low cytotoxic concentrations whereas cells exposed to IC50 (inhibitory concentration 50%) treatment exhibit control-like mechanical behavior despite obvious membrane damages. Quercetin, a well-known antioxidant, reverses the glyphosate-induced mechanical phenotype.

Related citations

ELSEVIER FULL-TEXT ARTICLE

MeSH Terms, Substances

Sci Total Environ. 2012 Apr 1;421-422:124-8. doi: 10.1016/j.scitotenv.2012.01.040. Epub 2012 Feb 25.

Phosphorus nutrition alters herbicide toxicity on Daphnia magna.

Lessard CR[1], Frost PC.
Author information

Abstract

We examined the effects of algal phosphorus (P) content on the toxicity of a common herbicide, WeatherMAXRoundup (WMR), to Daphnia magna. The growth, reproduction, and survival of D. magna were assessed with animals consuming different food P content and exposed to different concentrations of WMR. While the effects of WMR on mortality increased with time of exposure, we found no interactive effects between food P content and WMR on daphnid survival over any of time periods examined (4, 10, or 20 days). In contrast, we found interactive effects of WMR and dietary P content on Daphnia juvenile growth (measured after 6 days) with the greatest effects of WMR on animals consuming P-rich food. Interactive effects of WMR and food P content were also found on some aspects of Daphnia's reproduction (number of broods and total offspring production) with P-deprived animals most affected by WMR exposure. Our results demonstrate that P-nutrition can alter the toxicity of WMR on key life-history traits of D. magna but that the nature and strength of these effects differ among the traits examined. The effects of P-nutrition on WMR-toxicity likely reflect changes in the exposure to and/or incorporation of WMR into animal bodies associated with changes in growth resulting from poor nutrition and the ability of animals to repair ensuing damage. Given the widely variable nutritional state of animals in nature, this differential toxicity of WMR with food quality warrants further study and should be incorporated in future risk assessments of this widely used chemical.

Related citations
ELSEVIER FULL-TEXT ARTICLE
Publication Types, MeSH Terms, Substances

J Appl Toxicol. 2013 Jul;33(7):695-9. doi: 10.1002/jat.2712. Epub 2012 Feb 15.

Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide.

Mesnage R[1], Clair E, Gress S, Then C, Székács A, Séralini GE.

Author information

Abstract

The study of combined effects of pesticides represents a challenge for toxicology. In the case of the new growing generation of genetically modified (GM) plants with stacked traits, glyphosate-based herbicides (likeRoundup) residues are present in the Roundup-tolerant edible plants (especially corns) and mixed with modified Bt insecticidal toxins that are produced by the GM plants themselves. The potential side effects of these combined pesticides on human cells are investigated in this work. Here we have tested for the very first time Cry1Ab and Cry1Ac Bt toxins (10 ppb to 100 ppm) on the human embryonic kidney cell line 293, as well as their combined actions with Roundup, within 24 h, on three biomarkers of cell death: measurements ofmitochondrial succinate dehydrogenase, adenylate kinase release by membrane alterations and caspase 3/7 inductions. Cry1Ab caused cell death from 100 ppm. For Cry1Ac, under such conditions, no effects were detected. The Roundup tested alone from 1 to 20 000 ppm is necrotic and apoptotic from 50 ppm, far below agricultural dilutions (50% lethal concentration 57.5 ppm). The only measured significant combined effect was that Cry1Ab and Cry1Ac reduced caspases 3/7 activations induced by Roundup; this could delay the activation of apoptosis. There was the same tendency for the other markers. In these results, we argue that modified Bt toxins are not inert on nontarget human cells, and that they can present combined side-effects with other residues of pesticides specific to GM plants.

Related citations

Full Text Online Wiley Online Library

Publication Types, MeSH Terms, Substances

Arch Toxicol. 2012 May;86(5):805-13. doi: 10.1007/s00204-012-0804-8. Epub 2012 Feb 14.

Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells.

Koller VJ[1], Fürhacker M, Nersesyan A, Mišík M, Eisenbauer M, Knasmueller S.

Author information

Abstract

Glyphosate (G) is the largest selling herbicide worldwide; the most common formulations (Roundup, R) contain polyoxyethyleneamine as main surfactant. Recent findings indicate that G exposure may cause DNA damage and cancer in humans. Aim of this investigation was to study the cytotoxic and genotoxic properties of G and R (UltraMax) in a buccal epithelial cell line (TR146), as workers are exposed via inhalation to the herbicide. R induced acute cytotoxic effects at concentrations > 40 mg/l after 20 min, which were due to membrane damage and impairment of mitochondrial functions. With G, increased release of extracellular lactate dehydrogenase indicative for membrane damage was observed at doses > 80 mg/l. Both G and R induced DNA migration in single-cell gel electrophoresis assays at doses > 20 mg/l. Furthermore, an increase of nuclear aberrations that reflect DNA damage was observed. The frequencies of micronuclei and nuclear buds were elevated after 20-min exposure to 10-20 mg/l, while nucleoplasmatic bridges were only enhanced by R at the highest dose (20 mg/l). R was under all conditions more active than its active principle (G). Comparisons with results of earlier studies with lymphocytes and cells from internal organs indicate that epithelial cells are more susceptible to the cytotoxic and DNA-damaging properties of the herbicide and its formulation. Since we found genotoxic effects after short exposure to concentrations that correspond to a 450-fold dilution of spraying used in agriculture, our findings indicate that inhalation may cause DNA damage in exposed individuals.

Related citations

SpringerLink FULL-TEXT ARTICLE

MeSH Terms, Substances

Mutat Res. 2012 Mar 18;743(1-2):1-9. doi: 10.1016/j.mrgentox.2011.10.017. Epub 2012 Jan 14.

DNA damage in fish (Anguilla anguilla) exposed to a glyphosate-based herbicide -- elucidation of organ-specificity and the role of oxidative stress.

Guilherme S[1], Gaivão I, Santos MA, Pacheco M.

Author information

Abstract

Organophosphate herbicides are among the most dangerous agrochemicals for the aquatic environment. In this context, Roundup(®), a glyphosate-based herbicide, has been widely detected in natural water bodies, representing a potential threat to non-target organisms, namely fish. Thus, the main goal of the present study was to evaluate the genotoxic potential of Roundup(®) in the teleost fish Anguilla anguilla, addressing the possible causative involvement of oxidative stress. Fish were exposed to environmentally realistic concentrations of this herbicide (58 and 116 μgL(-1)) during one or three days. The standard procedure of the comet assay was applied to gill and liver cells in order to determine organ-specific genetic damage. Since liver is a central organ in xenobiotic metabolism, nucleoids of hepatic cells were also incubated with a lesion-specific repair enzyme (formamidopyrimidine DNA glycosylase - FPG), in order to recognise oxidised purines. Antioxidants were determined in both organs as indicators of pro-oxidant state. In general, both organs displayed an increase in DNA damage for the two Roundup(®) concentrations and exposure times, although liver showed to be less susceptible to the lower concentration. The enzyme-modified comet assay showed the occurrence of FPG-sensitive sites in liver only after a 3-day exposure to the higher Roundup(®) concentration. The antioxidant defences were in general unresponsive, despite a single increment of catalase activity in gills (116 μgL(-1), 3-day) and a decrease of superoxide dismutase activity in liver (58 μgL(-1), 3-day). Overall, the mechanisms involved in Roundup(®)-induced DNA strand-breaks showed to be similar in both organs. Nevertheless, it was demonstrated that the type of DNA damage varies with the concentration and exposure duration. Hence, after 1-day exposure, an increase on pro-oxidant state is not a necessary condition for the induction of DNA-damaging effects of Roundup(®). By increasing the duration of exposure to three days, ROS-dependent processes gained preponderance as a mechanism of DNA-damage induction in the higher concentration.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Int J Hyg Environ Health. 2012 Nov;215(6):570-6. doi: 10.1016/j.ijheh.2011.12.002. Epub 2012 Jan 18.

Estimating maternal and prenatal exposure to glyphosate in the community setting.

McQueen H[1], Callan AC, Hinwood AL.

Author information

Abstract

Glyphosate is a herbicide in common use, in both agricultural and residential settings. Controlled residue studies show that glyphosate persists in food crops, allowing for the potential of a large number of people to be exposed. Glyphosate is generally considered safe however there are a number of studies suggesting formulations or additives that may have adverse health effects. To assess the degree of exposure of pregnant women, this study measured glyphosate in composite food samples and estimated exposure based on food frequency questionnaire. 43 pregnant women were recruited and completed a self administered questionnaire with a food frequency component and provided a composite food sample. Twenty food samples were analysed with very low glyphosate concentrations (mean 0.08 mg/kg, range 0.002-0.5 mg/kg) with residues detected in more than 75% of the samples. Maternal dietary exposure was very low (0.001 mg/kg bw/day) and was considerably lower than the predicted National Estimated Daily Intake of glyphosate (0.02 mg/kg bw/day). The estimated exposure based on measured glyphosate in composite food samples corresponded to 0.4% of the acceptable daily intake for glyphosate, and the predicted concentration from dietary information was 4% which is comparable to the National Estimated Daily Intake of 5.5% of the Acceptable Daily Intake ofglyphosate. Prenatal exposures were estimated to be significantly lower. While residues of glyphosate are present in food, this study demonstrates that exposure concentrations are low and confirms the current models used to estimate glyphosate exposure.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

J Insect Sci. 2011;11:144. doi: 10.1673/031.011.14401.

Foraging range of honey bees, Apis mellifera, in alfalfa seed production fields.

Hagler JR[1], Mueller S, Teuber LR, Machtley SA, Van Deynze A.

Author information

Abstract

A study was conducted in 2006 and 2007 designed to examine the foraging range of honey bees, Apis mellifera (Hymenoptera: Apidae), in a 15.2 km(2) area dominated by a 128.9 ha glyphosate-resistant RoundupReady® alfalfa seed production field and several non-Roundup Ready alfalfa seed production fields (totaling 120.2 ha). Each year, honey bee self-marking devices were placed on 112 selected honey bee colonies originating from nine different apiary locations. The foraging bees exiting each apiary location were uniquely marked so that the apiary of origin and the distance traveled by the marked (field-collected) bees into each of the alfalfa fields could be pinpointed. Honey bee self-marking devices were installed on 14.4 and 11.2% of the total hives located within the research area in 2006 and 2007, respectively. The frequency of field-collectedbees possessing a distinct mark was similar, averaging 14.0% in 2006 and 12.6% in 2007. A grand total of 12,266 bees were collected from the various alfalfa fields on seven sampling dates over the course of the study. The distances traveled by marked bees ranged from a minimum of 45 m to a maximum of 5983 m. On average, marked bees were recovered ~ 800 m from their apiary of origin and the recovery rate of markedbees decreased exponentially as the distance from the apiary of origin increased. Ultimately, these data will be used to identify the extent of pollen-mediated gene flow from Roundup Ready to conventional alfalfa.

Arch Toxicol. 2012 Apr;86(4):663-73. doi: 10.1007/s00204-011-0788-9. Epub 2011 Nov 26.

Glyphosate impairs male offspring reproductive development by disrupting gonadotropin expression.

Romano MA[1], Romano RM, Santos LD, Wisniewski P, Campos DA, de Souza PB, Viau P, Bernardi MM, Nunes MT, de Oliveira CA.

Author information

Abstract

Sexual differentiation in the brain takes place from late gestation to the early postnatal days. This is dependent on the conversion of circulating testosterone into estradiol by the enzyme aromatase. Theglyphosate was shown to alter aromatase activity and decrease serum testosterone concentrations. Thus, the aim of this study was to investigate the effect of gestational maternal glyphosate exposure (50 mg/kg, NOAEL for reproductive toxicity) on the reproductive development of male offspring. Sixty-day-old male rat offspring were evaluated for sexual behavior and partner preference; serum testosterone concentrations, estradiol, FSH and LH; the mRNA and protein content of LH and FSH; sperm production and the morphology of the seminiferous epithelium; and the weight of the testes, epididymis and seminal vesicles. The growth, the weight and age at puberty of the animals were also recorded to evaluate the effect of the treatment. The most important findings were increases in sexual partner preference scores and the latency time to the first mount; testosterone and estradiol serum concentrations; the mRNA expression and protein content in the pituitary gland and the serum concentration of LH; sperm production and reserves; and the height of the germinal epithelium of seminiferous tubules. We also observed an early onset of puberty but no effect on the body growth in these animals. These results suggest that maternal exposure to glyphosate disturbed the masculinization process and promoted behavioral changes and histological and endocrine problems inreproductive parameters. These changes associated with the hypersecretion of androgens increased gonadal activity and sperm production.

Comment in

- Comment on "Glyphosate impairs male offspring reproductive development by disrupting gonadotropin expression" by Romano et al. 2012. [Arch Toxicol. 2012]

Related citations

Publication Types, MeSH Terms, Substances

Aquat Toxicol. 2012 Jan 15;106-107:104-13. doi: 10.1016/j.aquatox.2011.10.018. Epub 2011 Nov 3.

Genotoxicity of diuron and glyphosate in oyster spermatozoa and embryos.

Akcha F[1], Spagnol C, Rouxel J.

Author information

Abstract

We investigated the effects of genotoxicant exposure in gametes and embryos to find a possible link betweengenotoxicity and reproduction/developmental impairment, and explore the impact of chemical genotoxicity on population dynamics. Our study focused on the genotoxic effects of two herbicides on oyster gametes and embryos: glyphosate (both as an active substance and in the Roundup formulation) and diuron. France is Europe's leading consumer of agrochemical substances and as such, contamination of France's coastal waters by pesticides is a major concern. Glyphosate and diuron are among the most frequently detected herbicides in oyster production areas; as oyster is a specie with external reproduction, its gametes and embryos are in direct contact with the surrounding waters and are hence particularly exposed to these potentially dangerous substances. In the course of this study, differences in genotoxic and embryotoxic responses were observed in the various experiments, possibly due to differences in pollutant sensitivity between the tested genitor lots. Glyphosate and Roundup had no effect on oyster development at the concentrations tested, whereas diuron significantly affected embryo-larval development from the lowest tested concentration of 0.05 µg L^{-1}, i.e. an environmentally realistic concentration. Diuron may therefore have a significant impact on oyster recruitment rates in the natural environment. Our spermiotoxicity study revealed none of the tested herbicides to be cytotoxic for oyster spermatozoa. However, the alkaline comet assay showed diuron to have a significant genotoxic effect on oyster spermatozoa at concentrations of 0.05 µg L^{-1} upwards. Conversely, no effects due to diuron exposure were observed on sperm mitochondrial function or acrosomal membrane integrity. Although our initial results showed no negative effect on sperm function, the possible impact on fertilization rate and the consequences of the transmission of damaged DNA for oyster development and physiological performances, requires further investigation. A likely hypothesis to explain the embryotoxic and genotoxic effects of diuron is that it may act via causing oxidative stress.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

J Med Food. 2011 Oct;14(10):1263-72. doi: 10.1089/jmf.2010.0202. Epub 2011 Aug 22.

Protective effect of Ginkgo biloba L. leaf extract against glyphosate toxicity in Swiss albino mice.

Cavuşoğlu K[1], Yapar K, Oruç E, Yalçın E.

Author information

Abstract

The aim of the present study was to investigate the protective role of Ginkgo biloba L. leaf extract against the active agent of Roundup® herbicide (Monsanto, Creve Coeur, MO, USA). The Swiss Albino mice were randomly divided into six groups, with each group consisting of six animals: Group I (control) received an intraperitoneal injection of dimethyl sulfoxide (0.2 mL, once only), Group II received glyphosate at a dose of 50 mg/kg of body weight, Group III received G. biloba at a dose of 50 mg/kg of body weight, Group IV received G. biloba at a dose of 150 mg/kg of body weight, Group V received G. biloba (50 mg/kg of body weight) and glyphosate (50 mg/kg of body weight), and Group VI received G. biloba (150 mg/kg of body weight) and glyphosate (50 mg/kg of body weight). The single dose of glyphosate was given intraperitoneally. Animals from all the groups were sacrificed at the end of 72 hours, and their blood, bone marrow, and liver and kidney tissues were analyzed for aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine, malondialdehyde (MDA), and glutathione (GSH) levels and the presence of micronucleus (MN), chromosomal aberrations (CAs), and pathological damages. The results indicated that serum AST, ALT, BUN, and creatinine levels significantly increased in mice treated with glyphosate alone compared with the other groups (P<.05). Besides, glyphosate-induced oxidative damage caused a significant decrease in GSH levels and a significant increase in MDA levels of the liver and kidney tissues. Moreover,glyphosate alone-treated mice presented higher frequencies of CAs, MNs, and abnormal metaphases compared with the controls (P<.05). These mice also displayed a lower mean mitotic index than the controls (P<.05). Treatment with G. biloba produced amelioration in indices of hepatotoxicity, nephrotoxicity, lipid peroxidation, and genotoxicity relative to Group II. Each dose of G. biloba provided significant protection against glyphosate-induced toxicity, and the strongest effect was observed at a dose of 150 mg/kg of body weight. Thus, in vivo results showed that G. biloba extract is a potent protector against glyphosate-induced toxicity, and its protective role is dose-dependent.

Acta Biol Hung. 2011 Sep;62(3):290-301. doi: 10.1556/ABiol.62.2011.3.8.

Evaluation of Roundup-induced toxicity on genetic material and on length growth of barley seedlings.

Truta E[1], Vochita G, Rosu CM, Zamfirache MM, Olteanu Z.

Author information

Abstract

The study was performed in order to evaluate Roundup-induced genotoxic effects in Hordeum vulgare L. cv. Madalin root meristems and to analyze herbicide impact on length growth of barley seedlings. Caryopses were treated for 3 hours and 6 hours with 0.1%, 0.5%, 1.0% and 2.0% Roundup solutions (v/v), containing 0.36 mg ml-1, 1.8 mg ml-1, 3.6 mg ml-1 and 7.2 mg ml-1 glyphosate active ingredient. Mitotic index decreased in both exposure times with concentration increase. In 3-h treatment, its average values decreased from 4.73 ± 0.31% to 1.51 ± 0.43%, whereas in 6-h treatment this parameter declined from 3.86 ± 0.92% to 0.62 ± 0.15%. The highest ana-telophase aberration rates were noted in 3-h treatments (8.91%, 9.19%, 9.47%, 11.25%, comparatively to control - 5.99%). Roundup enhanced the number of metaphase disturbances proving its noxious effect on normal functioning of mitotic spindle. Seedling growth was negatively influenced at all tested concentrations in both exposure times. The length decreased as concentration increased, so that the average length is 7.5-9 times smaller than in control at the maximum concentration, in both exposures.

Related citations

FULL TEXT ON JOURNAL WEBSITE

Publication Types, MeSH Terms, Substances

Arch Environ Contam Toxicol. 2012 Jan;62(1):107-17. doi: 10.1007/s00244-011-9686-7. Epub 2011 Jun 4.

Exposure to a commercial glyphosate formulation (Roundup®) alters normal gill and liver histology and affects male sexual activity of Jenynsia multidentata (Anablepidae, Cyprinodontiformes).

Hued AC[1], Oberhofer S, de los Ángeles Bistoni M.

Author information

Abstract

Roundup is the most popular commercial glyphosate formulation applied in the cultivation of genetically modified glyphosate-resistant crops. The aim of this study was to evaluate the histological lesions of the neotropical native fish, Jenynsia multidentata, in response to acute and subchronic exposure to Roundup and to determine if subchronic exposure to the herbicide causes changes in male sexual activity of individuals exposed to a sublethal concentration (0.5 mg/l) for 7 and 28 days. The estimated 96-h LC50 was 19.02 mg/l for both male and female fish. Gill and liver histological lesions were evaluated through histopathological indices allowing quantification of the histological damages in fish exposed to different concentrations of the herbicide. Roundup induced different histological alterations in a concentration-dependent manner. In subchronic-exposure tests, Roundup also altered normal histology of the studied organs and caused a significant decrease in the number of copulations and mating success in male fish exposed to the herbicide. It is expected that in natural environments contaminated with Roundup, both general health condition andreproductive success of J. multidenatata could be seriously affected.

Genet Mol Biol. 2011 Jan;34(1):127-30. doi: 10.1590/S1415-47572010005000108. Epub 2011 Mar 1.

Evaluation of genetic damage induced by glyphosate isopropylamine salt using Tradescantia bioassays.

Alvarez-Moya C[1], Silva MR, Arámbula AR, Sandoval AI, Vasquez HC, González Montes RM.

Author information

Abstract

Glyphosate is noted for being non-toxic in fishes, birds and mammals (including humans). Nevertheless, the degree of genotoxicity is seriously controversial. In this work, various concentrations of a glyphosateisopropylamine salt were tested using two methods of genotoxicity assaying, viz., the pink mutation assay with Tradescantia (4430) and the comet assay with nuclei from staminal cells of the same plant. Staminal nuclei were studied in two different forms, namely nuclei from exposed plants, and nuclei exposed directly. Using the pink mutation assay, isopropylamine induced a total or partial loss of color in staminal cells, a fundamental criterion utilized in this test. Consequently, its use is not recommended when studyinggenotoxicity with agents that produce pallid staminal cells. The comet assay system detected statistically significant ($p < 0.01$) genotoxic activity by isopropylamine, when compared to the negative control in both the nuclei of treated plants and directly treated nuclei, but only the treated nuclei showed a dose-dependent increase. Average migration in the nuclei of treated plants increased, when compared to that in treated nuclei. This was probably due, either to the permanence of isopropylamine in inflorescences, or to the presence of secondary metabolites. In conclusion, isopropylamine possesses strong genotoxic activity, but its detection can vary depending on the test systems used.

KEYWORDS:

DNA damage; Tradescantia point mutation test; comet assay; glyphosate; plant genotoxicity test

Ecotoxicol Environ Saf. 2011 Jul;74(5):1363-9. doi: 10.1016/j.ecoenv.2011.04.020. Epub 2011 May 4.

Exposure of juvenile green frogs (Lithobates clamitans) in littoral enclosures to aglyphosate-based herbicide.

Edge CB[1], Gahl MK, Pauli BD, Thompson DG, Houlahan JE.

Author information

Abstract

The majority of studies on the toxicity of glyphosate-based herbicides to amphibians have focused on larval life stages exposed in aqueous media. However, adult and juvenile amphibians may also be exposed directly or indirectly to herbicides. The potential for such exposures is of particular interest in the littoral zone surrounding wetlands as this is preferred habitat for many amphibian species. Moreover, it may be argued that potential herbicide effects on juvenile or adult amphibians could have comparatively greater influence on overall recruitment, reproductive potential and thus stability of local populations than effects on larvae. In this experiment, juvenile green frogs (Lithobates clamitans) were exposed to two concentrations (2.16 and 4.27 kg a.e./ha) of a glyphosate-based herbicide formulation (VisionMax®), which were based on typical application scenarios in Canadian forestry. The experimental design employed frogs inhabiting in situ enclosures established at the edge of small naturalized wetlands that were split in half using an impermeable plastic barrier. When analyzed using nominal target application rates, exposure to the glyphosate-based herbicide had no significant effect on survival, body condition, liver somatic index or the observed rate of Batrachochytrium dendrobatidis infection. However, there were marginal trends in both ANOVA analysis and post-hoc regressions regarding B. dendrobatidis infection rates and liver somatic index in relation to measured exposure estimates. Results from this study highlight the importance of field research and the need to include multiple endpoints when examining potential effects of a contaminant on non-target organisms.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

New Phytol. 2011 Aug;191(3):840-9. doi: 10.1111/j.1469-8137.2011.03706.x. Epub 2011 Mar 28.

Glyphosate-drift but not herbivory alters the rate of transgene flow from single and stacked trait transgenic canola (Brassica napus) to nontransgenic B. napus and B. rapa.

Londo JP[1], Bollman MA, Sagers CL, Lee EH, Watrud LS.

Author information

Abstract

• Transgenic plants can offer agricultural benefits, but the escape of transgenes is an environmental concern. In this study we tested the hypothesis that glyphosate drift and herbivory selective pressures can change the rate of transgene flow between the crop Brassica napus (canola), and weedy species and contribute to the potential for increased transgene escape risk and persistence outside of cultivation. • We constructed plant communities containing single transgenic B. napus genotypes expressing glyphosate herbicide resistance (CP4 EPSPS), lepidopteran insect resistance (Cry1Ac), or both traits ('stacked'), plus nontransgenic B. napus, Brassica rapa and Brassica nigra. Two different selective pressures, a sublethal glyphosate dose and lepidopteran herbivores (Plutella xylostella), were applied and rates of transgene flow and transgenic seed production were measured. • Selective treatments differed in the degree in which they affected gene flow and production of transgenic hybrid seed. Most notably, glyphosate-drift increased the incidence of transgenic seeds on nontransgenic B. napus by altering flowering phenology and reproductive function. • The findings of this study indicate that transgenic traits may be transmitted to wild populations and may increase in frequency in weedy populations through the direct and indirect effects of selection pressures on gene flow.

Related citations

Full Text Online Wiley Online Library

Publication Types, MeSH Terms, Substances

Reprod Toxicol. 2011 May;31(4):528-33. doi: 10.1016/j.reprotox.2011.02.004. Epub 2011 Feb 18.

Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada.

Aris A[1], Leblanc S.

Author information

Abstract

Pesticides associated to genetically modified foods (PAGMF), are engineered to tolerate herbicides such asglyphosate (GLYP) and gluphosinate (GLUF) or insecticides such as the bacterial toxin bacillus thuringiensis (Bt). The aim of this study was to evaluate the correlation between maternal and fetal exposure, and to determine exposure levels of GLYP and its metabolite aminomethyl phosphoric acid (AMPA), GLUF and its metabolite 3-methylphosphinicopropionic acid (3-MPPA) and Cry1Ab protein (a Bt toxin) in Eastern Townships of Quebec, Canada. Blood of thirty pregnant women (PW) and thirty-nine nonpregnant women (NPW) were studied. Serum GLYP and GLUF were detected in NPW and not detected in PW. Serum 3-MPPA and CryAb1 toxin were detected in PW, their fetuses and NPW. This is the first study to reveal the presence of circulating PAGMF in women with and without pregnancy, paving the way for a new field in reproductive toxicology including nutrition and utero-placental toxicities.

