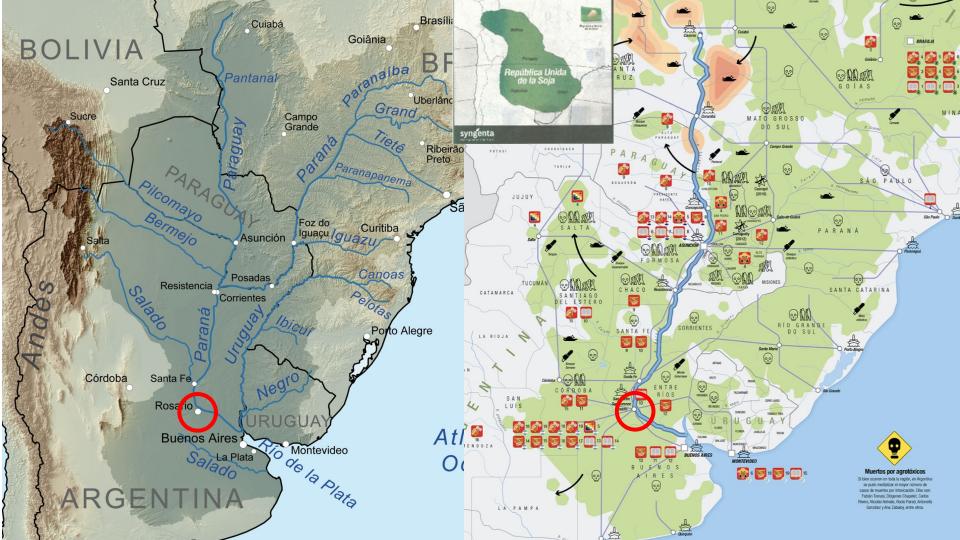
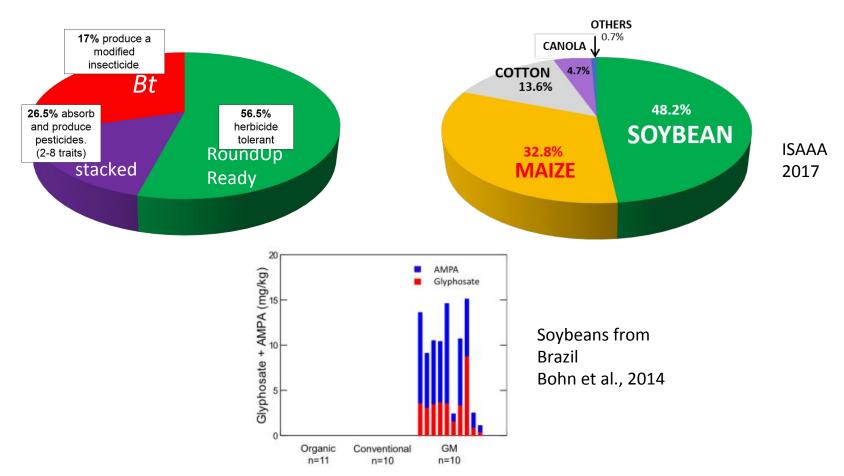
Rosario Argentina Glyphosate and Roundup: Scientific evidence of adverse impact on health and the environment Dr. Nicolas Defarge ASHA webinar, 18th sept 2020, planet Earth nicolas.defarge@gmail.com

Wetland area
Delta of the river Parana

City of Rosario (glyphosate banned!)





80% of GMOs are tolerant to herbicide(s), mostly to glyphosate









Harbour for loading of soja flour, few km upstream of Rosario (market of 9 billions US Dollars, mostly exported to China), Water quality of the main tributaries of the Paraná Basin: glyphosate and AMPA in surface water and bottom sediments

A. E. Ronco 🖂, D. J. G. Marino, M. Abelando, P. Almada & C. D. Apartin 🖂

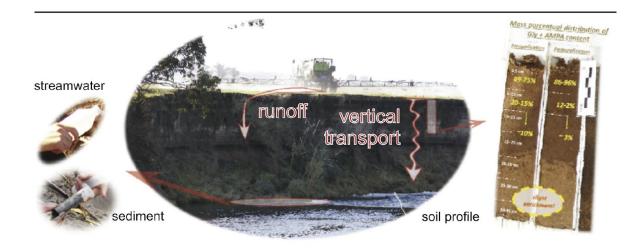
Environmental Monitoring and Assessment 188, Article number: 458 (2016) Cite this article

