

EFFECTS OF THE HERBICIDE GLYPHOSATE [N-(PHOSPHONOMETHYL) GLYCINE] ON BIODIVERSITY AND ORGANISMS IN THE SOIL – A REVIEW

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ABSTRACT

Glyphosate is an organophosphate herbicide manufactured by Monsanto, which eliminates annual and perennial weeds by inhibiting the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) involved in the production of aromatic amino acids in plants and microorganisms. As this herbicide is used extensively, there is a lot of research on its effect on plants, animals and microbes, and human health. Glyphosate contaminates different ecosystems by spray drift, volatilization, and erosion by wind of it adsorbed on soil particles. Soil and aquatic microbiota play a significant role in this process. This molecule is resistant to abiotic degradation. Degradation by microbes is important. The aim of this review is to provide a concise and comprehensive survey of certain relevant aspects related to its effect on the biodiversity in soil. The effect on human health is also discussed.

Keywords: biodiversity; environment; glyphosate; health; microorganisms; soil

Introduction

Glyphosate (N-phosphonomethyl glycine), was synthesised by Henri Martin of the Swiss pharmaceutical company Ciba and is the most widely used herbicide in the world. In the 1970s glyphosate was tested for its herbicidal activity (Duke and Powles 2008; Fu et al. 2017) and then sold by Monsanto in 1974 under the trade name Roundup® (Namratha et al. 2019), which consists of the active substance glyphosate (78.5%) (Çağlar and Kolankaya 2008), and a surfactant to facilitate the penetration of the active ingredient and increase its efficiency (Mesnage and Antoniou 2020).

Furthermore, glyphosate is a systemic, broad-spectrum, post-emergence and non-selective organophosphate (Zhan et al. 2018; Namratha et al. 2019), which can be used to control annual and perennial species of weeds and grasses (Singh and Singh 2014) in agricultural, forest and aquatic systems, and is applied as a foliar spray (Villarreal-Chiu et al. 2017; Yang et al. 2019). Some of the spray may fall directly on the surface of the soil or on non-targeted plants (Gomes et al. 2014). Its mode of action is to inhibit enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), which is involved in aromatic amino acid synthesis (Singh et al. 2019) as well as in reducing the rates of synthesis of proteins (Solomon 2016) and secondary metabolites that interfere with the vital energy pathways of plants and microorganisms (Zhan et al. 2018).

The shikimate pathway is present in plants and microorganisms, but not in mammals, including humans,

because they get amino acids from their diet (Aristilde et al. 2017). Excessive use of glyphosate and its persistence have adverse effects on human health and ecosystems (Sihtmäe et al. 2013), such as, genotoxicity, cytotoxicity, and reproductive toxicity, and can cause or trigger cancer, chronic kidney disease, hypothyroidism and birth defects (Manogaran et al. 2017). This herbicide can be transformed or degraded and removed from the environment, which is generally carried out by microbes, as the very stable bonds of glycolphosphate inhibit chemical degradation (Manogaran et al. 2017). Other studies have shown that bioremediation is a more promising way of removing chemical pollutants from the environment (Zhao et al. 2015). The purpose of this review is to present a summary of the scientific literature on the mode of action of glyphosate, the accumulation of its residues in humans, the air, water, and food products and to specify their effects on soil microorganisms, microbial biodiversity, plants and animals.

Proprieties and herbicidal activities of glyphosate

Glyphosate belongs to the glycine family (Ovono et al. 2019) and is non-volatile (Singh and Singh 2014). Glyphosate is an herbicide that is highly soluble in water (12 g l⁻¹) and insoluble in organic solvents due to a very stable carbon-phosphorus (C–P) bond (Hadi et al. 2013). The half-life of glyphosate in soil is 2–215 days and 2–91 days in an aquatic environment (Battaglin et al. 2014;

Mesnage and Antoniou 2020). Glyphosate can be adsorbed by humus and form complexes with the metal cations Fe^{2+} , Cu^{2+} , Mn^{2+} and Ni^{2+} (Singh and Singh 2014) and due to its phosphonic acid fraction it accumulates in soil (Lane et al. 2012; Zhao et al. 2015). A significant percentage of the glyphosate in soil can infiltrate the groundwater (Simonsen et al. 2008). This herbicide is effective against 100 annual species of grasses and broadleaved weeds, and more than 60 species of perennial weeds (Dill et al. 2010).