Comment in

- Comment: Aris and Leblanc "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada". [Reprod Toxicol. 2012]
- Bayer CropScience's position on the findings of glufosinate and its metabolite. [Reprod Toxicol. 2011]
- Comment on "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada" by A. Aris and S. Leblanc [Reprod. Toxicol. 31 (2011) 528-533]. [Reprod Toxicol. 2012]

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

J Occup Med Toxicol. 2011 Jan 20;6(1):3. doi: 10.1186/1745-6673-6-3.

Defined plant extracts can protect human cells against combined xenobiotic effects.

Gasnier C[1], Laurant C, Decroix-Laporte C, Mesnage R, Clair E, Travert C, Séralini GE.

Author information

Abstract

BACKGROUND:

Pollutants representative of common environmental contaminants induce intracellular toxicity in human cells, which is generally amplified in combinations. We wanted to test the common pathways of intoxication and detoxification in human embryonic and liver cell lines. We used various pollutants such as Roundup residues, Bisphenol-A and Atrazine, and five precise medicinal plant extracts called Circ1, Dig1, Dig2, Sp1, and Uro1 in order to understand whether specific molecular actions took place or not.

METHODS:

Kidney and liver are major detoxification organs. We have studied embryonic kidney and hepatic human cell lines E293 and HepG2. The intoxication was induced on the one hand by a formulation of one of the most common herbicides worldwide, Roundup 450 GT+ (glyphosate and specific adjuvants), and on the other hand by a mixture of Bisphenol-A and Atrazine, all found in surface waters, feed and food. The prevention and curative effects of plant extracts were also measured on mitochondrial succinate dehydrogenase activity, on the entry of radiolabelled glyphosate (in Roundup) in cells, and on cytochromes P450 1A2 and 3A4 as well as glutathione-S-transferase.

RESULTS:

Clear toxicities of pollutants were observed on both cell lines at very low sub-agricultural dilutions. The prevention of such phenomena took place within 48 h with the plant extracts tested, with success rates ranging between 25-34% for the E293 intoxicated by Roundup, and surprisingly up to 71% for the HepG2. By contrast, after intoxication, no plant extract was capable of restoring E293 viability within 48 h, however, two medicinal plant combinations did restore the Bisphenol-A/Atrazine intoxicated HepG2 up to 24-28%. The analysis of underlying mechanisms revealed that plant extracts were not capable of preventing radiolabelledglyphosate from entering cells; however Dig2 did restore the CYP1A2 activity disrupted by Roundup, and had only a mild preventive effect on the CYP3A4, and no effect on the glutathione S-transferase.

CONCLUSIONS:

Environmental pollutants have intracellular effects that can be prevented, or cured in part, by precise medicinal plant extracts in two human cell lines. This appears to be mediated at least in part by the cytochromes P450 modulation.

Ecotoxicol Environ Saf. 2011 May;74(4):852-9. doi: 10.1016/j.ecoenv.2010.12.005. Epub 2010 Dec 24.

Genetic, enzymatic and developmental alterations observed in Caiman latirostris exposed in ovo to pesticide formulations and mixtures in an experiment simulating environmental exposure.

Poletta GL[1], Kleinsorge E, Paonessa A, Mudry MD, Larriera A, Siroski PA.

Author information

Abstract

In South America, economic interests in last years have produced a constant increase in transgenic soybean cropping, with the corresponding rise in pesticide formulated products. The aim of this study was to determine the effects of pesticides formulations and mixtures on a South American caiman, Caiman latirostris, after in ovo exposure. We conducted a field-like experiment which simulates the environmental exposure that a caiman nest can receive in neighbouring croplands habitats. Experimental groups were Control group, Treatment 1: sprayed with a glyphosate herbicide formulation, and Treatment 2: sprayed with a pesticide mixture of glyphosate, endosulfan and cypermethrin formulations. Results demonstrated genotoxicity, enzymatic and metabolic alterations, as well as growth delay in caimans exposed in ovo to Treatments 1 and 2, showing a higher toxicity for the mixture. Integral evaluation through biomarkers of different biological meaning is highly informative as early indicators of contamination with pesticides and mixtures in this wildlife species.

Gynecol Obstet Fertil. 2010 Dec;38(12):747-53. doi: 10.1016/j.gyobfe.2010.08.030.

[Hypothetical link between endometriosis and xenobiotics-associated genetically modified food].

[Article in French]

Aris A[1], Paris K.

Author information

Abstract

Endometriosis is an oestrogen-dependent inflammatory disease affecting 10 % of reproductive-aged women. Often accompanied by chronic pelvic pain and infertility, endometriosis rigorously interferes with women's quality of life. Although the pathophysiology of endometriosis remains unclear, a growing body of evidence points to the implication of environmental toxicants. Over the last decade, an increase in the incidence of endometriosis has been reported and coincides with the introduction of genetically modified foods in our diet. Even though assessments of genetically modified food risk have not indicated any hazard on human health, xenobiotics-associated genetically modified food, such as pesticides residues and xenoproteins, could be harmful in the long-term. The "low-dose hypothesis", accumulation and biotransformation of pesticides-associated genetically modified food and the multiplied toxicity of pesticides-formulation adjuvants support this hypothesis. This review summarizes toxic effects (in vitro and on animal models) of some xenobiotics-associated genetically modified food, such as glyphosate and Cry1Ab protein, and extrapolates on their potential role in the pathophysiology of endometriosis. Their roles as immune toxicants, pro-oxidants, endocrine disruptors and epigenetic modulators are discussed.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Ecotoxicology. 2011 Jan;20(1):255-63. doi: 10.1007/s10646-010-0577-x. Epub 2010 Nov 18.

Effect of Roundup® (glyphosate formulation) in the energy metabolism andreproductive traits of Hyalella castroi (Crustacea, Amphipoda, Dogielinotidae).

Dutra BK[1], Fernandes FA, Failace DM, Oliveira GT.

Author information

Abstract

Roundup(®) (glyphosate formulation) is a nonselective and posts emergent herbicide used for controlling aquatic weeds and different concentrations are used in cultures around the world. The objective of this investigation was to examine the effects of Roundup(®) (glyphosate formulation) on the biochemical composition, levels of lipoperoxidation, Na(+)/K(+)ATPase activity and reproductive traits in the Hyalella castroi. Amphipods were collected in summer 2009, in the southern Brazilian highlands. In the laboratory, the animals were kept in aquariums under controlled conditions for 7 days, and after this period they were exposed to 0.36, 0.52, 1.08 and 2.16 mg/l of glyphosate for 7 days. After the period of exposure, the animals were immediately frozen for determination of glycogen, proteins, lipids, triglycerides, cholesterol, levels of lipoperoxidation, and Na(+)/K(+)ATPase activity. During each day of the cultivation reproductive traits (number of reproductive pairs, ovigerous females and eggs in the marsupium) were observed. All concentrations of Roundup(®) induced significant decreases in all biochemical parameters and Na(+)/K(+)ATPase activity, and significant increase in lipoperoxidation levels. Showing this form a potentially toxic effect at very low concentrations, this pattern of results can lead to significant changes in trophic structure of limnic environments because these amphipods are important links in food chain in these habitats.

Environ Toxicol Chem. 2011 Feb;30(2):455-68. doi: 10.1002/etc.394.

Comparing effects of low levels of herbicides on greenhouse- and field-grown potatoes (Solanum tuberosum L.), soybeans (Glycine max L.), and peas (Pisum sativum L.).

Pfleeger T[1], Olszyk D, Lee EH, Plocher M.
Author information

Abstract

Although laboratory toxicology tests are generally easy to perform, cost effective, and readily interpreted, they have been questioned for their environmental relevance. In contrast, field tests are considered realistic while producing results that are difficult to interpret and expensive to obtain. Toxicology tests were conducted on potatoes, peas, and soybeans grown in a native soil in pots in the greenhouse and were compared to plants grown outside under natural environmental conditions to determine toxicological differences between environments, whether different plant developmental stages were more sensitive to herbicides, and whether these species were good candidates for plant reproductive tests. The reproductive and vegetative endpoints of the greenhouse plants and field-grown plants were also compared. The herbicides bromoxynil, glyphosate, MCPA ([4-chloro-2-methylphenoxy] acetic acid), and sulfometuron-methyl were applied at below field application rates to potato plants at two developmental stages. Peas and soybeans were exposed to sulfometuron-methyl at similar rates at three developmental stages. The effective herbicide concentrations producing a 25% reduction in a given measure differed between experimental conditions but were generally within a single order of magnitude within a species, even though there were differences in plant morphology. This study demonstrated that potatoes, peas, and soybeans grown in pots in a greenhouse produce phytotoxicity results similar to those grown outside in pots; that reproductive endpoints in many cases were more sensitive than vegetative ones; and that potato and pea plants are reasonable candidates for asexual and sexual reproductive phytotoxicity tests, respectively. Plants grown in pots in a greenhouse and outside varied little in toxicity. However, extrapolating those toxicity results to native plant communities in the field is basically unknown and in need of research.

J Occup Med Toxicol. 2010 Oct 27;5:29. doi: 10.1186/1745-6673-5-29.

Dig1 protects against cell death provoked by glyphosate-based herbicides in human liver cell lines.

Gasnier C[1], Benachour N, Clair E, Travert C, Langlois F, Laurant C, Decroix-Laporte C, Séralini GE.

Author information

Abstract

BACKGROUND:

Worldwide used pesticides containing different adjuvants like Roundup formulations, which are glyphosate-based herbicides, can provoke some in vivo toxicity and in human cells. These pesticides are commonly found in the environment, surface waters and as food residues of Roundup tolerant genetically modified plants. In order to know their effects on cells from liver, a major detoxification organ, we have studied their mechanism of action and possible protection by precise medicinal plant extracts called Dig1.

METHODS:

The cytotoxicity pathways of four formulations of glyphosate-based herbicides were studied using human hepatic cell lines HepG2 and Hep3B, known models to study xenobiotic effects. We monitoredmitochondrial succinate dehydrogenase activity and caspases 3/7 for cell mortality and protection by Dig1, as well as cytochromes P450 1A1, 1A2, 3A4 and 2C9 and glutathione-S-transferase to approach the mechanism of actions.

RESULTS:

All the four Roundup formulations provoke liver cell death, with adjuvants having stronger effects than glyphosate alone. Hep3B are 3-5 times more sensitive over 48 h. Caspases 3/7 are greatly activated in HepG2 by Roundup at non-cytotoxic levels, and some apoptosis induction by Roundup is possible together with necrosis. CYP3A4 is specifically enhanced by Roundup at doses 400 times less than used in agriculture (2%). CYP1A2 is increased to a lesser extent together with glutathione-S-transferase (GST) down-regulation. Dig 1, non cytotoxic and not inducing caspases by itself, is able to prevent Roundup-induced cell death in a time-dependant manner with an important efficiency of up to 89%, within 48 h. In addition, we evidenced that it prevents Caspases 3/7 activation and CYP3A4 enhancement, and not GST reduction, but in turn it slightly inhibited CYP2C9 when added before Roundup.

CONCLUSION:

Roundup is able to provoke intracellular disruption in hepatic cell lines at different levels, but a mixture of medicinal plant extracts Dig1 can protect to some extent human cell lines against this pollutants. All this system constitutes a tool for studying liver intoxication and detoxification.

Integr Environ Assess Manag. 2010 Oct;6(4):725-34. doi: 10.1002/ieam.89.

Phytotoxicity assay for seed production using Brassica rapa L.

Olszyk D[1], Pfleeger T, Lee EH, Plocher M.

Author information

Abstract

Although pesticide drift can affect crop yield adversely, current plant testing protocols emphasize only the potential impacts on vegetative plant growth. The present study was conducted to determine whether a plant species with a short life cycle, such as Brassica rapa L. Wisconsin Fast Plants®, can be used to indicate potential effects on seed production of herbicides applied at relatively low levels (e.g., low field application rates [FAR]). The effects of ≤0.1 × FAR of aminopyralid, cloransulam, glyphosate, primisulfuron, or sulfometuron applied 14 d after emergence (DAE), were evaluated for B. rapa grown in mineral soil in pots under greenhouse conditions. Effects were expressed as the effective concentration of the herbicide producing a 25% reduction in a response (EC25) based on nonlinear regression. Brassica rapa seed dry weight was reduced by sulfometuron at an EC25 of 0.00014 × a field application rate (FAR) of 53 g active ingredient (a.i.) ha(-1), primisulfuron at 0.008 (experiment 1) or 0.0050 (experiment 2) × FAR of 40 g a.i. ha(-1), cloransulam at 0.022 × FAR of 18 g a.i. ha(-1), glyphosate at 0.0399 × FAR of 834 g a.i. ha(-1), and by aminopyralid at 0.005 × FAR of 123 g a.i. ha(-1), but only for 1 of 2 experiments. Reduced seed production occurred at less than the FAR that reduced shoot dry weight with sulfometuron and primisulfuron, whereas neither aminopyralid, cloransulam, nor glyphosate affected shoot dry weight. A short life cycle form of B. rapa could be used to indicate reduced seed production with plants grown only 1 week longer (~35 DAE) than as the current vegetative vigor test for nontarget herbicide effects on plants.

Related citations

Publication Types, MeSH Terms, Substances

Ann Bot. 2010 Dec;106(6):957-65. doi: 10.1093/aob/mcq190. Epub 2010 Sep 18.

Glyphosate drift promotes changes in fitness and transgene gene flow in canola (Brassica napus) and hybrids.

Londo JP[1], Bautista NS, Sagers CL, Lee EH, Watrud LS.

Author information

Abstract

BACKGROUND AND AIMS:

With the advent of transgenic crops, genetically modified, herbicide-resistant Brassica napus has become a model system for examining the risks and potential ecological consequences of escape of transgenes from cultivation into wild compatible species. Escaped transgenic feral B. napus and hybrids with compatible weedy species have been identified outside of agriculture and without the apparent selection for herbicide resistance. However, herbicide (glyphosate) exposure can extend beyond crop field boundaries, and a drift-level of herbicide could function as a selective agent contributing to increased persistence of transgenes in the environment.

METHODS:

The effects of a drift level (0·1 × the field application rate) of glyphosate herbicide and varied levels of plant competition were examined on plant fitness-associated traits and gene flow in a simulated field plot, common garden experiment. Plants included transgenic, glyphosate-resistant B. napus, its weedy ancestor B. rapa, and hybrid and advanced generations derived from them.

KEY RESULTS:

The results of this experiment demonstrate reductions in reproductive fitness for non-transgenic genotypes and a contrasting increase in plant fitness for transgenic genotypes as a result ofglyphosate-drift treatments. Results also suggest that a drift level of glyphosate spray may influence the movement of transgenes among transgenic crops and weeds and alter the processes of hybridization and introgression in non-agronomic habitats by impacting flowering phenology and pollen availability within the community.

CONCLUSIONS:

The results of this study demonstrate the potential for persistence of glyphosate resistance transgenes in weedy plant communities due to the effect of glyphosate spray drift on plant fitness. Additionally, glyphosate drift has the potential to change the gene-flow dynamics between compatible transgenic crops and weeds, simultaneously reducing direct introgression into weedy species while contributing to an increase in the transgenic seed bank.

Environ Toxicol Chem. 2010 Jan;29(1):111-21. doi: 10.1002/etc.12.

Potato (Solanum tuberosum) greenhouse tuber production as an assay for asexualreproduction effects from herbicides.

Olszyk D[1], Pfleeger T, Lee EH, Plocher M.
Author information

Abstract

The present study determined whether young potato plants can be used as an assay to indicate potential effects of pesticides on asexual reproduction. Solanum tuberosum (Russet Burbank) plants were grown from seed pieces in a mineral soil in pots under greenhouse conditions. Plants were treated with herbicides (cloransulam, dicamba, glyphosate, imazapyr, primsulfuron, sulfometuron, or tribenuron) at simulated drift levels [</=0.1 x standard field application rates (f.a.r.)], approximately 14 d after emergence (DAE). Plant height was measured approximately 14 d after treatment (DAT). Production of small tubers and shoot dry weight were determined at approximately 28 DAT. Imazapyr, sulfometuron, and tribenuron caused significant reductions in tuber fresh weight, with the effective concentrations producing a 25% potato tuber fresh weight (EC25) of 0.00038, 0.0016, and 0.0021 x f.a.r. of 1,124, 52, and 9 g active ingredient hectare(-1) (g a.i. HA(-1)), respectively. Primisulfuron, dicamba, and cloransulam also significantly reduced tuber fresh weight, but with higher EC25 values of 0.011, 0.07, and 0.010 to 0.2 x f.a.r. of 40, 558, and 18 g a.i. HA(-1), respectively. Glyphosate had little effect on tuber fresh weight, with a significant reduction in only one experiment. Sulfometuron reduced tuber fresh weight at an EC25 value lower than the EC25 values for shoot dry weight or plant height. For other herbicides, the reduction in tuber fresh weight occurred within the range of EC25 values for other responses. Although additional experiments are required to develop further a phytotoxicity test, these results indicated that tuber production in young potato plants (harvested approximately 42 DAE) may be an effective assay for below-ground asexual reproductive responses to herbicides, especially acetolactate synthase inhibitors.

Chem Res Toxicol. 2010 Oct 18;23(10):1586-95. doi: 10.1021/tx1001749. Epub 2010 Aug 9.

Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signaling.

Paganelli A[1], Gnazzo V, Acosta H, López SL, Carrasco AE.

Author information

Abstract

The broad spectrum herbicide glyphosate is widely used in agriculture worldwide. There has been ongoing controversy regarding the possible adverse effects of glyphosate on the environment and on human health. Reports of neural defects and craniofacial malformations from regions where glyphosate-based herbicides (GBH) are used led us to undertake an embryological approach to explore the effects of low doses ofglyphosate in development. Xenopus laevis embryos were incubated with 1/5000 dilutions of a commercial GBH. The treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening of the anterior-posterior (A-P) axis. Alterations on neural crest markers were later correlated with deformities in the cranial cartilages at tadpole stages. Embryos injected with pure glyphosateshowed very similar phenotypes. Moreover, GBH produced similar effects in chicken embryos, showing a gradual loss of rhombomere domains, reduction of the optic vesicles, and microcephaly. This suggests thatglyphosate itself was responsible for the phenotypes observed, rather than a surfactant or other component of the commercial formulation. A reporter gene assay revealed that GBH treatment increased endogenous retinoic acid (RA) activity in Xenopus embryos and cotreatment with a RA antagonist rescued the teratogenic effects of the GBH. Therefore, we conclude that the phenotypes produced by GBH are mainly a consequence of the increase of endogenous retinoid activity. This is consistent with the decrease of Sonic hedgehog (Shh) signaling from the embryonic dorsal midline, with the inhibition of otx2 expression and with the disruption of cephalic neural crest development. The direct effect of glyphosate on early mechanisms of morphogenesis in vertebrate embryos opens concerns about the clinical findings from human offspring in populations exposed to GBH in agricultural fields.

Bull Environ Contam Toxicol. 2010 Sep;85(3):264-8. doi: 10.1007/s00128-010-0089-7. Epub 2010 Jul 24.

Effects of glyphosate and 2,4-D on earthworms (Eisenia foetida) in laboratory tests.

Correia FV[1], Moreira JC.

Author information

Abstract

Laboratory tests were conducted to compare the effects of various concentrations of glyphosate and 2,4-D on earthworms (Eisenia foetida) cultured in Argissol during 56 days of incubation. The effects on earthworm growth, survival, and reproduction rates were verified for different exposure times. Earthworms kept inglyphosate-treated soil were classified as alive in all evaluations, but showed gradual and significant reduction in mean weight (50%) at all test concentrations. For 2,4-D, 100% mortality was observed in soil treated with 500 and 1,000 mg/kg. At 14 days, 30%-40% mortality levels were observed in all other concentrations. No cocoons or juveniles were found in soil treated with either herbicide. Glyphosate and 2,4-D demonstrated severe effects on the development and reproduction of Eisenia foetida in laboratory tests in the range of test concentrations.

Mutagenesis. 2010 Sep;25(5):523-30. doi: 10.1093/mutage/geq038. Epub 2010 Jul 19.

European eel (Anguilla anguilla) genotoxic and pro-oxidant responses following short-term exposure to Roundup--a glyphosate-based herbicide.

Guilherme S[1], Gaivão I, Santos MA, Pacheco M.

Author information

Abstract

The glyphosate-based herbicide, Roundup, is among the most used pesticides worldwide. Due to its extensive use, it has been widely detected in aquatic ecosystems representing a potential threat to non-target organisms, including fish. Despite the negative impact of this commercial formulation in fish, as described in literature, the scarcity of studies assessing its genotoxicity and underlying mechanisms is evident. Therefore, as a novel approach, this study evaluated the genotoxic potential of Roundup to blood cells of the European eel (Anguilla anguilla) following short-term (1 and 3 days) exposure to environmentally realistic concentrations (58 and 116 microg/l), addressing also the possible association with oxidative stress. Thus, comet and erythrocytic nuclear abnormalities (ENAs) assays were adopted, as genotoxic end points, reflecting different types of genetic damage. The pro-oxidant state was assessed through enzymatic (catalase, glutathione-S-transferase, glutathione peroxidase and glutathione reductase) and non-enzymatic (total glutathione content) antioxidants, as well as by lipid peroxidation (LPO) measurements. The Roundup potential to induce DNA strand breaks for both concentrations was demonstrated by the comet assay. The induction of chromosome breakage and/or segregational abnormalities was also demonstrated through the ENA assay, though only after 3-day exposure to both tested concentrations. In addition, the two genotoxic indicators were positively correlated. Antioxidant defences were unresponsive to Roundup. LPO levels increased only for the high concentration after the first day of exposure, indicating that oxidative stress caused by this agrochemical in blood was not severe. Overall results suggested that both DNA damaging effects induced by Roundup are not directly related with an increased pro-oxidant state. Moreover, it was demonstrated that environmentally relevant concentrations of Roundup can pose a health risk for fish populations.

Arch Environ Contam Toxicol. 2011 May;60(4):672-80. doi: 10.1007/s00244-010-9570-x. Epub 2010 Jul 10.

Influence of a combination of agricultural chemicals on embryos of the endangered gold-striped salamander (Chioglossa lusitanica).

Ortiz-Santaliestra ME[1], Fernández-Benéitez MJ, Lizana M, Marco A.

Author information

Abstract

Pollution from agrochemicals may be contributing to the global decline of amphibian populations. Environmentally relevant concentrations of a fertiliser, ammonium nitrate, and a commercial formulation of the herbicide glyphosate Roundup Plus were tested on the embryonic development of Chioglossa lusitanica. This study introduces new data at three different levels. First, we provide previously unknown information about hatchling traits of C. lusitanica. Second, we present the first ecotoxicological study of this endangered species, to which environmental pollution is considered a major threat. Third, we conduct the first experiment with an amphibian species exposed to a mixture of a glyphosate-based herbicide and a nitrogenous fertiliser. Control individuals hatched with an average (±SD) total length of 18.77 (±2.02) mm and at an average Harrison's developmental stage of 44.58 (±1.24). Mean hatching time among controls was 11.52 (±1.29) weeks. None of the chemicals or their interaction produced lethal effects; however, a significant interaction was found when analysing total length at hatching. Individuals exposed to the herbicide hatched at a larger size than controls, and this effect was especially clear when the fertiliser was added to the water. The absence of pollutant-related mortality or severe sublethal effects is in agreement with most studies indicating a high tolerance of amphibian embryos to agrochemicals. However, further research considering other life stages and additional natural factors (i.e., predators, food availability) is needed to estimate the ecological impact of chemical mixtures on C. lusitanica.

Chemosphere. 2010 Aug;80(9):1021-30. doi: 10.1016/j.chemosphere.2010.05.031. Epub 2010 Jun 25.

Joint effects of three plant protection products to the terrestrial isopod Porcellionides pruinosus and the collembolan Folsomia candida.

Santos MJ[1], Soares AM, Loureiro S.

Author information

Abstract

The effects of simultaneous application of plant protection products are of concern since the uses of different products pose an additional risk to non-target soil organisms. The effects of binary combinations of dimethoate, glyphosate and spirodiclofen, an insecticide an herbicide and an acaricide, on the avoidance behaviour of the terrestrial isopod Porcellionides pruinosus and the reproductive effort of Folsomia candida were assessed using the two reference models of concentration addition (CA) and independent action (IA). Results of single exposure to the three pesticides indicated a clear dose related avoidance response of the isopods in the highest concentrations tested of the three as well as a strong decrease in collembolan adult survival and concomitant number of juveniles produced. In the combined experiments, antagonism was found in 7 out of the 12 combinations, four combinations followed the reference models, and only in one combination synergism was detected (lower doses of glyphosate and spirodiclofen applied to P. pruinosus). In conclusion, it seems that mixing and applying these products, at the recommended field application rate, does not lead to enhanced toxicity, hence limited risk is associated with the joint application of these pesticides.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

J Toxicol. 2009;2009:308985. doi: 10.1155/2009/308985. Epub 2008 Dec 15.

Clastogenic effects of glyphosate in bone marrow cells of swiss albino mice.

Prasad S[1], Srivastava S, Singh M, Shukla Y.

Author information

Abstract

Glyphosate (N-(phosphonomethyl) glycine, C(3)H(8)NO(5)P), a herbicide, used to control unwanted annual and perennial plants all over the world. Nevertheless, occupational and environmental exposure to pesticides can pose a threat to nontarget species including human beings. Therefore, in the present study, genotoxic effects of the herbicide glyphosate were analyzed by measuring chromosomal aberrations (CAs) and micronuclei (MN) in bone marrow cells of Swiss albino mice. A single dose of glyphosate was given intraperitoneally (i.p) to the animals at a concentration of 25 and 50 mg/kg b.wt. Animals of positive control group were injected i.p. benzo(a)pyrene (100 mg/kg b.wt., once only), whereas, animals of control (vehicle) group were injected i.p. dimethyl sulfoxide (0.2 mL). Animals from all the groups were sacrificed at sampling times of 24, 48, and 72 hours and their bone marrow was analyzed for cytogenetic and chromosomal damage. Glyphosate treatment significantly increases CAs and MN induction at both treatments and time compared with the vehicle control ($P < .05$). The cytotoxic effects of glyphosate were also evident, as observed by significant decrease in mitotic index (MI). The present results indicate that glyphosate is clastogenic and cytotoxic to mouse bone marrow.

J Proteomics. 2010 Mar 10;73(5):951-64. doi: 10.1016/j.jprot.2009.12.008. Epub 2010 Jan 4.

Studies on glyphosate-induced carcinogenicity in mouse skin: a proteomic approach.

George J[1], Prasad S, Mahmood Z, Shukla Y.