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



Leonardo Lupi^a, Karina S.B. Miglioranza^{a,*}, Virginia C. Aparicio^b, Damian Marino^c, Francisco Bedmar^b, Daniel A. Wunderlin^d

GRAPHICAL ABSTRACT





Re-registration Challenges of Glyphosate in the European Union

REVIEW

published: 31 July 2018 doi: 10.3389/fenvs.2018.00078

And	rás Székács ^{1*} and Béla Darvas ²	10.3389/fenvs.2018.00078		
		AlGas		
SOUTH AMERICA				
Argentina (Buenos Aires Province)	100-700	Flow increased by rain caused the transport of the herbicide from the direct area of influence to downstream sites	2004	Peruzzo et al., 2008
Argentina (Buenos Aires Province)	Glyphosate: up to 298 AMPA: up to 235	Glyphosate and AMPA are present in the soil of the agricultural basin ($35-1502$ and $299-2256 \mu g/kg$, respectively), and reach surface water via surface run-off of soil particles		Aparicio et al., 2013
Argentina (Buenos Aires Province)	Glyphosate: up to 258 (in 69% of samples) AMPA: up to 5865 (in 69% of samples)	Surface stream, ground water sampled; the sampling site under urban-industrial land use had high concentrations in the spring (attributed to point pollution),	2010–2013	Caprile et al., 2017
Argentina (Formosa, Chaco, Santa Fé, Buenos Aires, Entre Rios Provinces)	Glyphosate: 0.2–1.8 (Galeguay River) up to 0.7 (in 15% of samples) (Paraná River) AMPA: 0.1–1.9 (Galeguay River) <0.3 (Paraná River)	Higher levels in the middle- and lower-course tributaries of Paraná River in accordance with the intensive agriculture in those regions; pollutant adsorption on suspended matter	2011–2012	Ronco et al., 2016
Argentina (Buenos Aires Province)	Glyphosate and AMPA: up to 0.5 (in 33 and 20% of samples, respectively) (Quequén Grande River)	Glyphosate and AMPA were registered in almost all matrices at different sampling times (pre- and post-application events).	2012–2013	Lupi et al., 2015
Argentina (Buenos Aires Province)	Glyphosate: up to 18.5 (in 78.9% of samples) AMPA: up to 47.5 (in 96.5% of samples)	Glyphosate and AMPA predominated in surface water and sediment samples in the El Crespo stream	2014–2015	Pérez et al., 2017
Argentina (Buenos Aires Province)	Glyphosate: up to 4.5 (in >40% of samples) AMPA: up to 0.9	In shallow lakes in the Pampa region	2015	Castro Berman et a 2018
Brazil (Rio de Janeiro region)	Glyphosate: 2.6–10.1, AMPA < 0.1 (LOD) in surface water glyphosate < 0.35 (LOD), AMPA < 0.1 (LOD) in ground water	Surface and ground water used for irrigation from the region of Rio de Janeiro tested	2017 D	Pinto et al., 2018



$RISK = HAZARD \times EXPOSURE$

Exposure is high! (in almost everybody's urine, Niemann et al., 2015): First pesticide active ingredient worldwide: 800 000 tons/year (Zhang et al., 2019) Regulatory « safety » thresholds 1000x higher than any other pesticide (e.g. US MRL: 400 ppm /alfalfa vs 0.1 ppm for any other a.i)

Exposure is the highest for GM fields workers...

 epidemiology: genotoxicity (DNA damage and chromosomal abberations in soybeans workers:

Brazil (Rio Grande do Sul, Benedetti et al., 2013)

Argentina (Manas et al., 2009)

Ecuador (Paz-y-Mino, 2007)