Glyphosate inhibits the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), which converts PEP (phosphoenolpyruvate) and S3P (shikimate-3-Phosphate) into 5-enolpyruvylshikimate-3-Phosphate (EPSP) (Cao et al. 2012). Current studies have shown that due to its structural similarity glyphosate competes with PEP (phosphoenolpyruvate) and then binds to the S3P-EPSPS complex to produce EPSP (Aristilde et al. 2017). This interaction is between the hydroxyl group 5 of S3P and glyphosate nitrogen (Rueda-Ruzafa et al. 2019), which is a common precursor of three aromatic amino acids, chorismate (Aristilde et al. 2017). So, glyphosate action is generated by the chelation of manganese necessary to reduce the MNF co-factor; which is a key element in the shikimate pathway (Shehata et al. 2013; Myers et al. 2016).

Then glyphosate induces the suppression of protein synthesis and secondary metabolites, e.g., flavonoids, lignin inducing cell death (Cao et al. 2012; Sviridov et al. 2015; Fu et al. 2017). The shikimate pathway is found only in microorganisms and plants, never in animals and humans (Samsel and Seneff 2013; Ovono et al. 2019), because they do not make their own aromatic amino acids (phenylalanine, tyrosine, and tryptophan), but obtain them from food (Padgett et al. 1995).

There are two classes of EPSPS: class I are naturally sensitive to glyphosate and occur in plants and many Gram-negative bacteria (e.g., *Escherichia coli* and *Salmonella typhimurium*), while class II EPSPS are involved in resistance to glyphosate and are found only in bacteria, including *Agrobacterium* sp. strain CP4 and *Pseudomonas* sp. PG2982 and some Gram-positive bacteria. Both have a similar structure but a different amino acid sequence (Fan et al. 2012; Rueda-Ruzafa et al. 2019).

Biodegradation of glyphosate

Glyphosate can either be degraded by biotic or abiotic means such as oxidation (with chlorine, permanganate, air or ozone), filtration and flocculation, adsorption, thermolysis and photodegradation, the latter of which is capable of breaking down glyphosate into non-toxic products such as carbon-dioxide, inorganic ions and water (Zhan et al. 2018).

This means of degradation is generally used in water and wastewater treatment plants, but it is expensive since

it is difficult to devise a single method because of the very stable bonds (carbon-phosphorus bond) in glyphosphate (Manogaran et al. 2017).

The main pathway of glyphosate degradation in soils is biodegradation by enzymes produced by some microorganisms, such as *Pseudomonas* sp. strain LBr (Jacob et al. 1988). Numerous bacteria of the genus *Escherichia*, *Pseudomonas*, *Agrobacterium*, *Klebsiella*, *Arthrobacter*, *Bacillus* and *Rhizobium*, and basidiomycete and ascomycete fungi (Ermakova et al. 2008) can degrade glyphosate in soil and water (Zhan et al. 2018). The main metabolites of this degradation are AMPA, sarcosine and acetyl glyphosate (Zhan et al. 2018). This degradation is considered to be a co-metabolic process because it produces nutrients (Zabaloy et al. 2012), which can be used by soil microorganisms as a source of phosphorus, carbon and nitrogen (Fu et al. 2017). It is important to optimize the conditions for degradation, which include pH, temperature, glyphosate concentration, biomass, and incubation period (Namratha et al. 2019).

The biodegradation of glyphosate takes place by two alternative pathways, one involving the cleavage of the C–P bond by the enzyme C–P lyase producing sarcosine, which is then broken down to glycine, used by microorganisms for the biosynthesis of proteins (Karpouzas and Singh 2006), and formaldehyde, which is then mineralised to carbon dioxide and water (Fig. 1), this pathway is used by bacteria that use glyphosate as a phosphorus source (Guijarro et al. 2018; Mesnage and Antoniou 2020) (Table 1). Among these microorganisms are *Pseudomonas* PG 2982, *Geobacillus caldxylosilyticus* T20 and *Pseudomonas* LBr strain, which are able to convert about 5% of the initially added glyphosate via the formation of sarcosine and glycine (Karpouzas and Singh 2006; Fu et al. 2017; Zhan et al. 2018), and fungi, including *Penicillium janthinellum*, *Penicillium simplicissimum*, *Mucor* sp. (Karpouzas and Singh 2006).

The second pathway is by the cleavage of the C–N bond of glyphosate by the enzyme glyphosate oxidoreductase releasing AMPA, which is the main metabolite of glyphosate and is then mineralized into methylamine and phosphate with a final decomposition producing CO_2 , NH_3 and glyoxylate, which *Ochrobactrum anthropi* GPK 3 uses as a source energy (Shushkova et al. 2010) (Fig. 1).