Author information

Abstract

Glyphosate is a widely used broad spectrum herbicide, reported to induce various toxic effects in non-target species, but its carcinogenic potential is still unknown. Here we showed the carcinogenic effects ofglyphosate using 2-stage mouse skin carcinogenesis model and proteomic analysis. Carcinogenicity study revealed that glyphosate has tumor promoting activity. Proteomic analysis using 2-dimensional gel electrophoresis and mass spectrometry showed that 22 spots were differentially expressed (>2 fold) onglyphosate, 7, 12-dimethylbenz[a]anthracene (DMBA) and 12-O-tetradecanoyl-phorbol-13-acetate (TPA) application over untreated control. Among them, 9 proteins (translation elongation factor eEF-1 alpha chain, carbonic anhydrase III, annexin II, calcyclin, fab fragment anti-VEGF antibody, peroxiredoxin-2, superoxide dismutase [Cu-Zn], stefin A3, and calgranulin-B) were common and showed similar expression pattern inglyphosate and TPA-treated mouse skin. These proteins are known to be involved in several key processes like apoptosis and growth-inhibition, anti-oxidant responses, etc. The up-regulation of calcyclin, calgranulin-B and down-regulation of superoxide dismutase [Cu-Zn] was further confirmed by immunoblotting, indicating that these proteins can be good candidate biomarkers for skin carcinogenesis induced by glyphosate. Altogether, these results suggested that glyphosate has tumor promoting potential in skin carcinogenesis and its mechanism seems to be similar to TPA.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Commun Agric Appl Biol Sci. 2010;75(3):367-72.

Side-effects of glyphosate on the life parameters of Eriopis connexa (Coleoptera: Coccinelidae) in Argentina.

Mirande L[1], Haramboure M, Smagghe G, Piñeda S, Schneider MI.
Author information

Abstract

In Argentina, transgenic soybean crop (Roundup Ready, RR) has undergone a major expansion over the last 15 years, with the consequent increase of glyphosate applications, a broad-spectrum and post emergence herbicide. Soybean crops are inhabited by several arthropods. Eriopis connexa Germar (Coleoptera: Coccinelidae) is a predator associated to soybean soft-bodies pest and have a Neotropical distribution. Nowadays, it is being considered a potentially biological control agent in South America. The objectives of this work were to evaluate the side-effects of glyphosate on larvae (third instar) and adults of this predator. Commercial compound and the maximum registered concentrations for field use were employed: GlifoGlex 48 (48% glyphosate, 192 mg a.i./litre, Gleba Argentina S.A.). The exposure was by ingestion through the treated prey (Rophalosiphum padi) or by drinking treated water during 48 h for treatment of the adult. The herbicide solutions were prepared using distilled water as solvent. The bioassays were carried out in the laboratory under controlled conditions: 23 +/- 0.5 degrees C, 75 +/- 5% RH and 16:8 (L:D) of photoperiod. Development time, weight of pupae, adult emergence, pre-oviposition period, fecundity and fertility were evaluated as endpoints. Larvae from glyphosate treatment molted earlier than controls. In addition, the weight of pupae, longevity, fecundity and fertility were drastically reduced in treated organisms. The reductions were more drastic when the treatments were performed at the third larval stage than as adult.
The reproduction capacity of the predator was the most affected parameter and could be related to a hormonal disruption by glyphosatein the treated organisms. This work can confirm the deleterious effects of this herbicide on beneficial organisms. Also, it agrees with prior studies carried out on other predators associated to soybean pest, such as Chrysoperla externa (Neuroptera: Chrysopidae) and Alpaida veniliae (Araneae: Araneidae).

Environ Biosafety Res. 2009 Jul-Sep;8(3):123-31. doi: 10.1051/ebr/2009013. Epub 2009 Oct 7.

Reproductive phenology of transgenic Brassica napus cultivars: Effect on intraspecific gene flow.

Simard MJ[1], Légère A, Willenborg CJ.

Author information

Abstract

Pollen-mediated gene flow in space is well documented and isolation distances are recommended to ensure genetic purity of Brassica napus seed crops. Isolation in time could also contribute to gene flow management but has been little investigated. We assessed the effects of asynchronous and synchronous flowering on intraspecific B. napus gene flow by seeding adjacent plots of transgenic spring canola cultivars, either resistant to glyphosate or glufosinate, over a 0-4 week interval and measuring outcrossing rates and seed-set. Outcrossing rates, evaluated in the center of the first adjacent row, were reduced to the lowest level in plots flowering first when the seeding interval > 2 weeks. Increasing the time gap increased outcrossing rates in plots flowering second up to a seeding interval of two weeks. Flowers that opened during the last week of the flowering period produced fewer seed (< 10% of total seed production) and a smaller fraction of outcrossed seed (-25%). Observed time gap effects were likely caused by extraneous pollen load during the receptivity of productive seed-setting early flowers. Clearly, manipulation of B. napus flowering development through staggered planting dates can contribute to gene flow management. The approach will need to be validated by additional site-years and increased isolation distances.

Neuro Endocrinol Lett. 2009;30 Suppl 1:2-12.

A review: oxidative stress in fish induced by pesticides.

Slaninova A[1], Smutna M, Modra H, Svobodova Z.
Author information

Abstract

The knowledge in oxidative stress in fish has a great importance for environmental and aquatic toxicology. Because oxidative stress is evoked by many chemicals including some pesticides, pro-oxidant factors' action in fish organism can be used to assess specific area pollution or world sea pollution. Hepatotoxic effect of DDT may be related with lipid peroxidation. Releasing of reactive oxygen species (ROS) after HCB exposure can be realized via two ways: via the uncoupling of the electron transport chain from monooxygenase activity and via metabolism of HCB major metabolite pentachlorophenol. Chlorothalonil disrupts mitochondrialmetabolism due to the impairment of NADPH oxidase function. Activation of spleen macrophages and a decrease of catalase (CAT) activity have been observed after endosulfan exposure. Excessive release of superoxide radicals after etoxazole exposure can cause a decrease of CAT activity and increase phagocytic activity of splenocytes. Anticholinergic activity of organophosphates leads to the accumulation of ROS and resulting lipid peroxidation. Carbaryl induces changes in the content of glutathione and antioxidant enzymes activities. The antioxidant enzymes changes have been observed after actuation of pesticides deltamethrin and cypermethrin. Bipyridyl herbicides are able to form redox cycles and thereby cause oxidative stress. Low concentrations of simazine do not cause oxidative stress in carps during sub-chronic tests while sublethal concentrations of atrazin can induce oxidative stress in bluegill sunfish. Butachlor causes increased activity of superoxide dismutase -catalase system in the kidney. Rotenon can inhibit the electron transport inmitochondria and thereby increase ROS production. Dichloroaniline, the metabolite of diuron, has oxidative effects. Oxidative damage from fenpyroximate actuation is related to the disruption of mitochondrial redox respiratory chain. Low concentration of glyphosate can cause mild oxidative stress.

Related citations

Publication Types, MeSH Terms, Substances

Chemosphere. 2010 Feb;78(7):871-6. doi: 10.1016/j.chemosphere.2009.11.027. Epub 2009 Dec 16.

Effects of the herbicide glyphosate on biological attributes of Alpaida veniliae (Araneae, Araneidae), in laboratory.

Benamú MA[1], Schneider MI, Sánchez NE.

Author information

Abstract

In the past decades there has been increasing interest in the study of arthropod predators as effective potential natural enemies to be used in the biological control of agricultural pests. In Argentina, transgenic soybean crops (Round-up Ready, RR) are inhabit by many spider species, some of them in high abundance, being indicative of an import potential for pest predation. This crop is associated with the use of glyphosate, a broad-spectrum herbicide, with low environmental impact, even though since the 80's, several negative effects have been deeply documented on mammals, fishes, amphibians, snails, earthworms, insects, etc. Nowadays, the effects on arthropod physiology, behavior and life history traits as end-points in ecotoxicological evaluations are being recognized. In transgenic soybean crops of Buenos Aires province (Argentina), Alpaida veniliae (Araneae, Araneidae) is one of the most abundant orb web weaver spiders. The purpose of this study was to address the effects of glyphosate on some biological attributes of A. veniliae, in laboratory. Results of this study showed no lethal direct effects of Glifoglex on this spider, but it is the first report in literature about sublethal effects of this herbicide on a spider's biological attributes. Negative effects on prey consumption, web building, fecundity, fertility and developmental time of progeny were observed. Although sublethal effects have received less attention than direct lethal effects, they are relevant from an ecological point of view, since the reduction of the arthropod performance may create risks to arthropod biodiversity conservation in agroecosystems.

Arch Toxicol. 2010 Apr;84(4):309-17. doi: 10.1007/s00204-009-0494-z. Epub 2009 Dec 12.

Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology.

Romano RM[1], Romano MA, Bernardi MM, Furtado PV, Oliveira CA.

Author information

Abstract

Glyphosate is a herbicide widely used to kill weeds both in agricultural and non-agricultural landscapes. Itsreproductive toxicity is related to the inhibition of a StAR protein and an aromatase enzyme, which causes an in vitro reduction in testosterone and estradiol synthesis. Studies in vivo about this herbicide effects in prepubertal Wistar rats reproductive development were not performed at this moment. Evaluations included the progression of puberty, body development, the hormonal production of testosterone, estradiol and corticosterone, and the morphology of the testis. Results showed that the herbicide (1) significantly changed the progression of puberty in a dose-dependent manner; (2) reduced the testosterone production, in semineferous tubules' morphology, decreased significantly the epithelium height ($P < 0.001$; control = 85.8 +/- 2.8 microm; 5 mg/kg = 71.9 +/- 5.3 microm; 50 mg/kg = 69.1 +/- 1.7 microm; 250 mg/kg = 65.2 +/- 1.3 microm) and increased the luminal diameter ($P < 0.01$; control = 94.0 +/- 5.7 microm; 5 mg/kg = 116.6 +/- 6.6 microm; 50 mg/kg = 114.3 +/- 3.1 microm; 250 mg/kg = 130.3 +/- 4.8 microm); (4) no difference in tubular diameter was observed; and (5) relative to the controls, no differences in serum corticosterone or estradiol levels were detected, but the concentrations of testosterone serum were lower in all treated groups ($P < 0.001$; control = 154.5 +/- 12.9 ng/dL; 5 mg/kg = 108.6 +/- 19.6 ng/dL; 50 mg/dL = 84.5 +/- 12.2 ng/dL; 250 mg/kg = 76.9 +/- 14.2 ng/dL). These results suggest that commercial formulation of glyphosate is a potent endocrine disruptor in vivo, causing disturbances in the reproductive development of rats when the exposure was performed during the puberty period.

Related citations

Publication Types, MeSH Terms, Substances

Arch Environ Contam Toxicol. 2010 May;58(4):973-84. doi: 10.1007/s00244-009-9410-z. Epub 2009 Oct 30.

Flow-cytometric analyses of viability biomarkers in pesticide-exposed sperm of three aquatic invertebrates.

Favret KP[1], Lynn JW.

Author information

Abstract

Toxicity studies on sperm often use fertilization success as the end point. This type of assay can be affected by sperm density, egg quality, and sperm-egg compatibility. Testing sperm viability biomarkers with flow cytometry is a fast, high-throughput technique for seminal analysis. In this study, we detected sperm viability biomarkers with several fluorescent reporter dyes using flow cytometry in three aquatic invertebrates (Crassostrea virginica, Dreissena polymorpha, and Lytechinus variegatus) after exposure to a pesticide and herbicide. The pesticide, Bayluscide, appeared to affect mitochondrial membrane potential in the sperm of all three species, as measured with MitoTracker Red CMXRos. A decrease in the percentage of sperm stained with SYBR-14 (indicating uncompromised plasma membrane) was observed in C. virginica and D. polymorpha sperm exposed to Bayluscide, but propidium iodide staining (indicating compromised plasma membranes) appeared to be inhibited by Bayluscide. Acrosome-reacted sperm, as measured by FITC-PNA, decreased after Bayluscide exposure in C. virginica and D. polymorpha sperm. The herbicide, Roundup Ready To-Use-Plus, did not affect the overall percentages of sperm stained with MitoTracker but did cause an increase in MitoTracker fluorescence intensity at 16 mg/L in D. polymorpha. Roundup also caused significant decreases in SYBR-14 staining, significant increases in propidium iodide staining, and significant increases in FITC-PNA staining in D. polymorpha sperm. By not having to rely on egg availability and optimal sperm density, sperm toxicity can be more accurately assessed with flow cytometry as being directly correlated to sperm viability rather than the possibility of altered toxicity results due to sperm-to-egg compatibility.

Occup Environ Med. 2010 May;67(5):323-9. doi: 10.1136/oem.2009.047175. Epub 2009 Oct 22.

Identifying pesticide use patterns among flower growers to assess occupational exposure to mixtures.

Schilmann A[1], Lacasaña M, Blanco-Muñoz J, Aguilar-Garduño C, Salinas-Rodríguez A, Flores-Aldana M, Cebrián ME.

Author information

Abstract

OBJECTIVES:

Exposure assessment to a single pesticide does not capture the complexity of the occupational exposure. Recently, pesticide use patterns analysis has emerged as an alternative to study these exposures. The aim of this study is to identify the pesticide use pattern among flower growers in Mexico participating in the study on the endocrine and reproductive effects associated with pesticide exposure.

METHODS:

A cross-sectional study was carried out to gather retrospective information on pesticide use applying a questionnaire to the person in charge of the participating flower growing farms. Information about seasonal frequency of pesticide use (rainy and dry) for the years 2004 and 2005 was obtained. Principal components analysis was performed.

RESULTS:

Complete information was obtained for 88 farms and 23 pesticides were included in the analysis. Six principal components were selected, which explained more than 70% of the data variability. The identified pesticide use patterns during both years were: 1. fungicides benomyl, carbendazim, thiophanate and metalaxyl (both seasons), including triadimephon during the rainy season, chlorotalonyl and insecticide permethrin during the dry season; 2. insecticides oxamyl, biphenthrin and fungicide iprodione (both seasons), including insecticide methomyl during the dry season; 3. fungicide mancozeb and herbicide glyphosate (only during the rainy season); 4. insecticides metamidophos and parathion (both seasons); 5. insecticides omethoate and methomyl (only rainy season); and 6. insecticides abamectin and carbofuran (only dry season). Some pesticides do not show a clear pattern of seasonal use during the studied years.

CONCLUSIONS:

The principal component analysis is useful to summarise a large set of exposure variables into smaller groups of exposure patterns, identifying the mixtures of pesticides in the occupational environment that may have an interactive effect on a particular health effect.

Related citations

BMJ Full Text

Publication Types, MeSH Terms, Substances

J Toxicol Environ Health A. 2009;72(15-16):986-97. doi: 10.1080/15287390902929741.

Biomonitoring of genotoxic risk in agricultural workers from five colombian regions: association to occupational exposure to glyphosate.

Bolognesi C[1], Carrasquilla G, Volpi S, Solomon KR, Marshall EJ.

Author information

Abstract

In order to assess possible human effects associated with glyphosate formulations used in the Colombian aerial spray program for control of illicit crops, a cytogenetic biomonitoring study was carried out in subjects from five Colombian regions, characterized by different exposure to glyphosate and other pesticides. Women of reproductive age (137 persons 15-49 yr old) and their spouses (137 persons) were interviewed to obtain data on current health status, history, lifestyle, including past and current occupational exposure to pesticides, and factors including those known to be associated with increased frequency of micronuclei (MN). In regions where glyphosate was being sprayed, blood samples were taken prior to spraying (indicative of baseline exposure), 5 d after spraying, and 4 mo after spraying. Lymphocytes were cultured and a cytokinesis-block micronucleus cytome assay was applied to evaluate chromosomal damage and cytotoxicity. Compared with Santa Marta, where organic coffee is grown without pesticides, the baseline frequency of binucleated cells with micronuclei (BNMN) was significantly greater in subjects from the other four regions. The highest frequency of BNMN was in Boyaca, where no aerial eradication spraying ofglyphosate was conducted, and in Valle del Cauca, where glyphosate was used for maturation of sugar cane. Region, gender, and older age (> or =35 yr) were the only variables associated with the frequency of BNMN measured before spraying. A significant increase in frequency of BNMN between first and second sampling was observed in Narino, Putumayo, and Valle immediately (<5 d) after spraying. In the post-spray sample, those who reported direct contact with the eradication spray showed a higher quantitative frequency of BNMN compared to those without glyphosate exposure. The increase in frequency of BNMN observed immediately after the glyphosate spraying was not consistent with the rates of application used in the regions and there was no association between self-reported direct contact with eradication sprays and frequency of BNMN. Four months after spraying, a statistically significant decrease in the mean frequency of BNMN compared with the second sampling was observed in Narino, but not in Putumayo and Valle del Cauca. Overall, data suggest that genotoxic damage associated with glyphosate spraying for control of illicit crops as evidenced by MN test is small and appears to be transient. Evidence indicates that the genotoxic risk potentially associated with exposure to glyphosate in the areas where the herbicide is applied for coca and poppy eradication is low.

Related citations

View full text

MeSH Terms, Substances

J Toxicol Environ Health A. 2009;72(15-16):949-60. doi: 10.1080/15287390902929691.

Regional differences in time to pregnancy among fertile women from five Colombian regions with different use of glyphosate.

Sanin LH[1], Carrasquilla G, Solomon KR, Cole DC, Marshall EJ.

Author information

Abstract

The objective of this study was to test whether there was an association between the use of glyphosate when applied by aerial spray for the eradication of illicit crops (cocaine and poppy) and time to pregnancy (TTP) among fertile women. A retrospective cohort study (with an ecological exposure index) of first pregnancies was undertaken in 2592 fertile Colombian women from 5 regions with different uses of glyphosate. Women were interviewed regarding potential reproductive, lifestyle, and work history predictors of TTP, which was measured in months. Fecundability odds ratios (fOR) were estimated using a discrete time analogue of Cox's proportional hazard model. There were differences in TTP between regions. In the final multivariate model, the main predictor was the region adjusted by irregular relationship with partner, maternal age at first pregnancy, and, marginally, coffee consumption and self-perception of water pollution. Boyaca, a region with traditional crops and. recently, illicit crops without glyphosate eradication spraying (manual eradication), displayed minimal risk and was the reference region. Other regions, including Sierra Nevada (control area, organic agriculture), Putumayo and Narino (illicit crops and intensive eradication spray program), and Valle del Cauca, demonstrated greater risk of longer TTP, with the highest risk for Valle del Cauca (fOR 0.15, 95% CI 0.12, 0.18), a sugar-cane region with a history of use of glyphosate and others chemicals for more than 30 yr. The reduced fecundability in some regions was not associated with the use of glyphosate for eradication spraying. The observed ecological differences remain unexplained and may be produced by varying exposures to environmental factors, history of contraceptive programs in the region, or psychological distress. Future studies examining these or other possible causes are needed.

Toxicol In Vitro. 2009 Oct;23(7):1380-6. doi: 10.1016/j.tiv.2009.07.028. Epub 2009 Jul 30.

Modeling placental transport: correlation of in vitro BeWo cell permeability and ex vivo human placental perfusion.

Poulsen MS[1], Rytting E, Mose T, Knudsen LE.

Author information

Abstract

The placental passage of three compounds with different physicochemical properties was recently investigated in ex vivo human placental perfusion experiments (caffeine, benzoic acid, and glyphosate) [Mose, T., Kjaerstad, M.B., Mathiesen, L., Nielsen, J.B., Edelfors, S., Knudsen, L.E., 2008. Placental passage of benzoic acid, caffeine, and glyphosate in an ex vivo human perfusion system. J. Toxicol. Environ. Health, Part A 71, 984-991]. In this work, the transport of these same three compounds, plus the reference compound antipyrine, was investigated using BeWo (b30) cell monolayers. Transport across the BeWo cells was observed in the rank order of caffeine>antipyrine>benzoic acid>glyphosate in terms of both the apparent permeability coefficient and the initial slope, defined as the linear rate of substance transferred to the fetal compartment as percent per time, a parameter used to compare the two experimental models. The results from the in vitro studies were in excellent agreement with the ex vivo results (caffeine approximately antipyrine>benzoic acid>glyphosate). However the transfer rate was much slower in the BeWo cells compared to the perfusion system. The advantages and limitations of each model are discussed in order to assist in the preparation, prediction, and performance of future studies of maternal-fetal transfer.

Clin Toxicol (Phila). 2009 Aug;47(7):670-7. doi: 10.1080/15563650903140399.

The epidemiology of glyphosate-surfactant herbicide poisoning in Taiwan, 1986-2007: a poison center study.

Chen YJ[1], Wu ML, Deng JF, Yang CC.

Author information

Abstract

BACKGROUND:

Glyphosate-surfactant herbicide (GlySH) is widely used in agriculture and has been associated with numerous toxicities following oral ingestion. However, there are many controversies with regard to the exact causes and determinants of developing severe/death outcome after exposure to GlySH.

METHODS:

We conducted an analysis of all GlySH exposures reported to the Taiwan National Poison Control Center between 1986 and 2007. Patients' baseline characteristics and clinical data were reviewed and analyzed.

RESULTS:

A total of 2,186 patients were eligible for analysis. Most of the exposures were related to oral ingestion (n = 2,023, 92.5%) and attempted suicide (n = 1,631, 74.6%). The mean age of exposure was 42.8 +/- 18.6 years. One hundred patients developed severe effects and 146 patients died following oral GlySH exposure, resulting in a case fatality rate of 7.2%. Shock (n = 85, 58.2%) and respiratory failure (n = 34, 23.3%) accounted for most fatalities. Four out of eight patients with injection exposure manifested severe (n = 3) or fatal outcome (n = 1). In a multivariate logistic regression analysis, increasing age, larger amount of exposure, longer elapsed time to presentation, attempted suicide, receipt of atropine therapy, and being exposed in certain calendar years were positively associated with the severity of poisoning following oral GlySH exposure.

CONCLUSION:

Age, ingested amount, delayed presentation, and reason for exposure were likely to be determinants of the severity of GlySH exposure. Because shock is the major cause of death and usually develops early after GlySH exposure, prompt fluid replacement therapy seems critical in the initial management of such exposures. Patients' airway should also be secured to avoid aspiration and subsequent respiratory failure.

Chemosphere. 2009 Sep;76(10):1451-5. doi: 10.1016/j.chemosphere.2009.05.029. Epub 2009 Jul 3.

Impact of glyphosate on the development, fertility and demography of Chrysoperla externa (Neuroptera: Chrysopidae): ecological approach.

Schneider MI[1], Sanchez N, Pineda S, Chi H, Ronco A.

Author information

Abstract

Few ecotoxicological studies have used life table analysis to evaluate the toxicity of pesticides on beneficial organisms. This study is the first report of the effect of the herbicide glyphosate on a predator insect, Chrysoperla externa, using a demographic approach. This predator is associated to soybean pests and has a potential role as a biological control agent in the Neotropical Region. The objective of this work was to evaluate the side-effects of glyphosate on the development, fertility and demography of C. externa, treated orally by ingestion of glyphosate-dipped eggs of Sitotroga cerealella in laboratory conditions. The data were analyzed using the age-stage, two-sex life table. Development from third larval instar to pupae and adult longevity were shorter in glyphosate-treatment than in the control. Adult pre-reproductive period was longer inglyphosate-treatment than in the control. Fecundity and fertility were deeply reduced, as well, being fertility greater affected. A high important reduction was registered in all population parameters. Most eggs fromglyphosate-treated cohort looked abnormal, smaller than control, dehydrated and became black 2d after oviposition. In addition, adults developed tumours in the abdomen region at 20d after emergence, being the effect more drastic in females than males. It is beyond the scope of our study to speculate on the effects of this herbicide on C. externa field populations. However, it seems likely that populations under continuous use of glyphosate would be exposed at greater detrimental effects in the long term.

Related citations

Publication Types, MeSH Terms, Substances

Environ Toxicol Pharmacol. 2009 Jul;28(1):37-41. doi: 10.1016/j.etap.2009.02.001. Epub 2009 Feb 11.

Genotoxicity of glyphosate assessed by the comet assay and cytogenetic tests.

Mañas F[1], Peralta L, Raviolo J, Ovando HG, Weyers A, Ugnia L, Cid MG, Larripa I, Gorla N.

Author information

Abstract

It was evaluated the genotoxicity of glyphosate which up to now has heterogeneous results. The comet assay was performed in Hep-2 cells. The level of DNA damage in the control group (5.42±1.83 arbitrary units) for tail moment (TM) measurements has shown a significant increase ($p<0.01$) with glyphosate at a range concentration from 3.00 to 7.50mM. In the chromosome aberrations (CA) test in human lymphocytes the herbicide (0.20-6.00mM) showed no significant effects in comparison with the control group. In vivo, the micronucleus test (MNT) was evaluated in mice at three doses rendering statistical significant increases at 400mg/kg (13.0±3.08 micronucleated erythrocytes/1000 cells, $p<0.01$). In the present study glyphosate wasgenotoxic in the comet assay in Hep-2 cells and in the MNT test at 400mg/kg in mice. Thiobarbituric acid reactive substances (TBARs) levels, superoxide dismutase (SOD) and catalase (CAT) activities were quantified in their organs. The results showed an increase in these enzyme activities.

Related citations

Toxicology. 2009 Aug 21;262(3):184-91. doi: 10.1016/j.tox.2009.06.006. Epub 2009 Jun 17.

Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines.

Gasnier C[1], Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE.

Author information

Abstract

Glyphosate-based herbicides are the most widely used across the world; they are commercialized in different formulations. Their residues are frequent pollutants in the environment. In addition, these herbicides are spread on most eaten transgenic plants, modified to tolerate high levels of these compounds in their cells. Up to 400 ppm of their residues are accepted in some feed. We exposed human liver HepG2 cells, a well-known model to study xenobiotic toxicity, to four different formulations and to glyphosate, which is usually tested alone in chronic in vivo regulatory studies. We measured cytotoxicity with three assays (Alamar Blue, MTT, ToxiLight), plus genotoxicity (comet assay), anti-estrogenic (on ERalpha, ERbeta) and anti-androgenic effects (on AR) using gene reporter tests. We also checked androgen to estrogen conversion by aromatase activity and mRNA. All parameters were disrupted at sub-agricultural doses with all formulations within 24h. These effects were more dependent on the formulation than on the glyphosate concentration. First, we observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in MDA-MB453-kb2 cells for the most active formulation (R400), then from 2 ppm the transcriptional activities on both estrogen receptors were also inhibited on HepG2. Aromatase transcription and activity were disrupted from 10 ppm. Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed.