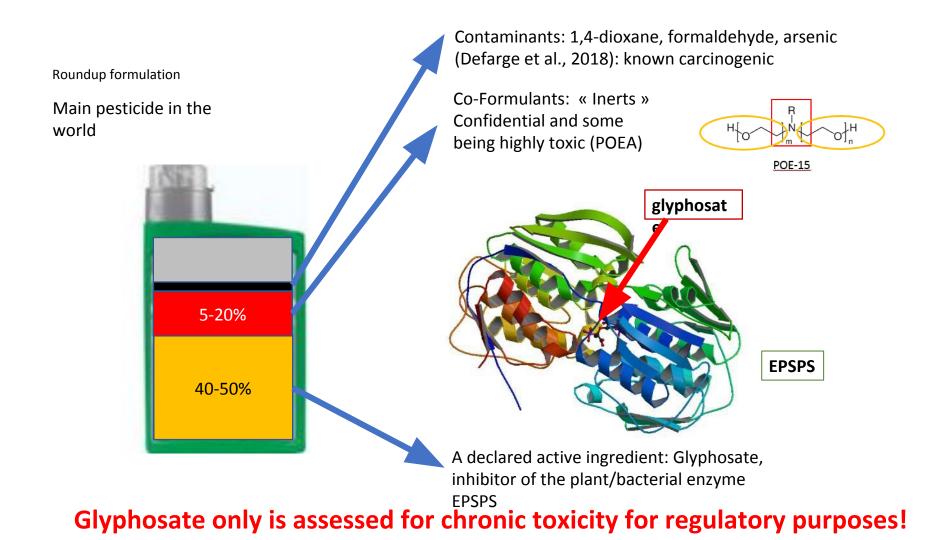
Exposure is high for the sprayed villages (pueblos fumigados)

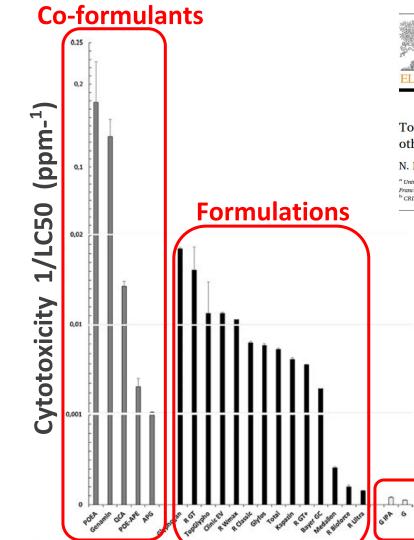


 epidemiology: sanitory camps in Argentina (pueblos fumigados)

a impressive survey by Dr. Verzenassi et al. involving over 100.000 people (to be published)

Cancers, miscarriages (spontaneous abortions), malformations were investigated.





10gy neporta 5 (2010) 150-10.

Contents lists available at ScienceDirect

Toxicology Reports



toxicology reports

journal homepage: www.elsevier.com/locate/toxrep

Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides

N. Defarge^a, J. Spiroux de Vendômois^b, G.E. Séralini^{a,*}

a University of Caen Normandy, Department of Biology and Network on Risks, Quality and Sustainable Environment MRSH, Esplanade de la Paix, 14032 Caen Cedex, France ^b CRIIGEN, 81 Rue Monceau, 75008 Paris, France



Glyphosate alone

.....

We performed the only existing study investigating the chronic effects of a pesticide formulation ! (and not the only declared active ingredient)

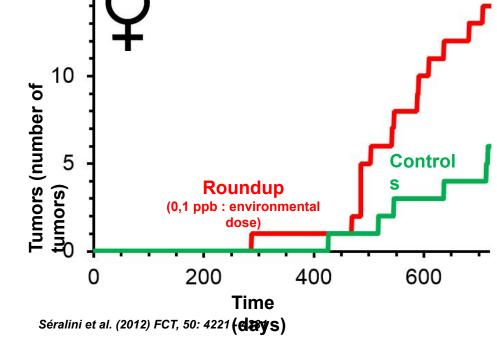
15

e formulation !RESEARCHOpeve ingredient)Republished study: long-term toxicity of a
Roundup herbicide and a Roundup-tolerant
genetically modified maize

Gilles-Eric Séralini^{1*}, Emilie Clair¹, Robin Mesnage¹, Steeve Gress¹, Nicolas Defarge¹, Manuela Malatesta², Didier Hennequin³ and Joël Spiroux de Vendômois¹

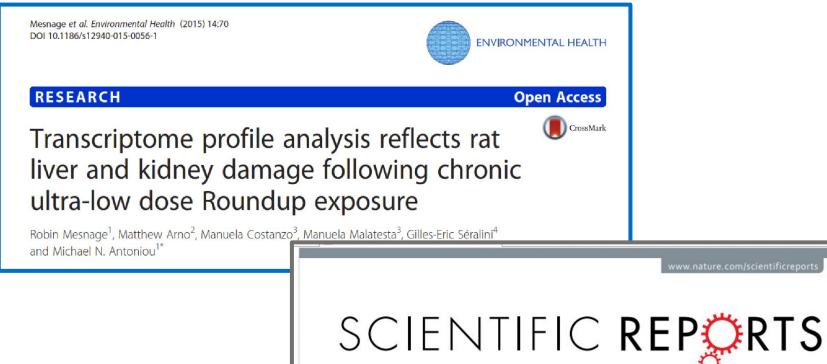
Séralini et al. Environmental Sciences Europe 2014, 26:14