This is the main natural pathway in the environment by which soil microorganisms use glyphosate as a source of nitrogen (Guijarro et al. 2018). The following microorganisms use this pathway: *S. meliloti* (Hove-Jensen et al. 2014), *Arthrobacter* sp. GLP-1 uses glycine for the biosynthesis of basic peptide proteins and amino acids (serine, threonine) (Shehata et al. 2013; Mesnage and Antoniou 2020), *Arthrobacter atrocyaneus* ATCC 13752 (Shehata et al. 2013; Fu et al. 2017). Strains 4ASW and 7b (Fu et al. 2017; Rueda-Ruzafa et al. 2019) of *Pseudomonas pseudomonalli* (Karpouzas and Singh 2006) and *Pseudomonas* sp. strain LBr (Shahata et al. 2013)

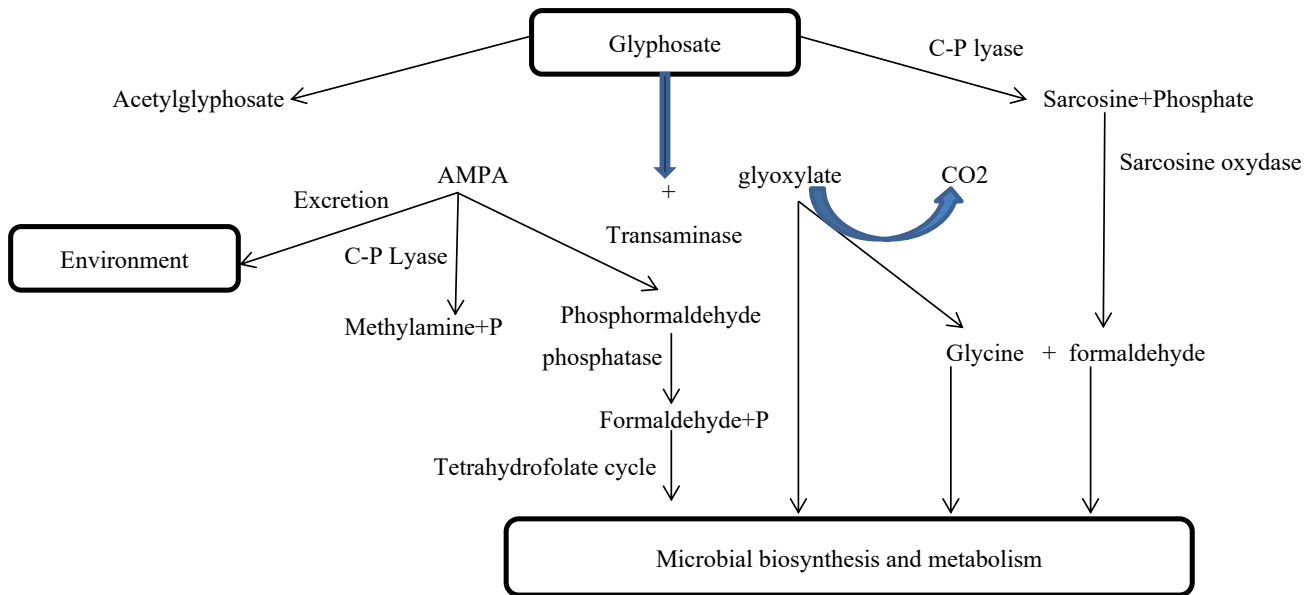


Fig 1. Pathways in the bacterial degradation of glyphosate.

Table 1 Glyphosate degrading microorganisms.