Ecotoxicol Environ Saf. 2009 Oct;72(7):2025-32. doi: 10.1016/j.ecoenv.2009.05.001. Epub 2009 Jun 2.

Effect of pesticides on cell survival in liver and brain rat tissues.

Astiz M[1], de Alaniz MJ, Marra CA.
Author information

Abstract

Pesticides are the main environmental factor associated with the etiology of human neurodegenerative disorders such as Parkinson's disease. Our laboratory has previously demonstrated that the treatment of rats with low doses of dimethoate, zineb or glyphosate alone or in combination induces oxidative stress (OS) in liver and brain. The aim of the present work was to investigate if the pesticide-induced OS was able to affect brain and liver cell survival. The treatment of Wistar rats with the pesticides (i.p. 1/250 LD50, three times a week for 5 weeks) caused loss of mitochondrial transmembrane potential and cardiolipin content, especially in substantia nigra (SN), with a concomitant increase of fatty acid peroxidation. The activation of calpain apoptotic cascade (instead of the caspase-dependent pathway) would be responsible for the DNA fragmentation pattern observed. Thus, these results may contribute to understand the effect(s) of chronic and simultaneous exposure to pesticides on cell survival.

Publication Types, MeSH Terms, Substances

J Toxicol Environ Health A. 2009;72(11-12):746-51. doi: 10.1080/15287390902841532.

Evaluation of pesticide toxicities with differing mechanisms using Caenorhabditis elegans.

Ruan QL[1], Ju JJ, Li YH, Liu R, Pu YP, Yin LH, Wang DY.

Author information

Abstract

The aim of this study was to (1) determine whether model organism Caenorhabditis elegans was sensitive to pesticides at the maximum concentration limits regulated by national agency standards, and (2) examine the multi-biological toxicities occurring as a result of exposure to pesticides. Five pesticides, namely, chlorpyrifos, imibacloprid, buprofezin, cyhalothrin, and glyphosate, with four different mechanisms of action were selected for the investigation. In accordance with national agency requirements, 4 exposed groups were used for each tested pesticide with the concentration scales ranging from 1.0 x 10(-3) to 1 mg/L. L4 larvae were exposed for 24 and 72 h, respectively. Endpoints of locomotion, propagation, and development were selected for the assay as parameters of toxicity. After exposure for 24 h, both the body bend frequency and head thrash frequency of nematodes exposed to chlorpyrifos, imibacloprid, and cyhalothrin decreased in a concentration-dependent manner, and there were significant differences between exposed groups at maximum concentration level (MCL) compared to control. The generation time of nematodes exposed to buprofezin 24 h significantly increased in a concentration-dependent manner in the highest exposed group. When exposed for 72 h, the body bend frequency and head thrash frequency of nematodes exposed to cyhalothrin markedly decreased at MCL. The generation time and brood size of nematodes exposed to buprofezin were reduced in a concentration-dependent manner. The behavior of nematodes was sensitive to pesticides with neurotoxic properties, while pesticides affecting insect growth modified the reproductive system. The effects of pesticides on nematodes exposed for 24 h appeared more sensitive than with exposure for 72 h. Caenorhabditis elegans may thus be used for assessing the adverse effects of pesticide residues in aquatic environment.

Environ Toxicol Chem. 2009 Sep;28(9):1920-9. doi: 10.1897/08-244.1.

Pea (Pisum sativum) seed production as an assay for reproductive effects due to herbicides.

Olszyk D[1], Pfleeger T, Lee EH, Plocher M.

Author information

Abstract

Even though herbicide drift can affect plant reproduction, current plant testing protocols emphasize effects on vegetative growth. In this study, we determined whether a short-growing season plant can indicate potential effects of herbicides on seed production. Pea (Pisum sativum cv. Dakota) plants were grown in mineral soil in pots under greenhouse conditions. Plants were treated with a variety of herbicides (dicamba, clopyralid, glufosinate, glyphosate, 2-methyl-4-chlorophenoxyacetic acid, primisulfuron, or sulfometuron) at below standard field application rates applied at a vegetative stage of growth (approximately 14 d after emergence) or at flowering (approximately 20 d after emergence). Pea seed production was greatly reduced by sulfometuron at the minimum concentration used (0.001 x field application rate), with an effective concentration producing a 25% reduction in seed dry weight of 0.00007 x field application rate. Primisulfuron and glyphosate had a 25% reduction in seed dry weight for seed dry weight of 0.0035 and 0.0096 x field application rate, respectively. Clopyralid and dicamba reduced pea seed dry weight at a 25% reduction in seed dry weight of approximately 0.07 x field application rate. Glufosinate only reduced pea seed weight in one experiment, with a 25% reduction in seed dry weight of 0.07 and 0.008 x field application rate at vegetative growth and flowering stages, respectively. Pea seed dry weight was not affected by 2-methyl-4-chlorophenoxyacetic acid. Plant developmental stage had no consistent effect on herbicide responses. Reduced seed production occurred with some herbicides (especially acetolactate synthase inhibitors), which caused little or no reduction in plant height or shoot biomass and little visible injury. Thus, pea may be a model species to indicate seed reproductive responses to herbicides, with seed production obtained by extending plant growth for usually only 7 d longer than the period usually used in the vegetative vigor test.

Environ Mol Mutagen. 2009 Dec;50(9):800-7. doi: 10.1002/em.20495.

Evaluation of genome damage and its relation to oxidative stress induced byglyphosate in human lymphocytes in vitro.

Mladinic M[1], Berend S, Vrdoljak AL, Kopjar N, Radic B, Zeljezic D.

Author information

Abstract

In the present study we evaluated the genotoxic and oxidative potential of glyphosate on human lymphocytes at concentrations likely to be encountered in residential and occupational exposure. Testing was done with and without metabolic activation (S9). Ferric-reducing ability of plasma (FRAP), thiobarbituric acid reactive substances (TBARS) and the hOGG1 modified comet assay were used to measure glyphosate's oxidative potential and its impact on DNA. Genotoxicity was evaluated by alkaline comet and analysis of micronuclei and other nuclear instabilities applying centromere probes. The alkaline comet assay showed significantly increased tail length (20.39 microm) and intensity (2.19%) for 580 microg/ml, and increased tail intensity (1.88%) at 92.8 microg/ml, compared to control values of 18.15 mum for tail length and 1.14% for tail intensity. With S9, tail length was significantly increased for all concentrations tested: 3.5, 92.8, and 580 microg/ml. Using the hOGG1 comet assay, a significant increase in tail intensity was observed at 2.91 microg/ml with S9 and 580 microg/ml without S9. Without S9, the frequency of micronuclei, nuclear buds and nucleoplasmic bridges slightly increased at concentrations 3.5 microg/ml and higher. The presence of S9 significantly elevated the frequency of nuclear instabilities only for 580 microg/ml. FRAP values slightly increased only at 580 microg/ml regardless of metabolic activation, while TBARS values increased significantly. Since for any of the assays applied, no clear dose-dependent effect was observed, it indicates that glyphosate in concentrations relevant to human exposure do not pose significant health risk.

Related citations

Publication Types, MeSH Terms, Substances

J Biol Chem. 2009 Apr 10;284(15):9854-60. doi: 10.1074/jbc.M809771200. Epub 2009 Feb 11.

Structural basis of glyphosate resistance resulting from the double mutation Thr97 -> Ile and Pro101 -> Ser in 5-enolpyruvylshikimate-3-phosphate synthase from Escherichia coli.

Funke T[1], Yang Y, Han H, Healy-Fried M, Olesen S, Becker A, Schönbrunn E.

Author information

Abstract

The shikimate pathway enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) is the target of the broad spectrum herbicide glyphosate. The genetic engineering of EPSPS led to the introduction ofglyphosate-resistant crops worldwide. The genetically engineered corn lines NK603 and GA21 carry distinct EPSPS enzymes. CP4 EPSPS, expressed in NK603 corn and transgenic soybean, cotton, and canola, belongs to class II EPSPS, glyphosate-insensitive variants of this enzyme isolated from certain Gram-positive bacteria. GA21 corn, on the other hand, was created by point mutations of class I EPSPS, such as the enzymes from Zea mays or Escherichia coli, which are sensitive to low glyphosate concentrations. The structural basis of the glyphosate resistance resulting from these point mutations has remained obscure. We studied the kinetic and structural effects of the T97I/P101S double mutation, the molecular basis for GA21 corn, using EPSPS from E. coli. The T97I/P101S enzyme is essentially insensitive to glyphosate (K(i) = 2.4 mm) but maintains high affinity for the substrate phosphoenolpyruvate (PEP) (K(m) = 0.1 mm). The crystal structure at 1.7-A resolution revealed that the dual mutation causes a shift of residue Gly(96) toward theglyphosate binding site, impairing efficient binding of glyphosate, while the side chain of Ile(97) points away from the substrate binding site, facilitating PEP utilization. The single site T97I mutation renders the enzyme sensitive to glyphosate and causes a substantial decrease in the affinity for PEP. Thus, only the concomitant mutations of Thr(97) and Pro(101) induce the conformational changes necessary to produce catalytically efficient, glyphosate-resistant class I EPSPS.

Chem Res Toxicol. 2009 Jan;22(1):97-105. doi: 10.1021/tx800218n.

Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells.

Benachour N[1], Séralini GE.

Author information

Abstract

We have evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup formulations, from 10(5) times dilutions, on three different human cell types. This dilution level is far below agricultural recommendations and corresponds to low levels of residues in food or feed. The formulations have been compared to G alone and with its main metabolite AMPA or with one known adjuvant of R formulations, POEA. HUVEC primary neonate umbilical cord vein cells have been tested with 293 embryonic kidney and JEG3 placental cell lines. All R formulations cause total cell death within 24 h, through an inhibition of themitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase measuring membrane damage. They also induce apoptosis via activation of enzymatic caspases 3/7 activity. This is confirmed by characteristic DNA fragmentation, nuclear shrinkage (pyknosis), and nuclear fragmentation (karyorrhexis), which is demonstrated by DAPI in apoptotic round cells. G provokes only apoptosis, and HUVEC are 100 times more sensitive overall at this level. The deleterious effects are not proportional to G concentrations but rather depend on the nature of the adjuvants. AMPA and POEA separately and synergistically damage cell membranes like R but at different concentrations. Their mixtures are generally even more harmful with G. In conclusion, the R adjuvants like POEA change human cell permeability and amplify toxicity induced already by G, through apoptosis and necrosis. The real threshold of G toxicity must take into account the presence of adjuvants but also G metabolism and time-amplified effects or bioaccumulation. This should be discussed when analyzing the in vivo toxic actions of R. This work clearly confirms that the adjuvants in Roundup formulations are not inert. Moreover, the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R formulation-treated crops.

Vopr Pitan. 2008;77(5):13-7.

[Medical and biological safety assessment of genetically modified maize event MON 88017. Report 2. Genotoxicologic, immunologic and allergologic examinations].

[Article in Russian]

Tyshko NV, Britsina MV, Gmoshinskiĭ IV, Zhanataev AK, Zakharova NS, Zorin SN, Mazo VK, Semenov BF.

Abstract

There are presented the results of genotoxicologic, immunologic and allergologic examinations which were conducted within the framework of integrated medical and biological assessment of genetically modified rootworm Diabrotica spp.--protected and glyphosate tolerant maize event MON 88017. Analysis of damages of DNA and structural chromosome aberrations, assessment of the allergenic potential and immunoreactive properties has not confirmed any genotoxic, allergenic and immunotoxic effect of maize event MON 88017.

Related citations

Publication Types, MeSH Terms, Substances

Mutat Res. 2009 Jan 31;672(2):95-102. doi: 10.1016/j.mrgentox.2008.10.007. Epub 2008 Oct 30.

Genotoxicity of the herbicide formulation Roundup (glyphosate) in broad-snouted caiman (Caiman latirostris) evidenced by the Comet assay and the Micronucleus test.

Poletta GL[1], Larriera A, Kleinsorge E, Mudry MD.

Author information

Abstract

The genotoxicity of pesticides is an issue of worldwide concern. The present study was undertaken to evaluate the genotoxic potential of a widely used herbicide formulation, Roundup (glyphosate), in erythrocytes of broad-snouted caiman (Caiman latirostris) after in ovo exposure. Caiman embryos were exposed at early embryonic stage to different sub-lethal concentrations of Roundup (50, 100, 200, 300, 400, 500, 750, 1000, 1250 and 1750microg/egg). At time of hatching, blood samples were obtained from each animal and two short-term tests, the Comet assay and the Micronucleus (MN) test, were performed on erythrocytes to assess DNA damage. A significant increase in DNA damage was observed at a concentration of 500microg/egg or higher, compared to untreated control animals ($p<0.05$). Results from both the Comet assay and the MN test revealed a concentration-dependent effect. This study demonstrated adverse effects of Roundup on DNA of C. latirostris and confirmed that the Comet assay and the MN test applied on caiman erythrocytes are useful tools in determining potential genotoxicity of pesticides. The identification of sentinel species as well as sensitive biomarkers among the natural biota is imperative to thoroughly evaluate genetic damage, which has significant consequences for short- and long-term survival of the natural species.

Related citations

Publication Types, MeSH Terms, Substances

Ecotoxicol Environ Saf. 2009 Mar;72(3):834-7. doi: 10.1016/j.ecoenv.2008.09.019. Epub 2008 Nov 14.

Genotoxicity of AMPA, the environmental metabolite of glyphosate, assessed by the Comet assay and cytogenetic tests.

Mañas F[1], Peralta L, Raviolo J, García Ovando H, Weyers A, Ugnia L, Gonzalez Cid M, Larripa I, Gorla N.

Author information

Abstract

Formulations containing glyphosate are the most widely used herbicides in the world. AMPA is the major environmental breakdown product of glyphosate. The purpose of this study is to evaluate the in vitrogenotoxicity of AMPA using the Comet assay in Hep-2 cells after 4h of incubation and the chromosome aberration (CA) test in human lymphocytes after 48h of exposition. Potential in vivo genotoxicity was evaluated through the micronucleus test in mice. In the Comet assay, the level of DNA damage in exposed cells at 2.5-7.5mM showed a significant increase compared with the control group. In human lymphocytes we found statistically significant clastogenic effect AMPA at 1.8mM compared with the control group. In vivo, the micronucleus test rendered significant statistical increases at 200-400mg/kg. AMPA was genotoxic in the three performed tests. Very scarce data are available about AMPA potential genotoxicity.

J Environ Qual. 2008 Oct 23;37(6):2070-82. doi: 10.2134/jeq2007.0376. Print 2008 Nov-Dec.

Effects of low concentrations of herbicides on full-season, field-grown potatoes.

Pfleeger T[1], Olszyk D, Plocher M, Yilma S.

Author information

Abstract

Current phytotoxicity plant test protocols for US pesticide registration require testing for effects on seedling emergence and early growth without regard to other important factors, such as plant reproduction. Yield and quality reduction can have significant economic and ecological effects. Therefore, field trials were conducted to determine if potato (Solanum tubersum L.) vegetative growth and tuber yield and quality were affected by herbicides at below recommended field rates. Potatoes were grown in fields at the Oregon State University Horticulture Farm with herbicides applied at below recommended field application rates 14 d after emergence (DAE) or at 28 DAE. Plant height was measured before and 14 d after application. Visual foliar injury was rated 14 d after application, and tuber yield and quality parameters were measured at harvest (120 DAE). Some tubers were grown in the greenhouse the following year to determine if there were carry-over effects. Potato vegetation and tuber yield quality were generally more affected by herbicides applied at 14 DAE than at 28 DAE. Tuber yield and quality parameters were more affected by lower herbicide rates than were plant height or injury. There were significant yield losses caused by low rates of sulfometuron methyl and imazapyr and, to a lesser extent, with glyphosate and cloransulam-methyl. Bromoxynil and MCPA ((4-chloro-2-methylphenoxy)acetic) acid had little effect on the plants. Vegetative responses did not accurately predict yield and quality responses of tubers; therefore, reproductive responses should be considered in phytotoxicity test protocols for pesticide registration in the USA.

Related citations

Publication Types, MeSH Terms, Substances

Toxicol In Vitro. 2008 Dec;22(8):1853-60. doi: 10.1016/j.tiv.2008.09.006. Epub 2008 Sep 18.

Hepatoma tissue culture (HTC) cells as a model for investigating the effects of low concentrations of herbicide on cell structure and function.

Malatesta M[1], Perdoni F, Santin G, Battistelli S, Muller S, Biggiogera M.

Author information

Abstract

Previous studies on mice fed genetically modified (GM) soybean demonstrated modifications of themitochondrial functions and of the transcription/splicing pathways in hepatocytes. The cause(s) of these alterations could not be conclusively established but, since the GM soybean used is tolerant to glyphosateand was treated with the glyphosate-containing herbicide Roundup , the possibility exists that the effects observed may be due to herbicide residues. In order to verify this hypothesis, we treated HTC cells with 1-10mM Roundup and analysed cellular features by flow cytometry, fluorescence and electron microscopy. Under these experimental conditions, the death rate and the general morphology of HTC cells were not affected, as well as most of the cytoplasmic organelles. However, in HTC-treated cells, lysosome density increased and mitochondrial membranes modified indicating a decline in the respiratory activity. Moreover, nuclei underwent morpho-functional modifications suggestive of a decreased transcriptional/splicing activity. Although we cannot exclude that other factors than the presence of the herbicide residues could be responsible for the cellular modifications described in GM-fed mice, the concordance of the effects induced by low concentrations of Roundup on HTC cells suggests that the presence of Roundup residues could be one of the factors interfering with multiple metabolic pathways.

Mutat Res. 2008 Aug-Sep;655(1-2):41-6. doi: 10.1016/j.mrgentox.2008.06.010.

Genotoxic effects of Roundup on the fish Prochilodus lineatus.

Cavalcante DG[1], Martinez CB, Sofia SH.
Author information

Abstract

Glyphosate-based herbicides, such as Roundup, represent the most extensively used herbicides worldwide, including Brazil. Despite its extensive use, the genotoxic effects of this herbicide are not completely understood and studies with Roundup show conflicting results with regard to the effects of this product on the genetic material. Thus, the aim of this study was to evaluate the genotoxic effects of acute exposures (6, 24 and 96 h) to 10 mg L(-1) of Roundup on the neotropical fish Prochilodus lineatus. Accordingly, fish erythrocytes were used in the comet assay, micronucleus test and for the analysis of the occurrence of nuclear abnormalities and the comet assay was adjusted for branchial cells. The results showed that Roundupproduces genotoxic damage in erythrocytes and gill cells of P. lineatus. The comet scores obtained for P. lineatus erythrocytes after 6 and 96 h of exposure to Roundup were significantly higher than respective negative controls. For branchial cells comet scores were significantly higher than negative controls after 6 and 24 h exposures. The frequencies of micronucleus and other erythrocyte nuclear abnormalities (ENAs) were not significantly different between Roundup exposed fish and their respective negative controls, for all exposure periods. In conclusion, the results of this work showed that Roundup produced genotoxic effects on the fish species P. lineatus. The comet assay with gill cells showed to be an important complementary tool for detecting genotoxicity, given that it revealed DNA damage in periods of exposure that erythrocytes did not. ENAs frequency was not a good indicator of genotoxicity, but further studies are needed to better understand the origin of these abnormalities.

Related citations

Publication Types, MeSH Terms, Substances

Int J Cancer. 2008 Oct 1;123(7):1657-63. doi: 10.1002/ijc.23589.

Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis.

Eriksson M[1], Hardell L, Carlberg M, Akerman M.

Author information

Abstract

We report a population based case-control study of exposure to pesticides as risk factor for non-Hodgkin lymphoma (NHL). Male and female subjects aged 18-74 years living in Sweden were included during December 1, 1999, to April 30, 2002. Controls were selected from the national population registry. Exposure to different agents was assessed by questionnaire. In total 910 (91 %) cases and 1016 (92%) controls participated. Exposure to herbicides gave odds ratio (OR) 1.72, 95% confidence interval (CI) 1.18-2.51. Regarding phenoxyacetic acids highest risk was calculated for MCPA; OR 2.81, 95% CI 1.27-6.22, all these cases had a latency period >10 years. Exposure to glyphosate gave OR 2.02, 95% CI 1.10-3.71 and with >10 years latency period OR 2.26, 95% CI 1.16-4.40. Insecticides overall gave OR 1.28, 95% CI 0.96-1.72 and impregnating agents OR 1.57, 95% CI 1.07-2.30. Results are also presented for different entities of NHL. In conclusion our study confirmed an association between exposure to phenoxyacetic acids and NHL and the association with glyphosate was considerably strengthened.

J Toxicol Environ Health A. 2008;71(15):984-91. doi: 10.1080/01932690801934513.

Placental passage of benzoic acid, caffeine, and glyphosate in an ex vivo human perfusion system.

Mose T[1], Kjaerstad MB, Mathiesen L, Nielsen JB, Edelfors S, Knudsen LE.

Author information

Abstract

Ex vivo perfusion of the human term placenta is a method to study placental transfer without extrapolation from animal to human and with no ethical concerns for mother and child. However, ex vivo placenta perfusion has a limited potential within chemical screening and testing as the method is time-consuming. This study was an attempt to construct data needed to develop quantitative structure-activity relationship (QSAR) models that are able to predict placental transfer of new compounds. Placental transfer is a biological activity that statistically may be related to the physiochemical properties of a given group of compounds. Benzoic acid, caffeine, and glyphosate were chosen as model compounds because they are small molecules with large differences in physiochemical properties. Caffeine crossed the placenta by passive diffusion. The initial transfer rate of benzoic acid was more limited in the first part of the perfusion compared to caffeine, but reached the same steady-state level by the end of perfusion. The transfer of glyphosate was restricted throughout perfusion, with a lower permeation rate, and only around 15% glyphosate in maternal circulation crossed to the fetal circulation during the study period.

Environ Pollut. 2008 Dec;156(3):1099-104. doi: 10.1016/j.envpol.2008.04.016. Epub 2008 Jun 6.

Is the growth stimulation by low doses of glyphosate sustained over time?

Cedergreen N[1].

Author information

Abstract

The herbicide, glyphosate, has been shown to stimulate growth in a range of species when applied at doses of 5-60 g a.e.ha(-1), corresponding to realistic spray drift events. This study investigates growth of shoot parameters over time to detect whether the glyphosate induced growth increase was sustained and had a final effect on reproduction. The results showed that an actual biomass growth rate increase took place within the first week after spraying with glyphosate doses <60 g a.e.ha(-1). This initial growth boost kept treated plants larger than untreated plants for up to six weeks, but at harvest there was no significant difference between control plants and treated plants. Possible effects of glyphosate hormesis on the competitive ability of spray drift affected plants are discussed.

Environ Sci Pollut Res Int. 2008 May;15(3):266-72.

Acute toxic hazard evaluations of glyphosate herbicide on terrestrial vertebrates of the Oregon coast range.

McComb BC[1], Curtis L, Chambers CL, Newton M, Bentson K.

Author information

Abstract

GOAL, SCOPE AND BACKGROUND: The degree to which dose responses of model organisms (lab rodents) can adequately predict dose responses of free-ranging wild mammals or amphibians is unknown, and the relative sensitivity of such species to body loading of a toxicant such as glyphosate is seldom reported. For relative effects of dosage, we compare sensitivity of nine wild vertebrate species to effects of high doses ofglyphosate in Swiss-Webster laboratory mice both by gavage and by intraperitoneal injection. We also evaluate sublethal effects of herbicide exposure on behavior and reproductive success of one mammal and one amphibian species. **METHODS:** Comparisons of acute toxicity of glyphosate were made with intraperitoneal dosings of technicalglyphosate isopropylamine salt to nine species of terrestrial vertebrates (five amphibians, four mammals) and compared with responses in Swiss-Webster laboratory mice. Animals collected from sites that had no recent herbicide application were allowed 7-14 days to equilibrate in captivity before treatment. **RESULTS:** Median lethal dose ranged from 800 to 1,340 mg kg(-1) in mammals, and 1,170 to >2,000 mg kg(-1) in amphibians, with Oregon vole being the most sensitive. White lab mice were in the middle of the mammalian range. Tailed frog, at >2,000 mg kg(-1) was the least sensitive. Calibration of IP sensitivity to oral administration by gavage indicated that roughly four times as much glyphosate must be administered to obtain a comparable estimate of lethality. Administration by gavage in highly concentrated solutions tended to cause physical injury, hence may prove less useful as a relative indicator of toxicity. When sublethal dosages were given to roughskin newts or chipmunks, mobility and use of cover appeared largely unaffected. **DISCUSSION:** Direct toxic effects of spraying glyphosate under normal forest management seem unlikely for the nine species examined. Nor could we detect significant indirect effects of exposure on behavior and use of cover features in two species. There may be effects on other aspects of the field biology of these animals, such as reproductive rates, which we did not investigate. Recent field data indicate that changes in habitat quality following herbicide application can result in high reproductive activity in species associated with the grasses and forbs that proliferate following field applications. **CONCLUSIONS:** When compared to field data on body burdens of wild mammals exposed after aerial application of glyphosate at maximum rates in forests, there seems to be a large margin of safety between dosages encountered and those causing either death or limitation of movement, foraging or shelter. **RECOMMENDATIONS AND PERSPECTIVES:** Margins of safety for small mammals and amphibians appear to be large under any probable exposure scenarios, however our results indicate high variability in responses among species. Uncertainty introduced into field studies from unknown sources of mortality (e.g, likely predation) must be considered when interpreting our results.

Commun Agric Appl Biol Sci. 2007;72(3):557-9.

Sublethal effects of two neurotoxican insecticides on Araneus pratensis (Araneae: Araneidae).

Benamú MA[1], Schneider MI, Pineda S, Sanchez NE, Gonzalez A.

Author information

Abstract

Spiders are important predators of several agricultural pests and they play an important role as indicators of ecosystem disturb. In Argentina, soybean crop has increased from the introduction of transgenic soybean resistant to glyphosate. This expansion produced an increase in the use of conventional and non-selective pesticides to control soybean pests. The objective of this work was to evaluate the side effects of subletal concentrations of two neurotoxican insecticides with a different mode of action: endosulfan (Glex, 35%, 25 mg/l a.i.) and spinosad (Tracer, 48%, 30 and 3 mg/l a.i) on Araneus pratensis. The insecticides were applied by ingestion of the treated prey (Musca domestica), and the effects on mortality, prey consumption, web building, mating, ootheca construction and fecundity were determined. Spinosad (30 mg/l a.i.) produced higher mortality than endosulfan (25 mg/l a.i.). Tremors and non-coordinated movements were observed in this treatment. The prey consumption was significantly reduced by the two insecticides (approximately 40% lower than control). The spider web building was significantly affected by the two insecticides, but spinosad had a greater effect. Though mating was not affected by both pesticides, abnormal oothecas and dehydrated eggs were observed. This work reports that sublethal concentrations representing approximately from 25 to 2.5% of the maximum field recommended concentrations (105 and 120 mg/l a.i., respectively) showed negative effects on A. pratensis. The consequences of these effects on role of A. pratensis as a natural mortality factor of soybean pests are discussed.