http://www.enveurope.com/content/26/1/14





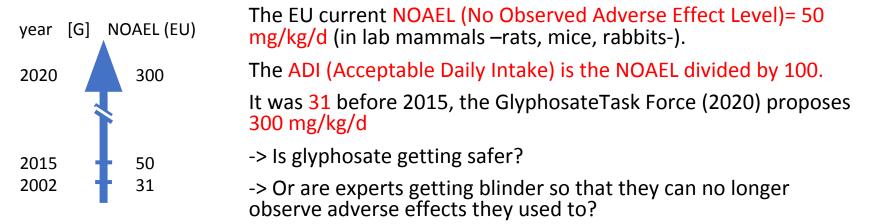
Open Access



 OPEN
 Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide

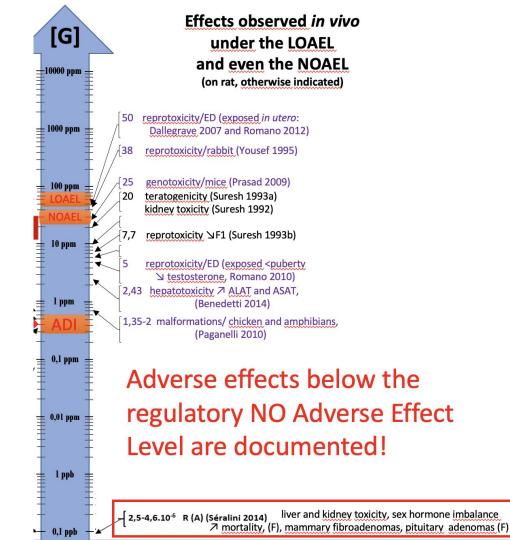
 Received: 22 July 2017
 Robin Mesnage¹, George Renney², Gilles-Eric Séralini³, Malcolm Ward² & Michael N, Antoniou¹

Health effects of Glyphosate and Roundup: Regulatory "Science"



Adverse effects below regulatory « safe » levels are documented!





Health effects of Glyphosate and Roundup: endocrine disruption



Toxicology Volume 376, 1 February 2017, Pages 2-14



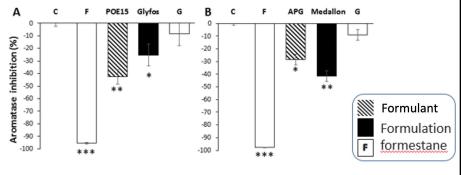
International Journal of **Environmental Research** and Public Health

MDPI

Article

Co-Formulants in Glyphosate-Based Herbicides Disrupt Aromatase Activity in Human Cells below Toxic Levels

Nicolas Defarge ^{1,3}, Eszter Takács ², Verónica Laura Lozano ¹, Robin Mesnage ^{1,3}, Joël Spiroux de Vendômois ³, Gilles-Eric Séralini ^{1,3,*} and András Székács ²



Co-formulants alone exert ED effects

Neonatal exposure to a glyphosate based herbicide alters the development of the rat uterus

Marlise Guerrero Schimpf, María M. Milesi, Paola I. Ingaramo, Enrique H. Luque, Jorgelina Varayoud 🖄 🖾 F Show more

https://doi.org/10.1016/j.tox.2016.06.004

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Highlights

- · Neonatal exposure to GBH lead to endometrial hyperplasia and increase proliferation.
- GBH disrupts proteins involved in uterine organogenetic differentiation.
- GBH exposure induced persistent increase of PR and Hoxa10 proteins.