Chemosphere. 2008 May;71(10):1816-22. doi: 10.1016/j.chemosphere.2008.02.001. Epub 2008 Apr 3.

Toxicity of the herbicide glyphosate to Chordodes nobilii (Gordiida, Nematomorpha).

Achiorno CL[1], Villalobos Cd, Ferrari L.

Author information

Abstract

Nematomorpha (horsehair worms) is a poorly known group of worm-like animals similar to nematodes. Adults are free-living and reproduction takes place in freshwater environments, where preparasitic larvae undergo development. All species have a parasitic juvenil stage and infection may result in the host's death, insects being the most frequent host. Most of the life cycle occurs in freshwater environments, which are often contaminated by different pollutants. Based on the lack of information on the toxicity of herbicides to horsehair worms, the objective of this study is to evaluate the effect of different concentrations of glyphosate(technical grade and formulated product) on Chordodes nobilii (Gordiida, Nematomorpha). Bioassays were performed with embryos and larvae (preparasitic stages), and adults (postparasitic stage). Test organisms were exposed for a short period of time to concentrations ranging between 0.1 and 8 mga.e.l(-1) of glyphosate(technical and formulated). Although embryo development was not inhibited, there was a significant decrease in the infective capacity of larvae derived from eggs that had been exposed to >or= 0.1mg/l. Similar results were obtained for directly exposed larvae. No differences in toxicity were detected between the active ingredient and formulated product. Adult exposed for 96 h to 1.76 mgl(-1) formulated Gly shown a mortality of 50%. Results indicate that C. nobilii is affected at glyphosate concentrations lower than those expected to be found in freshwater environments and those specified in the legislation.

Related citations

Publication Types, MeSH Terms, Substances

J Agric Food Chem. 2008 Feb 27;56(4):1517-23. doi: 10.1021/jf072581i. Epub 2008 Jan 16.

Genotoxic potential of glyphosate formulations: mode-of-action investigations.

Heydens WF[1], Healy CE, Hotz KJ, Kier LD, Martens MA, Wilson AG, Farmer DR.

Author information

Abstract

A broad array of in vitro and in vivo assays has consistently demonstrated that glyphosate and glyphosate-containing herbicide formulations (GCHF) are not genotoxic. Occasionally, however, related and contradictory data are reported, including findings of mouse liver and kidney DNA adducts and damage following intraperitoneal (ip) injection. Mode-of-action investigations were therefore undertaken to determine the significance of these contradictory data while concurrently comparing results from ip and oral exposures. Exposure by ip injection indeed produced marked hepatic and renal toxicity, but oral administration did not. The results suggest that ip injection of GCHF may induce secondary effects mediated by local toxicity rather than genotoxicity. Furthermore, these results continue to support the conclusion that glyphosate and GCHF are not genotoxic under exposure conditions that are relevant to animals and humans.

J Soc Biol. 2007;201(3):317-27.

[Sea urchin embryo, DNA-damaged cell cycle checkpoint and the mechanisms initiating cancer development].

[Article in French]

Bellé R[1], Le Bouffant R, Morales J, Cosson B, Cormier P, Mulner-Lorillon O.

Author information

Abstract

Cell division is an essential process for heredity, maintenance and evolution of the whole living kingdom. Sea urchin early development represents an excellent experimental model for the analysis of cell cycle checkpoint mechanisms since embryonic cells contain a functional DNA-damage checkpoint and since the whole sea urchin genome is sequenced. The DNA-damaged checkpoint is responsible for an arrest in the cell cycle when DNA is damaged or incorrectly replicated, for activation of the DNA repair mechanism, and for commitment to cell death by apoptosis in the case of failure to repair. New insights in cancer biology lead to two fundamental concepts about the very first origin of cancerogenesis. Cancers result from dysfunction of DNA-damaged checkpoints and cancers appear as a result of normal stem cell (NCS) transformation into acancer stem cell (CSC). The second aspect suggests a new definition of "cancer", since CSC can be detected well before any clinical evidence. Since early development starts from the zygote, which is a primary stem cell, sea urchin early development allows analysis of the early steps of the cancerization process. Although sea urchins do not develop cancers, the model is alternative and complementary to stem cells which are not easy to isolate, do not divide in a short time and do not divide synchronously. In the field of toxicology and incidence on human health, the sea urchin experimental model allows assessment of cancerrisk from single or combined molecules long before any epidemiologic evidence is available. Sea urchin embryos were used to test the worldwide used pesticide Roundup that contains glyphosate as the active herbicide agent; it was shown to activate the DNA-damage checkpoint of the first cell cycle of development. The model therefore allows considerable increase in risk evaluation of new products in the field of cancer and offers a tool for the discovery of molecular markers for early diagnostic in cancer biology. Prevention and early diagnosis are two decisive elements of human cancer therapy.

Related citations

Publication Types, MeSH Terms

Pest Manag Sci. 2008 Apr;64(4):392-401.

Simulation modelling to understand the evolution and management of glyphosateresistance in weeds.

Neve P[1].

Author information

Abstract

BACKGROUND:
A simulation model is used to explore the influence of biological, ecological, genetic and operational (management) factors on the probability and rate of glyphosate resistance in model weed species.

RESULTS:
Glyphosate use for weed control prior to crop emergence is associated with low risks of resistance. These low risks can be further reduced by applying glyphosate in sequence with other broad-spectrum herbicides prior to crop seeding. Post-emergence glyphosate use, associated with glyphosate-resistant crops, very significantly increases risks of resistance evolution. Annual rotation with conventional crops reduces these risks, but the proportion of resistant populations can only be reduced to close to zero by mixing two of three post-emergence glyphosate applications with alternative herbicide modes of action. Weed species that are prolific seed producers with high seed bank turnover rates are most at risk of glyphosateresistance evolution. The model is especially sensitive to the initial frequency of R alleles, and other genetic and reproductive parameters, including weed breeding system, dominance of the resistance trait and relative fitness, influence rates of resistance.

CONCLUSION:
Changing patterns of glyphosate use associated with glyphosate-resistant crops are increasing risks of evolved glyphosate resistance. Strategies to mitigate these risks can be explored with simulation models. Models can also be used to identify weed species that are most at risk of evolvingglyphosate resistance.

Related citations

Full Text Online Wiley Online Library

MeSH Terms, Substances

J Occup Med Toxicol. 2007 Nov 26;2:15.

Bias analysis applied to Agricultural Health Study publications to estimate non-random sources of uncertainty.

Lash TL[1].
Author information

Abstract

BACKGROUND:
The associations of pesticide exposure with disease outcomes are estimated without the benefit of a randomized design. For this reason and others, these studies are susceptible to systematic errors. I analyzed studies of the associations between alachlor and glyphosate exposure and cancerincidence, both derived from the Agricultural Health Study cohort, to quantify the bias and uncertainty potentially attributable to systematic error.

METHODS:
For each study, I identified the prominent result and important sources of systematic error that might affect it. I assigned probability distributions to the bias parameters that allow quantification of the bias, drew a value at random from each assigned distribution, and calculated the estimate of effect adjusted for the biases. By repeating the draw and adjustment process over multiple iterations, I generated a frequency distribution of adjusted results, from which I obtained a point estimate and simulation interval. These methods were applied without access to the primary record-level dataset.

RESULTS:
The conventional estimates of effect associating alachlor and glyphosate exposure with cancerincidence were likely biased away from the null and understated the uncertainty by quantifying only random error. For example, the conventional p-value for a test of trend in the alachlor study equaled 0.02, whereas fewer than 20% of the bias analysis iterations yielded a p-value of 0.02 or lower. Similarly, the conventional fully-adjusted result associating glyphosate exposure with multiple myeloma equaled 2.6 with 95% confidence interval of 0.7 to 9.4. The frequency distribution generated by the bias analysis yielded a median hazard ratio equal to 1.5 with 95% simulation interval of 0.4 to 8.9, which was 66% wider than the conventional interval.

CONCLUSION:
Bias analysis provides a more complete picture of true uncertainty than conventional frequentist statistical analysis accompanied by a qualitative description of study limitations. The latter approach is likely to lead to overconfidence regarding the potential for causal associations, whereas the former safeguards against such overinterpretations. Furthermore, such analyses, once programmed, allow rapid implementation of alternative assignments of probability distributions to the bias parameters, so elevate the plane of discussion regarding study bias from characterizing studies as "valid" or "invalid" to a critical and quantitative discussion of sources of uncertainty.

Hum Exp Toxicol. 2007 Sep;26(9):747-52.

Alteration of estrogen-regulated gene expression in human cells induced by the agricultural and horticultural herbicide glyphosate.

Hokanson R[1], Fudge R, Chowdhary R, Busbee D.

Author information

Abstract

Gene expression is altered in mammalian cells (MCF-7 cells), by exposure to a variety of chemicals that mimic steroid hormones or interact with endocrine receptors or their co-factors. Among those populations chronically exposed to these endocrine disruptive chemicals are persons, and their families, who are employed in agriculture or horticulture, or who use agricultural/horticultural chemicals. Among the chemicals most commonly used, both commercially and in the home, is the herbicide glyphosate. Although glyphosateis commonly considered to be relatively non-toxic, we utilized in vitro DNA microarray analysis of this chemical to evaluate its capacity to alter the expression of a variety of genes in human cells. We selected a group of genes, determined by DNA microarray analysis to be dysregulated, and used quantitative real-time PCR to corroborate their altered states of expression. We discussed the reported function of those genes, with emphasis on altered physiological states that are capable of initiating adverse health effects that might be anticipated if gene expression were significantly altered in either adults or embryos exposed in utero.

Bull Environ Contam Toxicol. 2007 Nov;79(5):529-32. Epub 2007 Sep 21.

Effect of pesticides on the reproductive output of Eisenia fetida.

Yasmin S[1], D'Souza D.
Author information

Abstract

We investigated the effects of three different pesticides (carbendazim, dimethoate, and glyphosate) and their mixture on the growth and reproduction of the earthworm species, Eisenia fetida. The study was conducted following the suggestion of the International Workshop on Earthworm Ecotoxicology. The results showed that the pesticide treatment had a marked negative impact on the growth and reproduction of earthworms. Carbendazim and dimethoate were found to cause greater harm to the selected earthworm species thanglyphosate.

Transgenic Res. 2008 Jun;17(3):417-24. Epub 2007 Aug 14.

Recovery of transgenic plants by pollen-mediated transformation in Brassica juncea.

Wang J[1], Li Y, Liang C.

Author information

Abstract

The aroA-M1 encoding the mutant of 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS) was introduced into the Brassica juncea genome by sonication-assisted, pollen-mediated transformation. The plasmid DNA and collected pollen grains were mixed in 0.3 mol/L sucrose solution and treated with mild ultrasonication. The treated pollen was then pollinated onto the oilseed stigmas after the stamens were removed artificially. Putative transgenic plants were obtained by screening germinating seeds on a medium containing glyphosate. Southern blot analysis of glyphosate-resistant plants indicated that the aroA-M1 gene had been integrated into the oilseed genome. Western blot analysis further confirmed that the EPSPS coded by aroA-M1 gene was expressed in transgenic plants. The transgenic plants exhibited increased resistance to glyphosate compared to untransformed plants. Some of those transgenic plants had considerably high resistance to glyphosate. The genetic analysis of T1 progeny further confirmed that the inheritance of the introduced genes followed the Mendelian rules. The results indicated that foreign genes can be transferred by pollen-mediated transformation combined with mild ultrasonication.

Related citations

Publication Types, MeSH Terms, Substances

Environ Toxicol Chem. 2007 Jul;26(7):1476-80.

Oviposition site selection: pesticide avoidance by gray treefrogs.

Takahashi M[1].
Author information

Abstract

Effects of glyphosate-formulated herbicides on nontarget organisms have received much recent attention. Although previous studies have explored the effects of pesticides on growth, development, and mortality of various amphibian species, no studies have tested the potential effects of herbicides on oviposition site selection by amphibians. Recent studies have found that a combination of pesticide and predatory cues lead to significantly increased mortality of tadpoles of several anuran species relative to that caused by pesticide alone. In the present study, I tested two hypotheses: First, adult gray treefrogs avoid oviposition sites based on the presence of glyphosate formulation (Roundup). Second, pesticide avoidance is manifested to a greater degree when combined with predatory cues. In the spring of 2006, I conducted an outdoor experiment using artificial ponds by setting up four treatments: Predatory fish cue, Roundup (2.4 mg glyphosate acid equivalent [a.e.]/L), a combination of predatory fish cue + Roundup, and a control. This experiment was designed to assess oviposition site choice among the four treatments by gray treefrogs based on the number of eggs laid in each treatment. Gray treefrogs avoided oviposition in pools contaminated with fish cue and/ or Roundupand placed the significant majority of their eggs in control pools, which suggests that breeding adults may be able to prevent lethal exposure of herbicide to their offspring through oviposition site selection. The present study provided the first evidence that the concentration of herbicide that is expected to be found in the field potentially alters oviposition site choice by amphibians. However, the concentration of 2.4 mg a.e./L is unlikely ubiquitous in nature. Thus, the further investigation of environmental relevancy of this finding is critical.

Related citations

Publication Types, MeSH Terms, Substances

Arch Toxicol. 2007 Sep;81(9):665-73. Epub 2007 Jul 19.

Pre- and postnatal toxicity of the commercial glyphosate formulation in Wistar rats.

Dallegrave E[1], Mantese FD, Oliveira RT, Andrade AJ, Dalsenter PR, Langeloh A.

Author information

Abstract

Glyphosate is the active ingredient and polyoxyethyleneamine is the surfactant present in the herbicideRoundup formulation commercialized in Brazil. The aim of this study was to assess the reproductive effects of glyphosate-Roundup on male and female offspring of Wistar rats exposed during pregnancy and lactation. Dams were treated orally with water or 50, 150 or 450 mg/kg glyphosate during pregnancy (21-23 days) and lactation (21 days). These doses do not correspond to human exposure levels. The results showed thatglyphosate-Roundup did not induce maternal toxicity but induced adverse reproductive effects on male offspring rats: a decrease in sperm number per epididymis tail and in daily sperm production during adulthood, an increase in the percentage of abnormal sperms and a dose-related decrease in the serum testosterone level at puberty, and signs of individual spermatid degeneration during both periods. There was only a vaginal canal-opening delay in the exposed female offspring. These findings suggest that in utero and lactational exposure to glyphosate-Roundup may induce significant adverse effects on the reproductive system of male Wistar rats at puberty and during adulthood.

Related citations

Publication Types, MeSH Terms, Substances

Int J Urol. 2007 May;14(5):375-83.

Report from the 1st Japanese Urological Association-Japanese Society of Medical Oncology joint conference, 2006: 'A step towards better collaboration between urologists and medical oncologists'.

Akaza H[1].
Author information

Erratum in

- Int J Urol. 2007 Aug;14(8):779.

Abstract

The 1st Japanese Urological Association-Japanese Society of Medical Oncology Joint Conference, titled 'A step towards better collaboration between urologists and medical oncologists', was held to coincide with the 44th Meeting of the Japan Society of Clinical Oncology, Tokyo, in October 2006. The main theme of the conference addressed the need for a subspecialty of medical oncologist within urology to keep abreast of advances in medical oncology. Urologists should become more involved in the postoperative management of urologic cancer. Consensus on the optimal way to move forward in the treatment of urological cancer is needed. The conference featured eight lectures surveying the present status of uro-oncology in Europe, the USA, Korea, Singapore, and Japan; the relationship between surgical oncologists and medical oncologists; global trends and international clinical trials in uro-oncology; and the future of urologic oncology. These were followed by a general discussion titled 'Achieving better collaboration between the surgical oncologist and the medical oncologist.' This report presents a roundup of the 1st Japanese Urological Association-Japanese Society of Medical Oncology Joint Conference.

Related citations

Publication Types, MeSH Terms

Arch Environ Contam Toxicol. 2007 Jul;53(1):126-33. Epub 2007 May 4.

Time- and dose-dependent effects of roundup on human embryonic and placental cells.

Benachour N[1], Sipahutar H, Moslemi S, Gasnier C, Travert C, Séralini GE.

Author information

Abstract

Roundup is the major herbicide used worldwide, in particular on genetically modified plants that have been designed to tolerate it. We have tested the toxicity and endocrine disruption potential of Roundup (Bioforce on human embryonic 293 and placental-derived JEG3 cells, but also on normal human placenta and equine testis. The cell lines have proven to be suitable to estimate hormonal activity and toxicity of pollutants. The median lethal dose (LD(50)) of Roundup with embryonic cells is 0.3% within 1 h in serum-free medium, and it decreases to reach 0.06% (containing among other compounds 1.27 mM glyphosate) after 72 h in the presence of serum. In these conditions, the embryonic cells appear to be 2-4 times more sensitive than the placental ones. In all instances, Roundup (generally used in agriculture at 1-2%, i.e., with 21-42 mMglyphosate) is more efficient than its active ingredient, glyphosate, suggesting a synergistic effect provoked by the adjuvants present in Roundup. We demonstrated that serum-free cultures, even on a short-term basis (1 h), reveal the xenobiotic impacts that are visible 1-2 days later in serum. We also document at lower non-overtly toxic doses, from 0.01% (with 210 microM glyphosate) in 24 h, that Roundup is an aromatase disruptor. The direct inhibition is temperature-dependent and is confirmed in different tissues and species (cell lines from placenta or embryonic kidney, equine testicular, or human fresh placental extracts). Furthermore,glyphosate acts directly as a partial inactivator on microsomal aromatase, independently of its acidity, and in a dose-dependent manner. The cytotoxic, and potentially endocrine-disrupting effects of Roundup are thus amplified with time. Taken together, these data suggest that Roundup exposure may affect humanreproduction and fetal development in case of contamination. Chemical mixtures in formulations appear to be underestimated regarding their toxic or hormonal impact.

Related citations

Publication Types, MeSH Terms, Substances

Environ Toxicol Pharmacol. 2007 May;23(3):308-13. doi: 10.1016/j.etap.2006.11.008. Epub 2006 Nov 26.

Chronic exposure to sub-lethal concentration of a glyphosate-based herbicide alters hormone profiles and affects reproduction of female Jundiá (Rhamdia quelen).

Soso AB[1], Barcellos LJ, Ranzani-Paiva MJ, Kreutz LC, Quevedo RM, Anziliero D, Lima M, Silva LB, Ritter F, Bedin AC, Finco JA.

Author information

Abstract

This work was carried out to verify the effect of a glyphosate-based herbicide on Jundiá hormones (cortisol, 17β-estradiol and testosterone), oocyte and swim-up fry production. Earthen ponds containing Jundiá females were contaminated with glyphosate (3.6mg/L); blood samples were collected from eight females from each treatment immediately before, or at 1, 10, 20, 30 and 40 days following contamination. A typical post-stress rise in cortisol levels was observed at the 20th and 40th days following exposure to glyphosate. At the 40th day, 17β-estradiol was decreased in the exposed females. A similar number of oocytes were stripped out from females from both groups; however, a lower number of viable swim-up fry were obtained from the herbicide exposed females, which also had a higher liver-somatic index (LSI). The results indicate that the presence ofglyphosate in water was deleterious to Rhamdia quelen reproduction, altering steroid profiles and egg viability.

Environ Biosafety Res. 2006 Jul-Sep;5(3):169-73. Epub 2007 Mar 28.

Gene flow from GM glyphosate-tolerant to conventional soybeans under field conditions in Japan.

Yoshimura Y [1], Matsuo K, Yasuda K.

Author information

Abstract

Natural out-crossing rates were evaluated for conventional soybeans (Glycine max (L.) Merr.) cultivated adjacent to genetically modified (GM) glyphosate-tolerant soybeans under field conditions during a four-year period in Japan. A total of 107 846 progeny of 2772 plants harvested from conventional varieties were screened for glyphosate herbicide tolerance. The highest out-crossing rates, 0.19% in 2001 and 0.16% in 2002, were observed in adjacent rows 0.7 m from the pollen source. The highest rate in 2004 was 0.052%, which was observed at 2.1 m. No out-crossing was observed in the rows 10.5 m from the pollen source over the four-year period. The farthest distances between receptor and pollen source at which out-crossing was observed were 7 m in 2001, 2.8 m in 2002, and 3.5 m in 2004. The greatest airborne pollen density during the flowering period, determined by Durham pollen samplers located between the rows of each variety, was 0.368 grains.cm(-2).day(-1), with the average value at 0.18 grains.cm(-2).day(-1), indicating that the possibility of out-crossing by wind is minimal. Thrips species and predatory Hemiptera visited the soybean flowers more frequently during the four-year period than any other common pollinators, such as bees.

Mutagenesis. 2007 Jul;22(4):263-8. Epub 2007 Apr 10.

Detection of cytogenetic and DNA damage in peripheral erythrocytes of goldfish (Carassius auratus) exposed to a glyphosate formulation using the micronucleus test and the comet assay.

Cavas T[1], Könen S.

Author information

Abstract

Glyphosate is a widely used broad-spectrum weed control agent. In the present study, an in vivo study on thegenotoxic effects of a technical herbicide (Roundup) containing isopropylamine salt of glyphosate was carried out on freshwater goldfish Carassius auratus. The fish were exposed to three doses of glyphosate formulation (5, 10 and 15 ppm). Cyclophosphamide at a single dose of 5 mg/l was used as positive control. Analysis of micronuclei, nuclear abnormalities and DNA damage were performed on peripheral erythrocytes sampled at intervals of 48, 96 and 144 h posttreatment. Our results revealed significant dose-dependent increases in the frequencies of micronuclei, nuclear abnormalities as well as DNA strand breaks. Our findings also confirmed that the alkaline comet assay and nuclear deformations in addition to micronucleus test on fish erythrocytes in vivo are useful tools in determining the potential genotoxicity of commercial herbicides.

Am J Bot. 2007 Apr;94(4):660-73. doi: 10.3732/ajb.94.4.660.

Transfer of glyphosate resistance: evidence of hybridization in Conyza (Asteraceae).

Zelaya IA[1], Owen MD, Vangessel MJ.
Author information

Abstract

Transfer of herbicide resistance genes between crops and weeds is relatively well documented; however, far less information exists for weed-to-weed interactions. The hybridization between the weedy diploids Conyza canadensis (2n = 18) and C. ramosissima (2n = 18) was investigated by monitoring transmission of the allele conferring resistance to N-phosphonomethyl glycine (glyphosate). In a multivariate quantitative trait analysis, we described the phylogenic relationship of the plants, whereas we tested seed viability to assess potential postzygotic reproductive barriers (PZRB) thus affecting the potential establishment of hybrid populations in the wild. When inflorescences were allowed to interact freely, approximately 3% of C. ramosissima or C. canadensis ova were fertilized by pollen of the opposing species and produced viable seeds; >95% of the ova were fertilized under no-pollen competition conditions (emasculation). The interspecific Conyza hybrid ( ) demonstrated an intermediate phenotype between the parents but superior resistance to glyphosate compared to the resistant C. canadensis parent. Inheritance of glyphosate resistance in the selfed ( ) followed the partially dominant nuclear, single-gene model; backcrosses confirmed successful introgression of the resistance allele to either parent. Negligible PZRB were observed in the hybrid progenies, confirming fertility of the C. canadensis × C. ramosissima nothotaxa. The implications of introgressive hybridization for herbicide resistance management and taxonomy of Conyza are discussed.

Plant Biotechnol J. 2006 Sep;4(5):477-87.

Expression of CP4 EPSPS in microspores and tapetum cells of cotton (Gossypium hirsutum) is critical for male reproductive development in response to late-stageglyphosate applications.

Chen YC[1], Hubmeier C, Tran M, Martens A, Cerny RE, Sammons RD, CaJacob C.

Author information

Abstract

Plants expressing Agrobacterium sp. strain CP4 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS) are known to be resistant to glyphosate, a potent herbicide that inhibits the activity of the endogenous plant EPSPS. The RR1445 transgenic cotton line (current commercial line for Roundup Ready Cotton) was generated using the figwort mosaic virus (FMV) 35S promoter to drive the expression of the CP4 EPSPS gene, and has excellent vegetative tolerance to glyphosate. However, with high glyphosate application rates at developmental stages later than the four-leaf stage (late-stage applications: applications that are inconsistent with the Roundup labels), RR1445 shows male sterility. Another transgenic cotton line, RR60, was generated using the FMV 35S promoter and the Arabidopsis elongation factor-1alpha promoter (AtEF1alpha) for the expression of CP4 EPSPS. RR60 has excellent vegetative and reproductive tolerance to applications of glyphosate at all developmental stages. Histochemical analyses were conducted to examine the male reproductive development at the cellular level of these cotton lines in response to glyphosateapplications, and to investigate the correlation between glyphosate injury and the expression of CP4 EPSPS in male reproductive tissues. The expression of CP4 EPSPS in RR60 was found to be strong in all malereproductive cell types. Conversely, CP4 EPSPS expression in RR1445 was low in pollen mother cells, male gametophytes and tapetum, three crucial male reproductive cell types. Our results indicate that the FMV 35S promoter, although expressing strongly in most vegetative tissues in plants, has extremely low activity in these cell types.

Related citations

Publication Types, MeSH Terms, Substances

Bull Environ Contam Toxicol. 2006 Nov;77(5):748-54.

Roundup Biactive modifies cadmium toxicity to Daphnia carinata.

Zalizniak L[1], Nugegoda D.

Author information

Reprod Toxicol. 2007 Feb;23(2):182-91. Epub 2006 Nov 11.

Effects of the herbicide Roundup on the epididymal region of drakes Anas platyrhynchos.

Oliveira AG[1], Telles LF, Hess RA, Mahecha GA, Oliveira CA.

Author information

Abstract

Exposure to the Roundup has been shown to affect StAR protein and aromatase expression and activity, pointing out that this herbicide may cause adverse effects in animal reproduction by affecting androgen and estrogen synthesis. We tested this hypothesis by investigating the in vivo effects of the Roundup on the testis and epididymal region of drake Anas platyrhynchos. The exposure to the herbicide resulted in alterations in the structure of the testis and epididymal region as well as in the serum levels of testosterone and estradiol, with changes in the expression of androgen receptors restricted to the testis. The harmful effects were more conspicuous in the proximal efferent ductules and epididymal ducts, suggesting higher sensitivity of these segments among the male genital organs. The effects were mostly dose dependent, indicating that this herbicide may cause disorder in the morphophysiology of the male genital system of animals.

Related citations

Publication Types, MeSH Terms, Substances

J Eukaryot Microbiol. 2006 Nov-Dec;53(6):435-44.

Ubiquinone synthesis and its regulation in Pneumocystis carinii.

Kaneshiro ES[1], Basselin M, Merali S, Kayser O.

Author information

Abstract

The opportunistic pathogen Pneumocystis causes a type of pneumonia in individuals with defective immune systems such as AIDS patients. Atovaquone, an analog of ubiquinone (coenzyme Q [CoQ]), is effective in clearing mild to moderate cases of the infection. Rat-derived Pneumocystis carinii was the first organism in which CoQ synthesis was clearly demonstrated to occur in both mitochondrial and microsomal subcellular fractions. Atovaquone inhibits microsomal CoQ synthesis with no effect on mitochondrial CoQ synthesis. We here report on additional studies evaluating CoQ synthesis and its regulation in the organism. Buparvaquone also inhibited CoQ synthesis and it reduced the synthesis of all four CoQ homologs in the microsomal but not the mitochondrial fraction. Glyphosate, which inhibits a reaction in the de novo synthesis of the benzoquinone moiety of CoQ reduced cellular ATP levels. Bacterial and plant quinones, and several chemically synthesized phenolics, flavanoids, and naphthoquinones that inhibit electron transport in other organisms were shown to reduce CoQ synthesis in P. carinii. The inhibitory action of naphthoquinone compounds appeared to depend on their molecular size and structural flexibility rather than redox potential. Results of experiments examining the synthesis of the polyprenyl chain of CoQ were consistent with negative feedback control of CoQ synthesis. These studies on P. carinii suggest that cellular sites and the control of CoQ synthesis in different organisms and cell types might be more diverse than previously thought.

J Chem Ecol. 2006 Dec;32(12):2733-48.

The role of indole and other shikimic acid derived maize volatiles in the attraction of two parasitic wasps.

D'Alessandro M[1], Held M, Triponez Y, Turlings TC.

Author information

Abstract

After herbivore attack, plants release a plethora of different volatile organic compounds (VOCs), which results in odor blends that are attractive to predators and parasitoids of these herbivores. VOCs in the odor blends emitted by maize plants (Zea mays) infested by lepidopteran larvae are well characterized. They are derived from at least three different biochemical pathways, but the relative importance of each pathway for the production of VOCs that attract parasitic wasps is unknown. Here, we studied the importance of shikimic acid derived VOCs for the attraction of females of the parasitoids Cotesia marginiventris and Microplitis rufiventris. By incubating caterpillar-infested maize plants in glyphosate, an inhibitor of the 5-enolpyruvylshikimate-3-phospate (EPSP) synthase, we obtained induced odor blends with only minute amounts of shikimic acid derived VOCs. In olfactometer bioassays, the inhibited plants were as attractive to naive C. marginiventris females as control plants that released normal amounts of shikimic acid derived VOCs, whereas naive M. rufiventris females preferred inhibited plants to control plants. By adding back synthetic indole, the quantitatively most important shikimic acid derived VOC in induced maize odors, to inhibited plants, we showed that indole had no effect on the attraction of C. marginiventris and that M. rufiventris preferred blends without synthetic indole. Exposing C. marginiventris females either to odor blends of inhibited or control plants during oviposition experiences shifted their preference in subsequent olfactometer tests in favor of the experienced odor. Further learning experiments with synthetic indole showed that C. marginiventris can learn to respond to this compound, but that this does not affect its choices between natural induced blends with or without indole. We hypothesize that for naïve wasps the attractiveness of an herbivore-induced odor blend is reduced due to masking by nonattractive compounds, and that during oviposition experiences in the presence of complex odor blends, parasitoids strongly associate some compounds, whereas others are largely ignored.

Ecol Appl. 2006 Oct;16(5):1967-74.

Relative fitness of transgenic vs. non-transgenic maize x teosinte hybrids: a field evaluation.

Guadagnuolo R[1], Clegg J, Ellstrand NC.

Author information

Abstract

Concern has been often expressed regarding the impact and persistence of transgenes that enter wild populations via gene flow. The impact of a transgene and its persistence are largely determined by the relative fitness of transgenic hybrids and hybrid derivatives compared to non-transgenic plants. Nevertheless, few studies have addressed this question experimentally in the field. Despite the economic importance of maize, and the fact that it naturally hybridizes with the teosinte taxon Zea mays ssp. mexicana, sometimes known as "chalco teosinte," the question has received little experimental attention in this system. Using aglyphosate-tolerant maize cultivar and chalco teosinte as parental lines, we carried out a field experiment testing (1) the relative fitness of maize x teosinte hybrids, compared to their parental taxa, as well as (2) the relative fitness of transgenic hybrids compared to non-transgenic hybrids created from the same parental stock. In order to evaluate the influence of the transgenic construct in different genetic backgrounds, our study included transgenic and non-transgenic pure maize progeny from the cultivar as well. We measured both vegetative and reproductive parameters. Our results demonstrated that hybrids have greater vigor and produced more seeds than the wild parent. However, in the absence of selective pressure from glyphosateherbicide, we did not observe any direct positive or negative impact of the transgene on the fitness or vigor of either the hybrids or pure maize progeny. We discuss our results in terms of the potential for spontaneous transgene flow and introgression from transgenic maize into sympatric teosinte.

Related citations

Publication Types, MeSH Terms

Mutagenesis. 2006 Nov;21(6):375-82. Epub 2006 Sep 23.

Comparative genotoxicity of the herbicides Roundup, Stomp and Reglone in plant and mammalian test systems.

Dimitrov BD[1], Gadeva PG, Benova DK, Bineva MV.

Author information

Abstract

The genotoxicities of the herbicides Roundup (glyphosate), Stomp (pendimethaline) and Reglone (diquat), were compared in plant (Crepis capillaris L.) and mouse bone marrow test systems using chromosomal aberrations and micronuclei. Roundup did not induce chromosomal aberrations or micronuclei in either test system. Reglone also did not induce chromosomal aberrations in either test system; however, it increased micronucleus frequency in both plant cells and mouse bone marrow polychromatic erythrocytes (PCEs). The responses of the two test systems to Stomp were quite different. Stomp did not induce chromosomal aberrations in the plant cells, but increased their incidence in mouse cells; Stomp increased the frequency of micronuclei in both test systems. The induction of micronuclei in plant cells may have been due to the spindle-destroying effect of the herbicide, since all concentrations of Stomp produced C-mitoses. The increased chromosomal aberration frequency in mouse bone marrow cells observed at later sampling times after administration of Stomp into animals suggests that the induction of aberrations may be due to biosynthesis of genotoxic metabolites. This conclusion was supported by the coincidence between the frequencies of chromosomal aberrations and of micronucleated PCEs in mouse cells. These data indicate that plant and animal assays are differentially responsive to some pesticides, and these differences may be due to metabolism and their responses to mitotic spindle disruption.

J Zhejiang Univ Sci B. 2006 Aug;7(8):623-6.

Invasion and control of water hyacinth (Eichhornia crassipes) in China.

Chu JJ[1], Ding Y, Zhuang QJ.

Author information

Abstract

By the time of primary 21st century, water hyacinth had become a serious environmental problem in China. Water hyacinth contributes to the major part of ecological hazards from the invasion of foreign plant species, which is estimated about USD 7 billion a year in values. In the past 10 years, herbicides glyphosate, 2,4-D and paraquat have been used in controlling water hyacinth in China. Although the herbicides provided effective control on the weed in some areas, they could not provide the sustainable inhibition on the weed population, while would lead to pollution of water at various levels. At present, the herbicide application on water hyacinth is forbidden in many areas of China such as Shanghai. In this situation, the asexualreproduction inhibitor, KWH02, was invented for controlling water hyacinth and it provided about 70% of growth inhibition without any risk of dead plant pollution. It has been about 10 years for bio-control of water hyacinth in China. Works focused on mainly the efficacy and safety of the utilization of foreign insects. Researches on microorganism herbicides to control water hyacinth were started and obtained primary achievements in recent years. Although there are different opinion on how to face the water hyacinth problem in China, it is accepted widely that the control methods should be high efficient and safe with low cost. Some practical measures for integrated management of water hyacinth are suggested.

Plant Physiol. 2006 Aug;141(4):1306-15. Epub 2006 Jun 9.

Glyphosate-induced anther indehiscence in cotton is partially temperature dependent and involves cytoskeleton and secondary wall modifications and auxin accumulation.

Yasuor H[1], Abu-Abied M, Belausov E, Madmony A, Sadot E, Riov J, Rubin B.

Author information

Abstract

Yield reduction caused by late application of glyphosate to glyphosate-resistant cotton (Gossypium hirsutum; GRC) expressing CP4 5-enol-pyruvylshikmate-3-P synthase under the cauliflower mosaic virus-35S promoter has been attributed to male sterility. This study was aimed to elucidate the factors and mechanisms involved in this phenomenon. Western and tissue-print blots demonstrated a reduced expression of the transgene in anthers of GRC compared to ovules of the same plants. Glyphosate application to GRC grown at a high temperature regime after the initiation of flower buds caused a complete loss of pollen viability and inhibition of anther dehiscence, while at a moderate temperature regime only 50% of the pollen grains were disrupted and anther dehiscence was normal. Glyphosate-damaged anthers exhibited a change in the deposition of the secondary cell wall thickenings (SWT) in the endothecium cells, from the normal longitudinal orientation to a transverse orientation, and hindered septum disintegration. These changes occurred only at the high temperature regime. The reorientation of SWT in GRC was accompanied by a similar change in microtubule orientation. A similar reorientation of microtubules was also observed in Arabidopsis (Arabidopsis thaliana) seedlings expressing green fluorescent protein tubulin (tubulin alpha 6) following glyphosate treatment.Glyphosate treatment induced the accumulation of high levels of indole-3-acetic acid in GRC anthers. Cotton plants treated with 2,4-dichlorophenoxyacetic acid had male sterile flowers, with SWT abnormalities in the endothecium layer similar to those observed in glyphosate-treated plants. Our data demonstrate thatglyphosate inhibits anther dehiscence by inducing changes in the microtubule and cell wall organization in the endothecium cells, which are mediated by auxin.

Commun Agric Appl Biol Sci. 2005;70(3):481-7.

Vegetative reproduction and chemical control with post-emergent herbicides of field bindweed (Convolvulus arvensis L.).

Gyenes V[1], Béres I, Lehoczky E, Kazinczi G, Nyári A.
Author information

Abstract

It is clearly seen from data that roots of Convolvulus arvensis L. have more and less intensive regenerative period during growing season. The more intensive period is in autumn, because in that time roots culminate nutrients, carbohydrate as starch and sugar. The less intensive regenerative or shoot-growing period is in spring, called "late spring bud dormancy". Experiments were conducted to get more information and further details about the regenerative capacity of roots close to and far from the collar of Convolvulus arvensis L. Root segments closer to collar have an intensive regenerative capacity than those ones further to collar. By data of Bakke et al. (1939) is well known, roots exhumed from deep soil layers are able to create shoots with low intensity. So finally we can exclaim that regenerative capacity is decreasing further to collar. Using mechanical weed control it is sufficient to till the upper layer of soil, but many times. Chemical treatments are most effective in the integrated weed control. It is clearly seen that auxin-type herbicide such as 2,4-D, fluroxipir, MCPA. dicamba give the best result. They gave 95% weed control effect used them separately or in combination with other herbicides. Combination of Banvel 480 S (dicamba) and Logran 75 WG (triasulfuron) introduced 95% weed control effect. Only one time got absolutely 100% weed control effect, in the case ofGlyphosate active substance. Caused total plant destruction. Excellent result was given with the application of Pledge 50WP (flumioxazin). Herbicides mentioned above are absolutely allowed to take an important and significant part in chemical plant protection against Convolvulus arvensis L. Other herbicides like Granstar 75DF (tribenuron-methyl), Basis 75DF (rimsulfuron + tifensulfuron-methyl) and Huszár (jodosulfuron-methyl-sodium + mefenpir-diethyl) are not so effective against Convolvulus arvensis L., as compared to the previous ones.

Commun Agric Appl Biol Sci. 2005;70(3):447-57.

Chemical control of ambrosia Artemisiifolia on non-crop areas: are there alternatives to glyphosate?

Lombard A[1], Gauvrit C, Chauvel B.

Author information

Abstract

We compared glyphosate, glufosinate and metsulfuron-methyl to control Ambrosia artemisiifolia under non-crop conditions. A laboratory study showed that A. artemisiifolia is an easy-to-wet species and that glufosinate and glyphosate are quickly absorbed by its leaves (nearly 100% in 24 h). Metsulfuron-methyl absorption was slower (about 50% in 24 h) but was strongly promoted by terpenic alcohol and esterified rapeseed oil. In the greenhouse, all three herbicides were efficacious against A. artemisiifolia, with ED50s of <23, 23 and 0.8 g ha(-1) for glufosinate, glyphosate and metsulfuron-methyl, respectively. These results were confirmed on a non-crop area for glufosinate and glyphosate, which at half the registered dose reached high efficacies at both the 4 to 6-node and flowering stages of A. artemisiifolia. By contrast, metsulfuron-methyl showed no efficacy. However, after treatment at the 4- to 6-node stage, new emergence of A. artemisiifolia led to the presence of vigorous plants that bore numerous flowers and produced high levels of pollen. After treatment at the flowering stage, flower production by A. artemisiifolia was not significantly affected, but achene weight was decreased by 60 to 70% and seed viability was only 8 to 13% for the treated plants, as compared to 85% for the control. No significant difference was observed between the two herbicides and between the doses. It is concluded that glufosinate can be an alternative to glyphosate for the chemical control of A. artemisiifolia on non-crop areas. However, with both herbicides, it is difficult to attain the two objectives of reducing seed production and pollen production by means of only one treatment.

Int J Hyg Environ Health. 2006 Jan;209(1):15-20. Epub 2005 Aug 29.

Cytogenetic effect of technical glyphosate on cultivated bovine peripheral lymphocytes.

Siviková K[1], Dianovský J.

Author information

Abstract

A technical herbicide containing isopropyl amine salt of glyphosate was tested for induction of chromosome aberrations (CA) and sister chromatid exchanges (SCE) in cultured bovine peripheral lymphocytes. Cultures were exposed to a glyphosate formulation at concentrations ranging from 28 to 1120 micromol/l without and with metabolic activation. No clastogenic effect of the herbicide was found. Its genotoxic effect was confirmed in the SCE assay after 24 h of incubation. A statistically significant elevation in SCE induction was observed in each of the donors after application of the product at doses ranging from 56 to 1120 micromol/l. The highest concentrations (560 and 1120 micromol/l) also caused reduction of mitotic and proliferation indices. In the 2 h-assay with metabolic activation a statistically significant frequency of SCE was observed only in cultures treated with the agent at a concentration of 140 micromol/l.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Biomedica. 2005 Sep;25(3):335-45.

[Cytotoxicity and genotoxicity of human cells exposed in vitro to glyphosate].

[Article in Spanish]

Monroy CM[1], Cortés AC, Sicard DM, de Restrepo HG.

Author information

Abstract

INTRODUCTION:

Glyphosate is a broad-spectrum non-selective herbicide, used to eliminate unwanted weeds in agricultural and forest settings. Herbicide action is achieved through inhibition of aromatic amino acid biosynthesis in plant cells. Since this is not a conserved mechanism between human and plant cells,glyphosate is considered to be a low health risk substance for humans. However, the occurrence of possible harmful side effects of glyphosate use is not well documented and controversial. Toxicity and genotoxicitystudies indicate that glyphosate is not harmful, although several investigations suggest that it can alter various cellular processes in animals. Therfore this has potential as a health and environmental risk factor in areas where glyphosate is widely used.

OBJECTIVES:

The present study evaluated glyphosate cytotoxic and genotoxic effects in normal human cells (GM38) and human fibrosarcoma (HT1080) cells.

MATERIALS AND METHODS:

Acute and chronic cytotoxicity were determined through the exposure of cultured cells to graded concentrations of glyphosate, and cell viability analysis was performed with crystal violet and Trypan blue staining. Genotoxicity was determined using the comet assay and data significance was evaluated with Dunnet's test.

RESULTS:

For chronic cytotoxicity a dose-dependent effect was observed in both GM38 and HT1080 cells after treatment with 5.2-8.5 mM and 0.9-3.0 mM glyphosate, respectively. In the acute cytotoxicity study, GM38 cells exposed to 4.0-7.0 mM glyphosate and HT1080 cells exposed to 4.5-5.8 mM glyphosate, had cell viability counts higher than 80%. Genotoxic effects were evidenced in GM38 cells at glyphosateconcentrations of 4.0-6.5 mM and in HT1080 cells at glyphosate concentrations of 4.75 -5.75 mM.

CONCLUSIONS:

The levels of cytotoxicity and genotoxicity of glyphosate occurring in mammalian cells suggested that its mechanism of action is not limited to plant cells.

Chemosphere. 2005 Dec;61(8):1115-22. Epub 2005 Apr 26.

Comparative effects of the Roundup and glyphosate on mitochondrial oxidative phosphorylation.

Peixoto F[1].
Author information

Abstract

The potential toxicity of the herbicide Roundup and its fundamental substance (glyphosate) was tested in bioenergetic functions of isolated rat liver mitochondria. Roundup stimulates succinate-supported respiration twice, with simultaneous collapse of transmembrane electrical potential, while glyphosate used in the same concentrations does not induce any significant effect. Additionally, Roundup depresses state 3 respiration by about 40%, at 15 mM, whereas uncoupled respiration in the presence of FCCP is depressed by about 50%. Depression of uncoupled respiratory activity is mediated through partial inhibition of mitochondrial complexes II and III, but not of complex IV. The phosphorylative system was affected by both a direct and an indirect effect on the F0F1 ATPase activity. The addition of uncoupled concentrations of Roundup to Ca2+-loadedmitochondria treated with Ruthenium Red resulted in non-specific membrane permeabilization, as evidenced by mitochondrial swelling in isosmotic sucrose medium. Therefore, the uncoupling of oxidative phosphorylation is also related to the non-specific membrane permeabilization induced by Roundup.Glyphosate alone does not show any relevant effect on the mitochondrial bioenergetics, in opposition toRoundup formulation products. The differences in the toxicity observed could be either attributed to some products of Roundup or to a synergic effect of glyphosate and formulation products. Bearing in mind thatmitochondria is provided with a variety of bioenergetic functions mandatory for the regulation of intracellular aerobic energy production and electrolyte homeostasis, these results question the safety of Roundup on animal health.

Environ Toxicol Chem. 2005 Sep;24(9):2336-40.

Toxicity of herbicides in highway runoff.

Huang X[1], Fong S, Deanovic L, Young TM.
Author information

Abstract

Previous field monitoring at two highway sites found highway-applied herbicides in storm water runoff at maximum concentrations ranging from 10 microg/L for glyphosate and diuron to as high as 200 microg/L for oryzalin. To determine whether these herbicides at these concentrations can cause any toxicity to aquatic organisms, a standard toxicity study was conducted. Storm water was collected along Highway 37, Sonoma County, California, USA, and the herbicides isoxaben, oryzalin, diuron, clopyralid, and glyphosate were spiked into the storm water at the highest concentrations observed during the five previous field-monitoring campaigns. Three different toxicity studies were conducted and the results showed the following: No significant reduction in reproduction or increase in mortality relative to the control for an 8-d Ceriodaphnia (water flea) toxicity test; no significant increase in mortality or decrease in biomass compared to the control during a 7-d Pimephales (fish) toxicity test; and, in a 96-h Selenastrum (algae) toxicity test, both the 10-microg/L diuron treatment and the combined 50-microg/L isoxaben plus 200-microg/L oryzalin treatment produced significant ($p < 0.05$) reductions in algal growth compared to the controls, although the 30-microg/L clopyralid or 10-microg/L glyphosate treatments did not exhibit any toxic effects.

Ying Yong Sheng Tai Xue Bao. 2005 Jun;16(6):1142-5.

[Effects of glyphosate on life histroy characteristics of freshwater rotifer Brachionus calyciflorus].

[Article in Chinese]

Chu Z[1], Yi Y, Xu X, Ge Y, Dong L, Chen F.

Author information

Abstract

The life table study on the life history characteristics of freshwater rotifer Brachionus calyciflorus under effects of different concentrations glyphosate showed that glyphosate had significant effects on the embryonic developmental time, duration of juvenile and reproductive periods, average lifespan, netreproductive rate, and intrinsic population increasing rate of the rotifer. The embryonic developmental time was significantly lengthened when exposed to 3 and 8 mg x L(-1) glyphosate, the juvenile period began to be lengthened significantly when exposed to 3 mg x L(-1) glyphosate, while the net reproductive rate and intrinsic population increasing rate decreased significantly when the rotifer was exposed to 8.00 and 10.50 mg x L(-1)glyphosate, respectively. Among all the parameters, intrinsic population increasing rate was the most sensitive parameter which could be used in monitoring the effects of glyphosate on the life history characteristics of B. calyciflorus.

Reprod Toxicol. 2005 Mar-Apr;19(4):501-4.

Effect of the herbicide glyphosate on liver lipoperoxidation in pregnant rats and their fetuses.

Beuret CJ[1], Zirulnik F, Giménez MS.

Author information

Abstract

Glyphosate is a post-emergence herbicide that acts on the synthesis of amino acids and other endogenous metabolites in plants. It is commonly used in agriculture, forestry, and nurseries for the control or destruction of herbaceous plants. Metabolic processes during development and pregnancy could be sensitive to changes induced by glyphosate such as lipid peroxidation. The present study has investigated the effects that 1%glyphosate oral exposure has on lipoperoxidation and antioxidant enzyme systems in the maternal serum and liver of pregnant rats and their term fetuses at 21 days of gestation. The results suggest that excessive lipid peroxidation induced with glyphosate ingestion leads to an overload of maternal and fetal antioxidant defense systems.

J Environ Sci Health B. 2005;40(1):59-67.

Alternative herbicides to manage Italian ryegrass (Lolium multiflorum lam) resistant to glyphosate at different phenological stages.

Christoffoleti PJ[1], Trentin R, Tocchetto S, Marochi A, Galli AJ, López-Ovejero RF, Nicolai M.

Author information

Abstract

During the growing season of 2002--2003, field and greenhouse experiments were conducted with the objective of evaluating the influence of Italian ryegrass phenological stages and management alternatives on the control of resistant biotypes to glyphosate. Three field experiments were conducted in Lagoa Vermelha, RS, Brazil and glyphosate was applied alone and in combinations with alternative herbicides. Two greenhouse experiments were also conducted at the Department of Crop Science, ESALQ/USP, Piracicaba, SP, Brazil. The Italian ryegrass resistant population was collected from Lagoa Vermelha, RS, Brazil. From the results it was possible to conclude that: (i) the more advanced the phenological stage of application, the more difficult the control of resistant Italian ryegrass by glyphosate, mainly by the rate of 960 g a.i. ha(-1); however, this rate applied at earlier phenological stage (five tillers), the control was higher than 90%; (ii) with the increment of glyphosate rate, it significant response was observed on the control at all stages of application; (iii) the mixture of glyphosate + clethodim (1440 + 72 g a.i. ha(-1)), paraquat + diuron (500 + 250 g a.i. ha(-1)), at all stages of application and clethodim (96 g a.i. ha(-1)) and paraquat + diuron (300 + 150 g a.i. ha(-1)) at the initial stages until pre-flowering were excellent alternatives for management of these populations; and (iv) the response of control was much faster for the mixture of glyphosate + clethodim, independently of growth stage.

Environ Health Perspect. 2005 Jan;113(1):49-54.

Cancer incidence among glyphosate-exposed pesticide applicators in the Agricultural Health Study.

De Roos AJ[1], Blair A, Rusiecki JA, Hoppin JA, Svec M, Dosemeci M, Sandler DP, Alavanja MC.

Author information

Abstract

Glyphosate is a broad-spectrum herbicide that is one of the most frequently applied pesticides in the world. Although there has been little consistent evidence of genotoxicity or carcinogenicity from in vitro and animal studies, a few epidemiologic reports have indicated potential health effects of glyphosate. We evaluated associations between glyphosate exposure and cancer incidence in the Agricultural Health Study (AHS), a prospective cohort study of 57,311 licensed pesticide applicators in Iowa and North Carolina. Detailed information on pesticide use and other factors was obtained from a self-administered questionnaire completed at time of enrollment (1993-1997). Among private and commercial applicators, 75.5% reported having ever used glyphosate, of which > 97% were men. In this analysis, glyphosate exposure was defined as a) ever personally mixed or applied products containing glyphosate; b) cumulative lifetime days of use, or "cumulative exposure days" (years of use times days/year); and c) intensity-weighted cumulative exposure days (years of use times days/year times estimated intensity level). Poisson regression was used to estimate exposure-response relations between glyphosate and incidence of all cancers combined and 12 relatively commoncancer subtypes. Glyphosate exposure was not associated with cancer incidence overall or with most of thecancer subtypes we studied. There was a suggested association with multiple myeloma incidence that should be followed up as more cases occur in the AHS. Given the widespread use of glyphosate, future analyses of the AHS will allow further examination of long-term health effects, including less common cancers.

Comment in

- Glyphosate results revisited. [Environ Health Perspect. 2005]

Free PMC Article

Related citations

MeSH Terms, Substances

J Econ Entomol. 2004 Oct;97(5):1517-23.

Field and semifield evaluation of impacts of transgenic canola pollen on survival and development of worker honey bees.

Huang ZY[1], Hanley AV, Pett WL, Langenberger M, Duan JJ.