Epigenetic effects of Glyphosate and Roundup

SCIENTIFIC REPORTS

Article Open Access Published: 23 April 2019

Assessment of Glyphosate Induced Epigenetic Transgenerational Inheritance of Pathologies and Sperm Epimutations: Generational Toxicology

Deepika Kubsad, Eric E. Nilsson, Stephanie E. King, Ingrid Sadler-Riggleman, Daniel Beck & Michael K. Skinner 🖂

 Scientific Reports
 9, Article number: 6372 (2019)
 Cite this article

 44k
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 1666
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Abstract

1

Ancestral environmental exposures to a variety of factors and toxicants have been shown to promote the epigenetic transgenerational inheritance of adult onset disease. One of the most widely used agricultural pesticides worldwide is the herbicide glyphosate (N-(phosphonomethyl)glycine), commonly known as Roundup. There are an increasing number of conflicting reports regarding the direct exposure toxicity (risk) of glyphosate, but no rigorous investigations on the generational actions. The current study using a transient exposure of gestating F0 generation female rats found negligible impacts of glyphosate on the directly exposed F0 generation, or F1 generation offspring pathology. In contrast, dramatic increases in pathologies in the F2 generation grand-offspring, and F3 transgenerational great-grandoffspring were observed. The transgenerational pathologies observed include prostate disease, obesity, kidney disease, ovarian disease, and parturition (birth) abnormalities. Epigenetic analysis of the F1, F2 and F3 generation sperm identified differential DNA methylation regions (DMRs). A number of DMR associated genes were identified and previously shown to be involved in pathologies. Therefore, we propose glyphosate can induce the transgenerational inheritance of disease and germline (e.g. sperm) epimutations. Observations suggest the generational toxicology of glyphosate needs to be considered in the disease etiology of future generations.

Glyphosate Primes Mammary Cells for Tumorigenesis by Reprogramming the Epigenome in a TET3-Dependent Manner

Manon Duforestel^{1,2,3,4†}, Arulraj Nadaradjane^{1,2,3,4†}, Gwenola Bougras-Cartron^{1,2,3,4†}, Joséphine Briand^{1,2,3,4†}, Christophe Olivier^{1,2,5}, Jean-Sébastien Frenel^{1,2,3,4†}, François M. Vallette^{1,2,3,4†}, Sophie A. Lelièvre^{6,7} and Pierre-François Cartron^{1,2,3,4†}

¹CRCINA, INSERM, Université de Nantes, Nantes, France ²Equipe Apoptose et Progression tumorale, LaBCT, Institut de Cancérologie de l'Ouest, Saint Herblain, France ³Cancéropole Grand-Ouest, réseau Epigénétique (RepiCGO), Nantes, France ⁴LabEX IGO, Université de Nantes, Nantes, France

⁵Service de toxicologie, Faculté de pharmacie de Nantes, Nantes, France
⁶Department of Basic Medical Sciences, Purdue University, West Lafayette, IN, United States
⁷Purdue University Center for Cancer Research, West Lafayette, IN, United States



Epigenomics and Epigenetics Front. Genet., 27 September 2019

The acknowledgment that pollutants might influence the epigenome raises serious concerns regarding their long-term impact on the development of chronic diseases. The herbicide glyphosate has been scrutinized for an impact on cancer incidence, but reports demonstrate the difficulty of linking estimates of exposure and response analysis. An approach to better apprehend a potential risk impact for cancer is to follow a synergistic approach, as cancer rarely occurs in response to one risk factor. The known influence of glyphosate on estrogen-regulated pathway makes it a logical target of investigation in breast cancer research. We have used nonneoplastic MCF10A cells in a repeated glyphosate exposure pattern over 21 days. Glyphosate triggered a significant reduction in DNA methylation, as shown by the level of 5-methylcytosine DNA; however, in contrast to strong demethylating agent and cancer promoter UP peptide, glyphosate-treated cells did not lead to tumor development. Whereas UP acts through a DNMT1/PCNA/UHRF1 pathway, glyphosate triggered increased activity of ten-eleven translocation (TET)3. Combining glyphosate with enhanced expression of microRNA (miR) 182-5p associated with breast cancer induced tumor development in 50% of mice. Culture of primary cells from resected tumors revealed a luminal B (ER+/PR-/HER2-) phenotype in response to glyphosate-miR182-5p exposure with sensitivity to tamoxifen and invasive and migratory potentials. Tumor development could be prevented either by specifically inhibiting miR 182-5p or by treating glyphosate-miR 182-5p-cells with dimethyloxallyl glycine, an inhibitor of TET pathway. Looking for potential epigenetic marks of TET-mediated gene regulation under glyphosate exposure, we identified MTRNR2L2 and DUX4 genes, the hypomethylation of which was sustained even after stopping glyphosate exposure for 6 weeks. Our findings reveal that low pressure but sustained DNA hypomethylation occurring via the TET pathway primes cells for oncogenic response in the presence of another potential risk factor. These results warrant further investigation of glyphosate-mediated breast cancer risk.