Author information

Abstract

A 2-yr field trial (2001 and 2002) and 1-yr semifield trial (2002) were conducted to evaluate the effect of transgenic herbicide (glyphosate) -tolerant canola Brassica napus L. pollen on larval and adult honey bee, Apis mellifera L., workers. In the field trial, colonies of honey bees were moved to transgenic or nontransgenic canola fields (each at least 40 hectares) during bloom and then sampled for larval survival and adult recovery, pupal weight, and hemolymph protein concentrations. No differences in larval survival, adult recovery, and pupal weight were detected between colonies placed in nontransgenic canola fields and those in transgenic canola fields. Colonies placed in the transgenic canola fields in the 2002 field experiment showed significantly higher hemolymph protein in newly emerged bees compared with those placed in nontransgenic canola field; however, this difference was not detected in the 2001 field experiment. In the semifield trial, bee larvae were artificially fed with bee-collected transgenic and nontransgenic canola pollen and returned to their original colonies. Larval survival, pupal survival, pupal weight, and hemolymph protein concentration of newly emerged adults were measured. There were no significant differences in any of the parameters measured between larvae that were fed transgenic canola pollen and those fed nontransgenic corn pollen. Results from this study suggest that transgenic canola pollen does not have adverse effects on honey bee development and that the use of transgenic canola dose not pose any threat to honey bees.

Bull Environ Contam Toxicol. 2004 Oct;73(4):644-51.

Effects of thiophanate-methyl and glyphosate on asexual and sexual reproductionin the rotifer Brachionus calyciflorus Pallas.

Xi YL[1], Feng LK.

Author information

Related citations

SpringerLink FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Arch Environ Contam Toxicol. 2004 Apr;46(3):362-71.

Evaluation of lethality and genotoxicity in the freshwater mussel Utterbackia imbecillis (Bivalvia: Unionidae) exposed singly and in combination to chemicals used in lawn care.

Conners DE[1], Black MC.
Author information

Abstract

Many chemicals, including fertilizers, herbicides, and insecticides, are routinely applied to turf in the care and maintenance of lawns. These chemicals have the potential to leach into nearby surface waters and adversely affect aquatic biota. In this study, we evaluated the lethal and genotoxic effects of chemicals used in lawn care on an early life stage of freshwater mussels (Utterbackia imbecillis). The chemicals tested were copper and commercial formulations of atrazine, glyphosate, carbaryl, and diazinon. Mussel glochidia were exposed to chemicals singly or in combination (equitoxic and environmentally realistic mixtures) for 24 h and toxic interactions were evaluated with Marking's additive index. Genotoxicity was quantified with the alkaline single-cell gel electrophoresis assay (Comet assay). In acute tests, copper was the most toxic of all chemicals evaluated (LC50 = 37.4 microg/L) and carbaryl was the most toxic of all pesticides evaluated (LC50 = 7.9 mg/L). In comparison to other aquatic organisms commonly used in toxicity tests (e.g., amphipods, cladocerans, and chironomids), mussel glochidia were as or more sensitive to the chemicals evaluated with the exception of diazinon, where mussels were observed to be less sensitive. The combined toxicity of equitoxic and environmentally realistic mixtures to mussels was additive. Genotoxic responses were observed in mussels exposed to copper, atrazine and diazinon at levels below their respective no-observed-effect concentrations. Together, these data indicate that freshwater mussels are among the most sensitive aquatic organisms tested for some chemicals commonly used in lawn care and that DNA damage may be useful as a screening tool to evaluate potential sublethal effects of lawn care products on non-target aquatic organisms.

Bull Environ Contam Toxicol. 2004 Feb;72(2):219-24.

As the worm turns: Eisenia fetida avoids soil contaminated by a glyphosate-based herbicide.

Verrell P[1], Van Buskirk E.

Author information

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Environ Toxicol Chem. 2004 Apr;23(4):823-31.

Multiple stress effects of Vision herbicide, pH, and food on zooplankton and larval amphibian species from forest wetlands.

Chen CY[1], Hathaway KM, Folt CL.

Author information

Abstract

As part of a multiple-tier research program, interactions of the herbicide Vision (glyphosate) with two stressors, pH and food level, were examined. Effects of the formulated product Vision were tested at two test concentrations (0.75 and 1.50 mg acid equivalent/L), two pH levels (pH 5.5 and 7.5), and under high and low food concentrations. Effects of each stressor alone and in combination were examined using two common wetland taxa: Zooplankton, Simocephalus vetulus, and tadpoles (Gosner stage 25) of Rana pipiens. For S. vetulus, survival, reproduction, and development time were measured; survival was measured for R. pipiens. For both species, significant effects of the herbicide were measured at concentrations lower than the calculated worst-case value for the expected environmental concentration ([EEC], 1.40 mg acid equivalent/L). Moreover, high pH (7.5) increased the toxic effects of the herbicide on all response variables for both species even though it improved reproductive rate of S. vetulus over pH 5.5 in the absence of herbicide. Stress due to low food alone also interacted with pH 5.5 to diminish S. vetulus survival. These results support the general postulate that multiple stress interactions may exacerbate chemical effects on aquatic biota in natural systems.

Med Pr. 2003;54(6):579-83.

[Glyphosate--a non-toxic pesticide?].

[Article in Polish]

Pieniazek D[1], Bukowska B, Duda W.

Author information

Abstract

Glyphosate is currently the most commonly applied herbicide and its use is still growing. Nowadays, over 50 commercial preparations containing this compound are used, and these formulations are much more toxic than their active compound, glyphosate, owing to the presence of many surfactants and carrier compounds. Toxicological investigations provide evidence that glyphosate is an extremely "safe" herbicide for animals. This is why its use in agriculture is universal. In June 1991, the Environmental Protection Agency (EPA) categorized this compound into class E (according to EPA there are five categories of carcinogenicity), which means that it is probably not carcinogenic to humans. Unfortunately, the study carried out by Swedish oncologists in 2001 showed that glyphosate may induce cancer of the lymphatic system. The results of the Swedish study have changed our opinion about "safety" of this herbicide. Investigations concerning both its accumulation and toxic effect in animals and plants are now under way in many laboratories.

Toxicol Lett. 2004 Feb 28;147(1):35-43.

Synergistic DNA damage by oxidative stress (induced by H2O2) and nongenotoxic environmental chemicals in human fibroblasts.

Lueken A[1], Juhl-Strauss U, Krieger G, Witte I.

Author information

Abstract

Genotoxic combination effects of oxidative stress (induced by H2O2) and eight nongenotoxic environmental chemicals (4-chloroaniline, 2,3,4,6-tetrachlorophenol, lindane, 2,4-dichloroacetic acid (2,4-D), m-xylene,glyphosate, nitrilotriacetic acid and n-hexanol) were determined in human fibroblasts. Genotoxicity was measured quantitatively by the single cell gel electrophoresis assay. The nongenotoxic chemicals were used in non cytotoxic concentrations. H2O2 was used in concentrations producing low (50 microM) and no cytotoxicity (40 microM). All environmental chemicals acted in a synergistic way with H2O2 except DMSO which effectively inhibited H2O(2)-induced DNA damage. The most effective enhancers were 4-chloroaniline, 2,3,4,6-tetrachlorophenol, m-xylene, and n-hexanol. Synergistic effects of hexanol/H2O2 were still evident at a concentration of 0.09 noec (no observed effect concentration). In contrast to synergistic DNA damage in the cell antagonism was found measuring DNA breakage in isolated PM2 DNA. From the results we concluded that synergisms between H2O2 and nongenotoxic chemicals may be a general phenomenon which is not observed on the level of isolated DNA.

Publication Types, MeSH Terms, Substances

Food Chem Toxicol. 2004 Jan;42(1):29-36.

A generational study of glyphosate-tolerant soybeans on mouse fetal, postnatal, pubertal and adult testicular development.

Brake DG[1], Evenson DP.

Author information

Abstract

The health safety of transgenic soybeans (glyphosate-tolerant or Roundup Ready) was studied using the mammalian testis (mouse model) as a sensitive biomonitor of potential toxic effects. Pregnant mice were fed a transgenic soybean or a non-transgenic (conventional) diet through gestation and lactation. After weaning, the young male mice were maintained on the respective diets. At 8, 16, 26, 32, 63 and 87 days after birth, three male mice and an adult reference mouse were killed, the testes surgically removed, and the cell populations measured by flow cytometry. Multi-generational studies were conducted in the same manner. The results showed that the transgenic foodstuffs had no effect on macromolecular synthesis or cell growth and differentiation as evidenced by no differences in the percentages of testicular cell populations (haploid, diploid, and tetraploid) between the transgenic soybean-fed mice and those fed the conventional diet. Additionally, there were no differences in litter sizes and body weights of the two groups. It was concluded that the transgenic soybean diet had no negative effect on fetal, postnatal, pubertal or adult testicular development.

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Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Occup Environ Med. 2003 Sep;60(9):E11.

Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men.

De Roos AJ[1], Zahm SH, Cantor KP, Weisenburger DD, Holmes FF, Burmeister LF, Blair A.
Author information

Abstract

BACKGROUND:

An increased rate of non-Hodgkin's lymphoma (NHL) has been repeatedly observed among farmers, but identification of specific exposures that explain this observation has proven difficult.

METHODS:

During the 1980s, the National Cancer Institute conducted three case-control studies of NHL in the midwestern United States. These pooled data were used to examine pesticide exposures in farming as risk factors for NHL in men. The large sample size (n = 3417) allowed analysis of 47 pesticides simultaneously, controlling for potential confounding by other pesticides in the model, and adjusting the estimates based on a prespecified variance to make them more stable.

RESULTS:

Reported use of several individual pesticides was associated with increased NHL incidence, including organophosphate insecticides coumaphos, diazinon, and fonofos, insecticides chlordane, dieldrin, and copper acetoarsenite, and herbicides atrazine, glyphosate, and sodium chlorate. A subanalysis of these "potentially carcinogenic" pesticides suggested a positive trend of risk with exposure to increasing numbers.

CONCLUSION:

Consideration of multiple exposures is important in accurately estimating specific effects and in evaluating realistic exposure scenarios.

Toxicol Lett. 2003 Apr 30;142(1-2):45-52.

The teratogenic potential of the herbicide glyphosate-Roundup in Wistar rats.

Dallegrave E[1], Mantese FD, Coelho RS, Pereira JD, Dalsenter PR, Langeloh A.

Author information

Abstract

The aim of this study was to assess the teratogenicity of the herbicide glyphosate-Roundup (as commercialized in Brazil) to Wistar rats. Dams were treated orally with water or 500, 750 or 1000 mg/kgglyphosate from day 6 to 15 of pregnancy. Cesarean sections were performed on day 21 of pregnancy, and number of corpora lutea, implantation sites, living and dead fetuses, and resorptions were recorded. Weight and gender of the fetuses were determined, and fetuses were examined for external malformations and skeletal alterations. The organs of the dams were removed and weighed. Results showed a 50%, mortality rate for dams treated with 1000 mg/kg glyphosate. Skeletal alterations were observed in 15.4, 33.1, 42.0 and 57.3% of fetuses from the control, 500, 750 and 1000 mg/kg glyphosate groups, respectively. We may conclude that glyphosate-Roundup is toxic to the dams and induces developmental retardation of the fetal skeleton.

Related citations

Publication Types, MeSH Terms, Substances

Toxicology. 2003 Mar 14;185(1-2):67-78.

The effects of acute pesticide exposure on neuroblastoma cells chronically exposed to diazinon.

Axelrad JC[1], Howard CV, McLean WG.

Author information

Abstract

Speculation about potential neurotoxicity due to chronic exposure to low doses of organophosphate (OP) pesticides is not yet supported by experimental evidence. The objective of this work was to use a cell culture model of chronic OP exposure to determine if such exposure can alter the sensitivity of nerve cells to subsequent acute exposure to OPs or other compounds. NB2a neuroblastoma cells were grown in the presence of 25 microM diazinon for 8 weeks. The OP was then withdrawn and the cells were induced to differentiate in the presence of various other pesticides or herbicides, including OPs and OP-containing formulations. The resulting outgrowth of neurite-like structures was measured by light microscopy and quantitative image analysis and the IC(50) for each OP or formulation was calculated. The IC(50) values in diazinon-pre-exposed cells were compared with the equivalent values in cells not pre-exposed to diazinon. The IC(50) for inhibition of neurite outgrowth by acute application of diazinon, pyrethrum, glyphosate or a commercial formulation of glyphosate was decreased by between 20 and 90% after pre-treatment with diazinon. In contrast, the IC(50) for pirimiphos methyl was unaffected and those for phosmet or chlorpyrifos were increased by between 1.5- and 3-fold. Treatment of cells with chlorpyrifos or with a second glyphosate-containing formulation led to the formation of abnormal neurite-like structures in diazinon-pre-exposed cells. The data support the view that chronic exposure to an OP may reduce the threshold for toxicity of some, but by no means all, environmental agents.

Related citations

MeSH Terms, Substances

Leuk Lymphoma. 2002 May;43(5):1043-9.

Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies.

Hardell L[1], Eriksson M, Nordstrom M.

Author information

Abstract

Increased risk for non-Hodgkin's lymphoma (NHL) following exposure to certain pesticides has previously been reported. To further elucidate the importance of phenoxyacetic acids and other pesticides in the etiology of NHL a pooled analysis was performed on two case-control studies, one on NHL and another on hairy cell leukemia (HCL), a rare subtype of NHL. The studies were population based with cases identified from cancerregistry and controls from population registry. Data assessment was ascertained by questionnaires supplemented over the telephone by specially trained interviewers. The pooled analysis of NHL and HCL was based on 515 cases and 1141 controls. Increased risks in univariate analysis were found for subjects exposed to herbicides (OR 1.75, CI 95% 1.26-2.42), insecticides (OR 1.43, CI 95% 1.08-1.87), fungicides (OR 3.11, CI 95% 1.56-6.27) and impregnating agents (OR 1.48, CI 95% 1.11-1.96). Among herbicides, significant associations were found for glyphosate (OR 3.04, CI 95% 1.08-8.52) and 4-chloro-2-methyl phenoxyacetic acid (MCPA) (OR 2.62, CI 95% 1.40-4.88). For several categories of pesticides the highest risk was found for exposure during the latest decades before diagnosis. However, in multivariate analyses the only significantly increased risk was for a heterogeneous category of other herbicides than above.

Related citations

Publication Types, MeSH Terms, Substances

Environ Health Perspect. 2002 Jun;110 Suppl 3:441-9.

Birth defects, season of conception, and sex of children born to pesticide applicators living in the Red River Valley of Minnesota, USA.

Garry VF[1], Harkins ME, Erickson LL, Long-Simpson LK, Holland SE, Burroughs BL.
Author information

Abstract

We previously demonstrated that the frequency of birth defects among children of residents of the Red River Valley (RRV), Minnesota, USA, was significantly higher than in other major agricultural regions of the state during the years 1989-1991, with children born to male pesticide applicators having the highest risk. The present, smaller cross-sectional study of 695 families and 1,532 children, conducted during 1997-1998, provides a more detailed examination of reproductive health outcomes in farm families ascertained from parent-reported birth defects. In the present study, in the first year of life, the birth defect rate was 31.3 births per 1,000, with 83% of the total reported birth defects confirmed by medical records. Inclusion of children identified with birth or developmental disorders within the first 3 years of life and later led to a rate of 47.0 per 1,000 (72 children from 1,532 live births). Conceptions in spring resulted in significantly more children with birth defects than found in any other season (7.6 vs. 3.7%). Twelve families had more than one child with a birth defect (n = 28 children). Forty-two percent of the children from families with recurrent birth defects were conceived in spring, a significantly higher rate than that for any other season. Three families in the kinships defined contributed a first-degree relative other than a sibling with the same or similar birth defect, consistent with a Mendelian inheritance pattern. The remaining nine families did not follow a Mendelian inheritance pattern. The sex ratio of children with birth defects born to applicator families shows a male predominance (1.75 to 1) across specific pesticide class use and exposure categories exclusive of fungicides. In the fungicide exposure category, normal female births significantly exceed male births (1.25 to 1). Similarly, the proportion of male to female children with birth defects is significantly lower (0.57 to 1; p = 0.02). Adverse neurologic and neurobehavioral developmental effects clustered among the children born to applicators of the fumigant phosphine (odds ratio [OR] = 2.48; confidence interval [CI], 1.2-5.1). Use of the herbicide glyphosateyielded an OR of 3.6 (CI, 1.3-9.6) in the neurobehavioral category. Finally, these studies point out that (a) herbicides applied in the spring may be a factor in the birth defects observed and (b) fungicides can be a significant factor in the determination of sex of the children of the families of the RRV. Thus, two distinct classes of pesticides seem to have adverse effects on different reproductive outcomes. Biologically based confirmatory studies are needed.

J Agric Food Chem. 2002 Jan 30;50(3):506-12.

Tolerance and accumulation of shikimic acid in response to glyphosateapplications in glyphosate-resistant and nonglyphosate-resistant cotton (Gossypium hirsutum L.).

Pline WA[1], Wilcut JW, Duke SO, Edmisten KL, Wells R.
Author information

Abstract

Measurement of shikimic acid accumulation in response to glyphosate inhibition of 5-enolpyruvylshikimate-3-phosphate synthase is a rapid and accurate assay to quantify glyphosate-induced damage in sensitive plants. Two methods of assaying shikimic acid, a spectrophotometric and a high-performance liquid chromatography (HPLC) method, were compared for their accuracy of recovering known amounts of shikimic acid spiked into plant samples. The HPLC method recovered essentially 100% of shikimic acid as compared with only 73% using the spectrophotometric method. Relative sensitivity to glyphosate was measured in glyphosate-resistant (GR) and non-GR cotton leaves, fruiting branches, and squares (floral buds) by assaying shikimic acid. Accumulation of shikimic acid was not observed in any tissue, either GR or non-GR, at rates of 5 mMglyphosate or less applied to leaves. All tissues of non-GR plants accumulated shikimic acid in response toglyphosate treatment; however, only fruiting branches and squares of GR plants accumulated a slight amount of shikimic acid. In non-GR cotton, fruiting branches and squares accumulated 18 and 11 times, respectively, more shikimic acid per micromolar of translocated glyphosate than leaf tissue, suggesting increased sensitivity to glyphosate of reproductive tissue over vegetative tissue. GR cotton leaves treated with 80 mM of glyphosate accumulated 57 times less shikimic acid per micromolar of translocated glyphosate than non-GR cotton but only 12.4- and 4-fold less in fruiting branches and squares, respectively. The increased sensitivity of reproductive structures to glyphosate inhibition may be due to a higher demand for shikimate pathway products and may provide an explanation for reports of fruit abortion from glyphosate-treated GR cotton.

Related citations

Publication Types, MeSH Terms, Substances

J Nematol. 2001 Dec;33(4):214-8.

Evaluation of Pea and Soybean as Trap Crops for Managing Heterodera glycines.

Chen SY, Porter PM, Reese CD, Klossner LD, Stienstra WC.

Abstract

Trap crops that stimulate nematode egg hatching but not reproduction have been reported as an effective means for managing certain nematodes. Studies were carried out at two field sites each year in 1998 and 1999 to evaluate the potential of trapping the soybean cyst nematode (Heterodera glycines) with soybean and pea in the corn year to manage the nematode in Minnesota. The trap crops were planted on the same day as corn at each site and later killed with the herbicide glyphosate. Nematode egg densities were determined at planting, 1 and 2 months after planting, and at harvest. Treatments included four seeding rates (0, 124,000, 247,000, and 494,000 seeds/ha) of resistant soybean as a trap crop and four kill dates (3, 4, 5, and 6 weeks after planting). No effects of the trap-crop and kill-date treatments on H. glycines population density, corn yield, and the followingyear soybean yield were observed at the two locations. In a second study, the experiment included four trap-crop comparisons (resistant soybean at 494,000 seeds/ha, susceptible soybean at 494,000 seeds/ha, pea at 1,482,000 seeds/ha, and no trap crop) and five kill dates (3, 4, 5, 6 weeks after planting, and no-kill). At the Waseca site, egg density at harvest was lower where resistant soybean was grown for 6 weeks and where pea was grown for 5 and 6 weeks compared with where no trap crop was grown. Maintaining pea plants for more than 5 weeks, however, reduced corn yield by 20% at the Waseca site. At the Lamberton site, egg density at harvest was lower where the susceptible soybean was grown for 5 weeks compared with where no trap crop was grown. Even with significant reduction of eggs in some treatments, use of soybean and pea as trap crops in the corn year was not an effective means for managing H. glycines.

KEYWORDS:

Glycine max; Heterodera glycines; Pisum sativum; management; pea; soybean; soybean cyst nematode; trap crop

Environ Health Perspect. 2001 Aug;109(8):851-7.

An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population.

Arbuckle TE[1], Lin Z, Mery LS.
Author information

Abstract

The toxicity of pesticides on human reproduction is largely unknown--particularly how mixtures of pesticide products might affect fetal toxicity. The Ontario Farm Family Health Study collected data by questionnaire on the identity and timing of pesticide use on the farm, lifestyle factors, and a complete reproductive history from the farm operator and eligible couples living on the farm. A total of 2,110 women provided information on 3,936 pregnancies, including 395 spontaneous abortions. To explore critical windows of exposure and target sites for toxicity, we examined exposures separately for preconception (3 months before and up to month of conception) and postconception (first trimester) windows and for early (< 12 weeks) and late (12-19 weeks) spontaneous abortions. We observed moderate increases in risk of early abortions for preconception exposures to phenoxy acetic acid herbicides [odds ratio (OR) = 1.5; 95% confidence interval (CI), 1.1-2.1], triazines (OR = 1.4; 95% CI, 1.0-2.0), and any herbicide (OR = 1.4; 95% CI, 1.1-1.9). For late abortions, preconception exposure to glyphosate (OR = 1.7; 95% CI, 1.0-2.9), thiocarbamates (OR = 1.8; 95% CI, 1.1-3.0), and the miscellaneous class of pesticides (OR = 1.5; 95% CI, 1.0-2.4) was associated with elevated risks. Postconception exposures were generally associated with late spontaneous abortions. Older maternal age (> 34 years of age) was the strongest risk factor for spontaneous abortions, and we observed several interactions between pesticides in the older age group using Classification and Regression Tree analysis. This study shows that timing of exposure and restricting analyses to more homogeneous endpoints are important in characterizing the reproductive toxicity of pesticides.

Mar Environ Res. 2000 Jul-Dec;50(1-5):263-6.

Effects of the herbicide Roundup on the ultrastructural pattern of hepatocytes in carp (Cyprinus carpio).

Szarek J[1], Siwicki A, Andrzejewska A, Terech-Majewska E, Banaszkiewicz T.
Author information

Abstract

Experimental studies were performed on healthy, 80-100 g carp (Cyprinus carpio). Fish were exposed by emersion in Roundup (205 mg of glyphosate/l or 410 mg of glyphosate/l) in concentrations of 40- to 20-fold lower than those used in practice. Electron microscopy revealed that the herbicide caused appearance of myelin-like structures in carp hepatocytes, swelling of mitochondria and disappearance of internal membrane of mitochondria in carp at both exposure concentrations. It means that Roundup was harmful to carp when used in applied concentrations. Results of these studies enhance our knowledge of ultrastructural pathomorphology of fish organs following exposure to Roundup.

Related citations

MeSH Terms, Substances

Toxicol In Vitro. 2001 Apr;15(2):143-51.

Herbicides and the microtubular apparatus of Nicotiana tabacum pollen tube: immunofluorescence and immunogold labelling studies.

Ovidi E[1], Gambellini G, Taddei AR, Cai G, Del Casino C, Ceci M, Rondini S, Tiezzi A.
Author information

Abstract

Herbicides are chemical compounds widely used in agriculture. As their intensive application is becoming a cause of environmental pollution, detailed and more sophisticated investigations are needed to understand better their consequences at the biological level. After herbicides are dispersed in the fields, they establish chemical interactions with both target and non-target plants. In both cases, herbicides can interact with the plant reproductive apparatus; consequently they could play a role during the fertilisation process in higher plants. Using an antibody to the alpha-tubulin subunit in immunofluorescence and immunoelectron microscopy techniques, we investigated the distribution of microtubules in Nicotiana tabacum pollen tubes grown under in vitro conditions in the presence of five different herbicides selected among those used frequently in central Italy. Herbicides have a specific effect on the microtubular apparatus of both pollen tube and generative cell. In addition to other tests and assays, these results suggest that the microtubule cytoskeleton of pollen tubes can be used as a bioindicator for studying the toxicity effects induced by herbicides.

MeSH Terms, Substances

Environ Res. 2001 Mar;85(3):226-31.

Effect of the herbicide glyphosate on enzymatic activity in pregnant rats and their fetuses.

Daruich J[1], Zirulnik F, Gimenez MS.

Author information

Abstract

To prevent health risk from environmental chemicals, particularly for progeny, we have studied the effects of the herbicide glyphosate on several enzymes of pregnant rats. Glyphosate is an organophosphorated nonselective agrochemical widely used in many countries including Argentina and acts after the sprout in a systemic way. We have studied three cytosolic enzymes: isocitrate dehydrogenase-NADP dependent, glucose-6-phosphate dehydrogenase, and malic dehydrogenase in liver, heart, and brain of pregnant Wistar rats. The treatment was administered during the 21 days of pregnancy, with 1 week as an acclimation period. The results suggest that maternal exposure to agrochemicals during pregnancy induces a variety of functional abnormalities in the specific activity of the enzymes in the studied organs of the pregnant rats and their fetuses.

Vet Parasitol. 2001 Feb 26;95(2-4):241-9.

In vitro quantitative analysis of (3)H-uracil incorporation by Sarcocytis neurona to determine efficacy of anti-protozoal agents.

Marsh AE[1], Mullins AL, Lakritz J.
Author information

Abstract

Parasite-specific incorporation of (3)H-uracil was used to assess the replication of Sarcocystis neurona, a protozoal parasite associated with equine protozoal myeloencephalitis (EPM). Anti-protozoal drugs, pyrimethamine (0.01, 0.1 and 1.0microg/ml PYR), sulfadiazine (5microg/ml; SDZ), sulfamethoxazole (5microg/ml; SMZ), diclazuril (100ng/ml; DCZ), atovaquone (0.04ng/ml; ATQ), tetracycline (5microg/ml; TET) and the herbicide glyphosate (1.5 and 4.5mM; GLY) were studied with varying S. neurona parasite densities (2x10(1)-1.2x10(6)merozoites/well). A microtiter plate format was used to test these compounds, and incorporation of (3)H-uracil was determined using a semi-automated plate harvester and liquid scintillation counter. When PYR, DCZ, ATQ, SMZ, SDZ, and TET were tested, the assay was most reliable when parasite densities were greater than 9.0x10(4) individual merozoites per well. When the herbicide GLY was tested, as few as 900 individual merozoites were sufficient to demonstrate reduction in parasite proliferation. Of the anti-protozoal drugs commonly used to treat EPM, PYR was the most potent anti-S. neurona agent tested. The herbicide GLY appears to be more potent than all of the other compounds tested in vitro; however information regarding in vivo use of GLY is not available, and central nervous system penetration by this compound is unlikely. Incorporation of (3)H-uracil by replicating S. neurona is quantitative and can be used in a semi-automated assay. This in vitro assay is capable of high throughput screening of candidate drugs that may have applications in a clinical setting. Further studies using a wider range of drug concentrations with optimal numbers of merozoites are necessary to determine true potency of these agents.