Health effects of Glyphosate and Roundup on the rodent gut microbiota



Toxicology Reports Volume 5, 2018, Pages 96-107



Sex-dependent impact of Roundup on the rat gut microbiome

Veronica L. Lozano ^{a, f}. Nicolas Defarge ^{e, g}. Louis-Marie Rocque ^{b, g}. Robin Mesnage ^{e, d}. Didier Hennequin ^a, Renaud Cassier ^b, Joël Spiroux de Vendômois ^e, Jean-Michel Panoff ^{a, g, g, f}. Gilles-Eric Séralini ^{a, g, f}. Caroline Amiel ^{a, g, f}. 🛛

Show more

https://doi.org/10.1016/j.toxrep.2017.12.005 Under a Creative Commons license Get rights and content open access

Highlights

- We have examined the long-term effects of Roundup on rat gut microbiota.
- 141 bacteria families were identified by a high-throughput sequencing approach.
- Roundup caused an alteration of the Firmicutes to Bacteroidetes ratio.
- An environmental concentration of Roundup has a sex-dependent impact on rat gut microbiome.



Neurotoxicology and Teratology Volume 67, May-June 2018, Pages 44-49

AL 1 12	Contraction of the second s
Brief (communication

Glyphosate based- herbicide exposure affects gut microbiota, anxiety and depression-like behaviors in mice

Yassine Aitbali ^a, Saadia Ba-M'hamed ^a, Najoua Elhidar ^b, Ahmed Nafis ^b, Nabila Soraa ^c, Mohamed Bennis ^a ^A ⊠ **⊡ Show more**

https://doi.org/10.1016/j.ntt.2018.04.002

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TERATOLOGY

Highlights

- Toxic effects of Glyphosate-based herbicide on mice gut microbiota and neurobehavior were investigated.
- Glyphosate-based herbicide exposure leads to despair behavior.
- Glyphosate-based herbicide changed the gut microbiota abundance and composition.

insects

Open Access Review

Effects of the Herbicide Glyphosate on Honey Bee Sensory and Cognitive Abilities: Individual Impairments with Implications for the Hive

by (Walter M. Farina 1.2.* ⊠ ⊙, (M. Sol Balbuena 1.2 ⊠ ⊙, (Lucila T. Herbert 1.2 ⊠, (Carolina Mengoni Goñalons 1.2 ⊠ ⊙ and (Diego E. Vázquez 1.2 ⊠ ⊙

¹ Laboratorio de Insectos Sociales, Departamento de Biodiversidad y Biología Experimental, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Buenos Aires 1428, Argentina

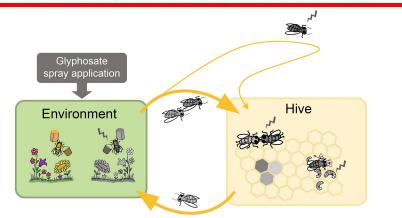
² Biología Molecular y Neurociencias (IFIBYNE), Instituto de Fisiología, CONICET-Universidad de Buenos Aires, Buenos Aires 1428, Argentina

* Author to whom correspondence should be addressed.

Insects 2019, 10(10), 354; https://doi.org/10.3390/insects10100354

Received: 21 September 2019 / Accepted: 14 October 2019 / Published: 18 October 2019

effects can be detected using experimental approaches. GLY negatively affects associative learning processes of foragers, cognitive and sensory abilities of young hive bees and promotes delays in brood development. An integrated approach that