Related citations

Publication Types, MeSH Terms, Substances

Plant J. 2001 Feb;25(3):261-70.

Plastid-expressed 5-enolpyruvylshikimate-3-phosphate synthase genes provide high level glyphosate tolerance in tobacco.

Ye GN[1], Hajdukiewicz PT, Broyles D, Rodriguez D, Xu CW, Nehra N, Staub JM.
Author information

Abstract

Plastid transformation (transplastomic) technology has several potential advantages for biotechnological applications including the use of unmodified prokaryotic genes for engineering, potential high-level gene expression and gene containment due to maternal inheritance in most crop plants. However, the efficacy of a plastid-encoded trait may change depending on plastid number and tissue type. We report a feasibility study in tobacco plastids to achieve high-level herbicide resistance in both vegetative tissues and reproductiveorgans. We chose to test glyphosate resistance via over-expression in plastids of tolerant forms of 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS). Immunological, enzymatic and whole-plant assays were used to prove the efficacy of three different prokaryotic (Achromobacter, Agrobacterium and Bacillus) EPSPS genes. Using the Agrobacterium strain CP4 EPSPS as a model we identified translational control sequences that direct a 10,000-fold range of protein accumulation (to >10% total soluble protein in leaves). Plastid-expressed EPSPS could provide very high levels of glyphosate resistance, although levels of resistance in vegetative and reproductive tissues differed depending on EPSPS accumulation levels, and correlated to the plastid abundance in these tissues. Paradoxically, higher levels of plastid-expressed EPSPS protein accumulation were apparently required for efficacy than from a similar nuclear-encoded gene. Nevertheless, the demonstration of high-level glyphosate tolerance in vegetative and reproductive organs using transplastomic technology provides a necessary step for transfer of this technology to other crop species.

Environ Health Perspect. 2000 Aug;108(8):769-76.

Roundup inhibits steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression.

Walsh LP[1], McCormick C, Martin C, Stocco DM.
Author information

Abstract

Recent reports demonstrate that many currently used pesticides have the capacity to disrupt reproductivefunction in animals. Although this reproductive dysfunction is typically characterized by alterations in serum steroid hormone levels, disruptions in spermatogenesis, and loss of fertility, the mechanisms involved in pesticide-induced infertility remain unclear. Because testicular Leydig cells play a crucial role in malereproductive function by producing testosterone, we used the mouse MA-10 Leydig tumor cell line to study the molecular events involved in pesticide-induced alterations in steroid hormone biosynthesis. We previously showed that the organochlorine insecticide lindane and the organophosphate insecticide Dimethoate directly inhibit steroidogenesis in Leydig cells by disrupting expression of the steroidogenic acute regulatory (StAR) protein. StAR protein mediates the rate-limiting and acutely regulated step in steroidogenesis, the transfer of cholesterol from the outer to the inner mitochondrial membrane where the cytochrome P450 side chain cleavage (P450scc) enzyme initiates the synthesis of all steroid hormones. In the present study, we screened eight currently used pesticide formulations for their ability to inhibit steroidogenesis, concentrating on their effects on StAR expression in MA-10 cells. In addition, we determined the effects of these compounds on the levels and activities of the P450scc enzyme (which converts cholesterol to pregnenolone) and the 3beta-hydroxysteroid dehydrogenase (3beta-HSD) enzyme (which converts pregnenolone to progesterone). Of the pesticides screened, only the pesticide Roundup inhibited dibutyryl [(Bu)(2)]cAMP-stimulated progesterone production in MA-10 cells without causing cellular toxicity. Roundup inhibited steroidogenesis by disrupting StAR protein expression, further demonstrating the susceptibility of StAR to environmental pollutants.

J Toxicol Environ Health A. 2000 Jul 28;60(6):423-39.

In vitro studies of cellular and molecular developmental toxicity of adjuvants, herbicides, and fungicides commonly used in Red River Valley, Minnesota.

Lin N[1], Garry VF.
Author information

Abstract

Recent epidemiologic studies showed increased frequency of birth defects in pesticide applicators and general population of the Red River Valley, Minnesota. These studies further indicated that this crop growing area used more chlorophenoxy herbicides and fungicides than elsewhere in Minnesota. Based on frequency of use and known biology, certain herbicides, pesticide additives, fungicides, and mycotoxins are suspect agents. To define whether these agents affect developmental endpoints in vitro, 16 selected agrochemicals were examined using the MCF-7 breast cancer cell line. In the flow cytometric assay, cell proliferation in this estrogen-responsive cell line indicates xenobiotic-mediated estrogenic effects. Cell viability, morphology, ploidy, and apoptosis were incorporated in this assay. Data showed that the adjuvants X-77 and Activate Plus induced significant cell proliferation at 0.1 and 1 microg/ml. The commercial-grade herbicides 2,4-D LV4 and 2,4-D amine induced cell proliferation at 1 and 10 microg/ml. The reagent-grade 2,4-D products failed to induce proliferation over the same concentration range, suggesting that other ingredients in the commercial products, presumably adjuvants, could be a factor in these results. The fungicides triphenyltin and mancozeb induced apoptosis at concentrations of 4.1 microg/ml (10(-5) M) and 50 microg/ml, respectively. Triphenyltin also induced aneuploidy (C2/M arrest) at 0.41 microg/ml (10(-6) M). Data provide a mechanistic step to understanding human reproductive and developmental effects in populations exposed to these agrochemicals, and initiative to focusing limited resources for future in vivo animal developmental toxicity studies.

Related citations

Publication Types, MeSH Terms, Substances, Grant Support

Environ Mol Mutagen. 2000;36(1):40-6.

Use of the Drosophila wing spot test in the genotoxicity testing of different herbicides.

Kaya B[1], Creus A, Yanikoğlu A, Cabré O, Marcos R.

Author information

Abstract

Four herbicides, namely propanil, maleic hydrazide, glyphosate, and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), were investigated for genotoxicity in the wing spot test of Drosophila melanogaster. The herbicides were administered by chronic feeding to 3-day-old larvae. Two different crosses, a standard (ST) and a high-bioactivation (HB) cross, involving the flare-3 (flr(3)) and the multiple wing hairs (mwh) markers, were used. The HB cross uses flies characterized by an increased cytochrome P-450-dependent bioactivation capacity, which permits a more efficient biotransformation of promutagens and procarcinogens. In both crosses, the wings of the two types of progeny, which are inversion-free marker heterozygotes and balancer heterozygotes, were analyzed. Maleic hydrazide and glyphosate proved to be more genotoxic in the ST cross, whereas propanil appeared to be slightly more genotoxic in the HB cross. On the other hand, the herbicide 2,4,5-T increased the mutation frequency for only the small single spots in the ST cross.

Related citations

Full Text Online Wiley Online Library

Publication Types, MeSH Terms, Substances

Regul Toxicol Pharmacol. 2000 Apr;31(2 Pt 1):117-65.

Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans.

Williams GM[1], Kroes R, Munro IC.
Author information

Abstract

Reviews on the safety of glyphosate and Roundup herbicide that have been conducted by several regulatory agencies and scientific institutions worldwide have concluded that there is no indication of any human health concern. Nevertheless, questions regarding their safety are periodically raised. This review was undertaken to produce a current and comprehensive safety evaluation and risk assessment for humans. It includes assessments of glyphosate, its major breakdown product [aminomethylphosphonic acid (AMPA)], itsRoundup formulations, and the predominant surfactant [polyethoxylated tallow amine (POEA)] used inRoundup formulations worldwide. The studies evaluated in this review included those performed for regulatory purposes as well as published research reports. The oral absorption of glyphosate and AMPA is low, and both materials are eliminated essentially unmetabolized. Dermal penetration studies with Roundup showed very low absorption. Experimental evidence has shown that neither glyphosate nor AMPA bioaccumulates in any animal tissue. No significant toxicity occurred in acute, subchronic, and chronic studies. Direct ocular exposure to the concentrated Roundup formulation can result in transient irritation, while normal spray dilutions cause, at most, only minimal effects. The genotoxicity data for glyphosate and Roundup were assessed using a weight-of-evidence approach and standard evaluation criteria. There was no convincing evidence for direct DNA damage in vitro or in vivo, and it was concluded that Roundup and its components do not pose a risk for the production of heritable/somatic mutations in humans. Multiple lifetime feeding studies have failed to demonstrate any tumorigenic potential for glyphosate. Accordingly, it was concluded thatglyphosate is noncarcinogenic. Glyphosate, AMPA, and POEA were not teratogenic or developmentally toxic. There were no effects on fertility or reproductive parameters in two multigeneration reproduction studies withglyphosate. Likewise there were no adverse effects in reproductive tissues from animals treated withglyphosate, AMPA, or POEA in chronic and/or subchronic studies. Results from standard studies with these materials also failed to show any effects indicative of endocrine modulation. Therefore, it is concluded that the use of Roundup herbicide does not result in adverse effects on development, reproduction, or endocrine systems in humans and other mammals. For purposes of risk assessment, no-observed-adverse-effect levels (NOAELs) were identified for all subchronic, chronic, developmental, and reproduction studies withglyphosate, AMPA, and POEA. Margins-of-exposure for chronic risk were calculated for each compound by dividing the lowest applicable NOAEL by worst-case estimates of chronic exposure. Acute risks were assessed by comparison of oral LD50 values to estimated maximum acute human exposure. It was concluded that, under present and expected conditions of use, Roundup herbicide does not pose a health risk to humans.

Related citations

Publication Types, MeSH Terms, Substances

Cancer. 1999 Aug 15;86(4):729-31.

A case-control study of non-Hodgkin lymphoma and exposure to pesticides.

Acquavella J, Farmer D, Cullen MR.

Comment on

- A case-control study of non-Hodgkin lymphoma and exposure to pesticides. [Cancer. 1999]

Related citations

Publication Types, MeSH Terms, Substances

Mutat Res. 1998 Jul 17;403(1-2):13-20.

Genotoxicity and oxidative stress induced by pesticide exposure in bovine lymphocyte cultures in vitro.

Lioi MB[1], Scarfì MR, Santoro A, Barbieri R, Zeni O, Di Berardino D, Ursini MV.
Author information

Abstract

The genotoxic activity of the pesticides gliphosate, vinclozolin and DPX-E9636 was studied in in vitro cultures of bovine lymphocytes, using chromosome aberration (CA) and sister chromatid exchange (SCE) frequencies as genetic end-points and a variation of glucose 6-phosphate dehydrogenase (G6PD) enzyme activity as a marker of changes in the normal cell redox state. Results indicated a statistically significant increase of structural aberrations, sister chromatid exchanges and G6PD activity, suggesting that the pesticides tested induce either oxidative stress or a mutagenic effect in this species. The evaluation of both mitotic index and cell viability, after pesticide exposure, demonstrates a high cytotoxic effect which is always associated with the observed genotoxic effect.

Publication Types, MeSH Terms, Substances

Am J Epidemiol. 1997 Dec 15;146(12):1025-36.

Male pesticide exposure and pregnancy outcome.

Savitz DA[1], Arbuckle T, Kaczor D, Curtis KM.
Author information

Abstract

Potential health effects of agricultural pesticide use include reproductive outcomes. For the Ontario Farm Family Health Study, the authors sampled Ontario farms from the 1986 Canadian Census of Agriculture, identified farm couples, and obtained questionnaire data concerning farm activities, reproductive health experience, and chemical applications. Male farm activities in the period from 3 months before conception through the month of conception were evaluated in relation to miscarriage, preterm delivery, and small-for-gestational-age births. Among the 1,898 couples with complete data (64% response), 3,984 eligible pregnancies were identified. Miscarriage was not associated with chemical activities overall but was increased in combination with reported use of thiocarbamates, carbaryl, and unclassified pesticides on the farm. Preterm delivery was also not strongly associated with farm chemical activities overall, except for mixing or applying yard herbicides (odds ratio = 2.1, 95% confidence interval 1.0-4.4). Combinations of activities with a variety of chemicals (atrazine, glyphosate, organophosphates, 4-[2,4-dichlorophenoxy] butyric acid, and insecticides) generated odds ratios of two or greater. No associations were found between farm chemicals and small-for-gestational-age births or altered sex ratio. Based on these data, despite limitations in exposure assessment, the authors encourage continued evaluation of male exposures, particularly in relation to miscarriage and preterm delivery.

Comment in

- Re: "Male pesticide exposure and pregnancy outcome". [Am J Epidemiol. 1999]

Free full text

Related citations

Publication Types, MeSH Terms, Substances, Grant Support

Environ Mol Mutagen. 1997;29(3):277-88.

Genotoxicity of select herbicides in Rana catesbeiana tadpoles using the alkaline single-cell gel DNA electrophoresis (comet) assay.

Clements C[1], Ralph S, Petras M.
Author information

Abstract

Pesticides are broadly used for pest control in agriculture despite possible negative impacts they may pose to the environment. Thus, we examined the DNA damage caused by five herbicides commonly used in southern Ontario (Canada). Erythrocytes from Rana catesbeiana (bullfrog) tadpoles were evaluated for DNA damage following exposure to selected herbicides, using the alkaline single-cell gel DNA electrophoresis (SCG) or "comet" assay [Singh et al. (1988): Exp Cell Res 175:184-191; Ralph et al. (1996): Eviron Mol Mutagen 28:112-120]. This approach involves detection, under alkaline conditions, of DNA fragments that upon electrophoresis migrate from the nuclear care, resulting in a comet formation. The herbicides tested, along with their active ingredients, were AAtrex Nine-O (atrazine), Dual-960E (metalochlor), Roundup (glyphosate), Sencor-500F (metribuzin), and Amsol (2,4-D amine). Tadpoles were exposed in the laboratory for a 24-hr period to several concentrations of the herbicides dissolved in dechlorinated water. Methyl methanesulphonate was used as a positive control. The herbicides AAtrex Nine-O-, Dual-960E-, Roundup-, and Sencor-500F-treated tadpoles showed significant DNA damage when compared with unexposed control animals, whereas, Amsol-treated tadpoles did not. Unlike the other responding herbicides, Sencor-500F did not show a relationship between dosage and DNA damage. In summary, the results indicate that at least some of the herbicides currently used in southern Ontario are capable of inducing DNA damage in tadpoles.

Related citations

Publication Types, MeSH Terms, Substances

J Environ Sci Health B. 1996 Jan;31(1):99-115.

A sensitive sperm-motility test for the assessment of cytotoxic effect of pesticides.

Yousef MI[1], Bertheussen K, Ibrahim HZ, Helmi S, Seehy MA, Salem MH.

Author information

Abstract

A sensitive sperm-motility test for the evaluation of cytotoxic effects of carbofuran and glyphosate in a defined protein-free culture medium is described. The sperm motility was compared to that obtained with a protein-containing medium. The use of protein-free medium considerably increased the sensitivity of sperm cells from rabbit and human to the toxic effects of the pesticide. The respective IC50 values (the concentration needed to cause 50% inhibition of sperm motility) in protein-free medium of carbofuran andglyphosate were 321 and 48.2 microM with human sperm, and 116 and 23.5 microM with rabbit sperm. Whereas, the corresponding values in protein-containing medium were 920 and 740 microM, and 910 and 500 microM with human and rabbit sperm, respectively. Our results show that testing human and rabbit sperm in protein-free medium proves to be a more sensitive method than that in protein-containing medium. Additionally, the use of rabbit sperm is a more sensitive test system than human sperm. This study suggests that the rabbit sperm test appears to have a potential for the assessment of toxicity on human reproduction.

Related citations

MeSH Terms, Substances

J Environ Sci Health B. 1995 Jul;30(4):513-34.

Toxic effects of carbofuran and glyphosate on semen characteristics in rabbits.

Yousef MI[1], Salem MH, Ibrahim HZ, Helmi S, Seehy MA, Bertheussen K.

Author information

Abstract

The present study was undertaken to investigate the effect of chronic treatment with two sublethal doses of Carbofuran (carbamate insecticide) and Glyphosate (organophosphorus herbicide) on body weight and semen characteristics in mature male New Zealand white rabbits. Pesticide treatment resulted in a decline in body weight, libido, ejaculate volume, sperm concentration, semen initial fructose and semen osmolality. This was accompanied with increases in the abnormal and dead sperm and semen methylene blue reduction time. The hazardous effect of these pesticides on semen quality continued during the recovery period, and was dose-dependent. These effects on sperm quality may be due to the direct cytotoxic effects of these pesticides on spermatogenesis and/or indirectly via hypothalami-pituitary-testis axis which control the reproductiveefficiency.

Mutat Res. 1993 Jun;300(1):29-36.

Genotoxicity testing of the herbicide Roundup and its active ingredient glyphosateisopropylamine using the mouse bone marrow micronucleus test, Salmonella mutagenicity test, and Allium anaphase-telophase test.

Rank J[1], Jensen AG, Skov B, Pedersen LH, Jensen K.

Author information

Abstract

The genotoxic potential of the herbicide Roundup and its active agent, glyphosate isopropylamine salt, was studied in three different assays. No clastogenic effects were found in the mouse bone marrow micronucleus test for either of the two agents. In the Salmonella assay only Roundup was tested. It showed a weak mutagenic effect for the concentrations 360 micrograms/plate in TA98 (without S9) and 720 micrograms/plate in TA100 (with S9). These concentrations are close to the toxic level. The anaphase-telophase Allium test showed no effect for the glyphosate isopropylamine salt, but a significant increase in chromosome aberrations appeared after treatment with Roundup at concentrations of 1.44 and 2.88 mg/l when calculated as glyphosateisopropylamine. The most frequent aberrations observed could be characterized as disturbances of the spindle.

Mutat Res. 1992 May 1;279(1):9-13.

Importance of the type of soil for the induction of micronuclei and the growth of primary roots of Vicia faba treated with the herbicides atrazine, glyphosate and maleic hydrazide.

De Marco A[1], De Simone C, Raglione M, Testa A, Trinca S.

Author information

Abstract

Research was carried out on the genotoxic effects (induction of micronucleated cells in primary root tips) and toxic effects (reduction in primary root growth) in young plants of Vicia faba grown in soils with different organic matter contents and treated with the herbicides atrazine, glyphosate and maleic hydrazide. The data obtained show that the genotoxic effects are noticeably influenced by the interactions between the herbicide and the type of soil in which the Vicia faba have grown. While maleic hydrazide proved to be highly clastogenic for young plants grown in both soils, atrazine was genotoxic only in young plants grown in soil poor in organic matter. Glyphosate did not induce micronuclei under either soil condition, but induced a significant toxic effect.

Related citations

ELSEVIER FULL-TEXT ARTICLE

Publication Types, MeSH Terms, Substances

Toxicology. 1990 Apr 17;61(2):205-9.

Modification of the transport of protons and Ca2+ ions across mitochondrialcoupling membrane by N-(phosphonomethyl)glycine.

Olorunsogo OO[1].

Author information

Abstract

The proton permeability of mitochondrial membranes suspended in 0.15 N NH4Cl was enhanced by N-(phosphonomethyl)glycine (PMG), a broad-spectrum and a non-selective herbicide, in a concentration-dependent manner. Significant decreases in light scattering by these membranes were observed at concentrations greater than or equal to 600 microM PMG. The effect of PMG is therefore several times lower than that of FCCP, a classical uncoupler of oxidative phosphorylation. Using a sensitive pH-glass electrode, PMG significantly enhanced the movement of protons into mitochondrial matrix. Furthermore, the rate of PMG-induced release of Ca2+ ions following its accumulation by energized mitochondria was only slightly over one-half that induced by FCCP (1 microM). Whereas Ca2+ or Mg2+ only marginally reduced the effect induced by PMG, inclusion of glycine into the reaction media did not have any influence whatsoever on the effect induced by PMG. These results indicate that, although PMG increases the permeability of themitochondrial membrane to protons and to Ca2+, the herbicide does not seem to act like a true protonophore. Its uncoupling effect may, therefore, be due to its ability to act both as a chelator and a mild protonophore.

Biochem Pharmacol. 1983 Sep 15;32(18):2775-9.

Hypolipidemia and peroxisome proliferation induced by phenoxyacetic acid herbicides in rats.

Vainio H, Linnainmaa K, Kähönen M, Nickels J, Hietanen E, Marniemi J, Peltonen P.

Abstract

Male Wistar rats were treated daily by gavage with two phenoxy herbicides, 2,4-dichlorophenoxyacetic acid (2,4-D)(100-200 mg/kg body wt) and 4-chloro-2-methylphenoxyacetic acid (MCPA) (100-200 mg/kg body wt), and with the chemically different glyphosate N-phosphonomethyl glycine (300 mg/kg body wt) 5 days per week for 2 weeks. A hypolipidemic drug, clofibrate [ethyl-2-(4-chlorophenoxy)-2-methylpropionate], which is structurally related to phenoxy acids, was used as a positive control (200 mg/kg body wt). 2,4-D and MCPA had several effects similar to those of clofibrate: all three compounds induced proliferation of hepatic peroxisomes, decreased serum lipid levels, and increased hepatic carnitine acetyltransferase and catalase activities. 2,4-D and MCPA, but not clofibrate, decreased lipoprotein lipase activity in the adipose tissue to about a third of the control value but did not change the lipoprotein lipase activity in the heart muscle. The data suggest that these compounds cause hypolipidemia not by enhancing the storage of peripheral lipids in adipose tissue but by preferentially increasing lipid utilization in the liver. Glyphosate caused no peroxisome proliferation or hypolipidemia, suggesting that these effects are associated with the structural similarity between phenoxy acid herbicides and clofibrate.

Related citations

Publication Types, MeSH Terms, Substances

Acta Pharmacol Toxicol (Copenh). 1983 Aug;53(2):103-12.

Effects of phenoxyherbicides and glyphosate on the hepatic and intestinal biotransformation activities in the rat.

Hietanen E, Linnainmaa K, Vainio H.

Abstract

The effects of phenoxyacid herbicides 2,4-D (2,4-dichlorophenoxyacetic acid) and MCPA (4-chloro-2-methylphenoxyacetic acid), clofibrate, and glyphosate on hepatic and intestinal drug metabolizing enzyme activities were studied in rats intragastrically exposed for 2 weeks. The hepatic ethoxycoumarin O-deethylase activity increased about 2-fold with MCPA. Both 2,4-D and MCPA increased the hepatic epoxide hydrolase activity and decreased the hepatic glutathione S-transferase activity. MCPA also increased the intestinal activities of ethoxycoumarin O-deethylase and epoxide hydrolase. Glyphosate decreased the hepatic level of cytochrome P-450 and monooxygenase activities and the intestinal activity of aryl hydrocarbon hydroxylase. Clofibrate decreased the hepatic activities of UDPglucuronosyltransferase with p-nitrophenol or methylumbelliferone as the substrate. Also 2,4-D decreased the hepatic activity of UDPglucuronosyltransferase with p-nitrophenol as the substrate. MCPA decreased the intestinal activities of UDPglucuronosyltransferase with either p-nitrophenol or methylumbelliferone as the substrate. The results indicate that phenoxyacetic acids, especially MCPA, may have potent effects on the metabolism of xenobiotics. Glyphosate, not chemically related to phenoxyacids, seems to inhibit monooxygenases. Whether these changes are related to the toxicity of these xenobiotics remains to be clarified in further experiments.

Related citations

Publication Types, MeSH Terms, Substances, Grant Support

Biochem Pharmacol. 1982 Jun 15;31(12):2191-2.

Defective nicotinamide nucleotide transhydrogenase reaction in hepaticmitochondria of N-(phosphonomethyl)-glycine treated rats.

Olorunsogo O.

Related citations

MeSH Terms, Substances

Toxicol Lett. 1982 Jan;10(1):91-5.

Inhibition of energy-dependent transhydrogenase reaction by N-)phosphonomethyl) glycine in isolated rat liver mitochondria.

Olorunsogo OO.

Abstract

The pattern of interaction of various concentrations of N-phosphonomethyl derivative of glycine (PMG) with membrane-bound nicotinamide nucleotide transhydrogenase has been investigated in intact mitochondriaisolated from rat liver. Lower concentrations of PMG (less than 1.50 . 10(-4)M) had no significant effect (12% inhibition) on the activity of the enzyme when the reaction was supported by energy generated from succinate oxidation. Inhibition increased as the concentration of the herbicide was raised: at 3.12 . 10(-4) the degree was 28% and at 1.25 . 10(-3)M PMG, 46% (maximal inhibition). Similar results were obtained when ATP was used as the source of energy. These observations indicate that like thyroxine, an uncoupler of oxidative phosphorylation, PMG interacts with both oxidative phosphorylation and energy-dependent transhydrogenase reaction.

Related citations

MeSH Terms, Substances

Toxicol Lett. 1980 Dec;7(2):149-52.

Inhibition of succinate-linking reduction of pyridine nucleotide in rat livermitochondria 'in vivo' by N-(phosphonomethyl)glycine.

Olorunsogo OO, Bababunmi EA.

Abstract

The pattern of the interaction of N-(phosphonomethyl)glycine (PMG), a broad-spectrum and non-selective herbicide with succinate-linked reduction of pyridine nucleotide, was investigated in liver mitochondria isolated 5 h after albino rats were given i.p. injections of PMG. Although there was no appreciable inhibition of the reduction of pyridine nucleotide at dosage levels less than 150 mg PMG/kg, the extent of inhibition increased as the dose was raised to 240 mg PMG/kg. Maximal inhibition of 34.5% and 45.4% were obtained at 240 mg PMG/kg when externally added ATP and high-energy intermediate, respectively, were used as the source of energy. These findings suggest that the inhibitory effect of PMG may be due to its uncoupling effect on oxidative phosphorylation.

Related citations

MeSH Terms, Substances

Bull Environ Contam Toxicol. 1979 Jun;22(3):357-64.

Effect of glyphosate on rat liver mitochondria in vivo.

Olorunsogo OO, Bababunmi EA, Bassir O.

Related citations