Glyphosate perturbs the gut microbiota of honey bees



Erick V. S. Motta, Kasie Raymann, and O Nancy A. Moran

Abstract

Glyphosate, the primary herbicide used globally for weed control, targets the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) enzyme in the shikimate pathway found in plants and some microorganisms. Thus, glyphosate may affect bacterial symbionts of animals living near agricultural sites, including pollinators such as bees. The honey bee gut microbiota is dominated by eight bacterial species that promote weight gain and reduce pathogen susceptibility. The gene encoding EPSPS is present in almost all sequenced genomes of bee gut bacteria, indicating that they are potentially susceptible to glyphosate. We demonstrated that the relative and absolute abundances of dominant gut microbiota species are decreased in bees exposed to glyphosate at concentrations documented in the environment. Glyphosate exposure of young workers increased mortality of bees subsequently exposed to the opportunistic pathogen *Serratia marcescens*. Members of the bee gut microbiota varied in susceptibility to glyphosate, largely corresponding to whether they possessed an EPSPS of class I (sensitive to glyphosate) or class II (insensitive to glyphosate). This basis for differences in sensitivity was confirmed using in vitro experiments in which the EPSPS gene from bee gut bacteria was cloned into *Escherichia coli*. All strains of the core bee gut species, *Snodgrassella alvi*, encode a sensitive class I EPSPS, and reduction in *S. alvi* levels was a consistent experimental result. However, some *S. alvi* strains appear to possess an alternative mechanism of glyphosate resistance. Thus, exposure of bees to glyphosate can perturb their beneficial gut microbiota, potentially affecting bee health and their effectiveness as pollinators.

Adverse effects of Glyphosate and Roundup on the environment

> Sci Rep. 2015 Aug 5;5:12886. doi: 10.1038/srep12886.

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

Mailin Gaupp-Berghausen ¹, Martin Hofer ², Boris Rewald ², Johann G Zaller ¹

Research Article | Published: 11 April 2016

Multiple effects of a commercial Roundup® formulation on the soil filamentous fungus *Aspergillus nidulans* at low doses: evidence of an unexpected impact on energetic metabolism

Valérie Nicolas, Nathalie Oestreicher & Christian Vélot 🖂

Published: March 2003

Induction of Mortality and Malformation in *Scinax nasicus* Tadpoles Exposed to Glyphosate Formulations

R. C. Lajmanovich, M. T. Sandoval & P. M. Peltzer

 Bulletin of Environmental Contamination and Toxicology
 70, 0612–0618(2003)
 Cite this article

 550
 Accesses
 80
 Citations
 1
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Heliyon. 2019 Oct; 5(10): e02601. Published online 2019 Oct 25. doi: <u>10.1016/j.heliyon.2019.e02601</u> PMCID: PMC6820099 PMID: <u>31687490</u>

First evaluation of novel potential synergistic effects of glyphosate and arsenic mixture on *Rhinella arenarum* (Anura: Bufonidae) tadpoles

<u>Rafael C. Lajmanovich</u>, ^{a,d,*} <u>Paola M. Peltzer</u>, ^{a,d} <u>Andrés M. Attademo</u>, ^{a,d} <u>Candela S. Martinuzzi</u>, ^{a,d} <u>María F. Simoniello</u>, ^b <u>Carlina L. Colussi</u>, ^a <u>Ana P. Cuzziol Boccioni</u>, ^{a,d} <u>and Mirna Sigrist</u>^c





Adverse effects of Glyphosate and Roundup on the environment

Article Arthropod decline in grasslands and forests is associated with landscape-level drivers

https://doi.org/10.1038/s41586-019-1684-3

Received: 8 February 2019

Accepted: 16 September 2019

Published online: 30 October 2019

Recent rep arthropod biodiversi arthropod causal rela groups are linked to or arthropods and 2017 at diversity in across site number of consistent independe higher cov with annua by 41% and in three-ve differed act arthropod Arthropod Our results and are (at implies that effects of la

Sebastian Seibold¹²⁴, Martin M. Gossner², Nadja K. Simons¹⁴, Nico Blüthgen³, Jörg Müller¹², Didem Ambarlu¹⁰, Christian Ammer², Jürgen Bauhus³, Markus Fischer³, Jan C. Habel¹³⁰, Karl Eduard Linsenmair³, Thomas Nauss¹², Caterina Penone³, Daniel Prati²⁷, Peter Schall⁷, Ernst-Detlef Schulze¹³, Juliane Vogt³, Stephan Wöllauer¹² & Wolfgang W. Weisser¹

in Environmental Science

frontiers

OPINION published: 31 October 2019 doi: 10.3389/fenvs.2019.00177



Biodiversity Decline as a Consequence of an Inappropriate Environmental Risk Assessment of Pesticides

Carsten A. Brühl 1* and Johann G. Zaller²

¹ Community Ecology and Ecotoxicology, iES Landau, Institute for Environmental Sciences, University of Koblenz-Landau, Landau, Germany, ² Department of Integrative Biology and Biodiversity Research, Institute of Zoology, University of Natural Resources and Life Sciences (BOKU), Vienna, Austria

Keywords: ecotoxicology, plant protection products, agroecology, regulatory, EU

thanks for your attention!

nicolas.defarge@gmail.com