Microorganism	Origin	Degradation pathway and source	Metabolites detected	References
Bacteria				
Strains				
<i>Achromobacter</i> sp. MPS 12A	Sites contaminated with AMPA	Sarcosine pathway as the sole source of phosphorus	Sarcosine, Glycine, Formaldehyde	Sviridov et al. (2011)
<i>Arobacterium radiobacter</i>	Sludge from water treatment plant	Sarcosine pathway as the sole source of phosphorus	No data	Wackett et al. (1987)
<i>Arthrobacter atrocyaneus</i> ATCC 13752	Collection of microorganisms and cell cultures Germany	AMPA pathway as the sole source of phosphorus	AMPA CO ₂	Pipke and Amrhein (1988)
<i>Bacillus cereus</i> CB4	Glyphosate contaminated soil China	Both AMPA and sarcosine pathway as sole sources of phosphorus and carbon	AMPA Glyoxylate Sarcosine Glycine Formaldehyde	Fan et al. (2012)
<i>Enterobacter cloacae</i> K7	Rhizoplane of various plants in Russia	Sarcosine pathway as the sole source of phosphorus	Sarcosine Glycine	Kryuchkova et al. (2014)
<i>Flavobacterium</i> sp. GD1	Monsanto activated sludges	AMPA pathway as the sole source of phosphorus	AMPA Phosphate	Balthazor and Hallas (1986)
<i>Pseudomonas pseudomallei</i> 22	Soil	AMPA putative pathway of the sole source of phosphorus	No data	Peñaloza-Vazquez et al. (1995)
<i>Pseudomonas</i> sp. SG-1	Aerobic digester liquid	AMPA pathway as the sole source of phosphorus	AMPA	Talbot et al. (1984)
<i>Pseudomonas</i> sp. LBr	Glyphosate process waste stream	Both AMPA (95%) and sarcosine (5%) pathways as sources of phosphorus	AMPA Glycine	Jacob et al. (1988)
<i>Rhizobiaceae melliloti</i> 1021	Spontaneous mutation of a wild type strain	Sarcosine pathway as the sole source of phosphorus	Sarcosine Glycine	Liu et al. (1991)
<i>Streptomyces</i> sp. StC	Raw sludge from a municipal sewage treatment plant	Sarcosine pathway as the sole source of phosphorus, nitrogen or nitrogen and phosphorus	Sarcosine Glycine	Obojska et al. (1999)
<i>Comamonas odontotermitis</i> P2	Glyphosate-contaminated soil in Australia	Both AMPA and sarcosine pathways (putative) as the sole sources of carbon and phosphorus	No data	Firdous et al. (2017)

Microorganism	Origin	Degradation pathway and source	Metabolites detected	References
<i>Pseudomonas</i> sp. strains GA07, GA09, GC04	Glyphosate contaminated soil China	Both AMPA and Sarcosine pathways as the sole sources of carbon and phosphorus	AMPA Glyoxylate Glycine Formaldehyde	Zhao et al. (2015)
<i>Enterobacter</i> sp. strain Bisph2	sandy soil Algeria	AMPA pathway as the sole source of phosphorus	No data	Benslama and Boulahrouf (2016)
<i>Ochrobactrum</i> sp. GDOS	Soil	Sarcosine pathway as the sole source of phosphorus	AMPA	Hadi et al. (2013)
<i>Achromobacter</i> sp. MPK 7A	Glyphosate contaminated soil	AMPA pathway as the sole source of phosphorus	Sarcosine	Ermakova et al. (2017)
Fungi				
<i>Aspergillus oryzae</i> A-F02	Sludge of glyphosate manufacture	AMPA pathway	AMPA Methylamine	Fu et al. (2017)
<i>Penicillium chrysogenum</i>	Soil	AMPA pathway putative source of nitrogen	No data	Klimek et al. (2001)
<i>Aspergillus niger Scopulariopsis</i> sp. <i>Trichoderma harzianum</i>	Soil	AMPA pathway as the sole source of phosphorus	AMPA	Krzysko-Lupicka and Orlik (1997)

Table 2 Glyphosate doses degraded or tolerated by bacteria.

Microorganisms	Doses of glyphosate	Comments	References
<i>Aeromonas acetobacter</i> sp.	100 mg l ⁻¹ 100 to 250 mg l ⁻¹ 7.2 mg ml ⁻¹	Increase in number of bacteria sensitive to this dose of glyphosate Strong degradation	Moneke et al. (2010)
<i>Bacillus cereus</i> strain CB4	6 g l ⁻¹ for 7 days 12g	94.16% degradation in 5 days Inhibition of degradation	Fan et al. (2012)
<i>Bacillus subtilis</i> Bs-15	5000 mg l ⁻¹	In treated soil 66.97% degradation was recorded 71.57% in untreated soil	Yu et al. (2015)
<i>Enterobacter cloacae</i> K7	5 mM	40% degradation	Kryuchkova et al. (2014)
<i>Comamonas odontotermitis</i> P2	1.5 g l ⁻¹	Complete degradation of glyphosate within 104h	Firdous et al. (2017)
<i>Pseudomonas</i> sp. LBr	0.5–0.7 mM	Glyphosate degraded at this dose	Jacob et al. (1988)
<i>Fusarium solani</i> H30 <i>Fusarium solani</i> H50 <i>Fusarium oxysporum</i> H80	1 to 1.5 mM 2.0 mM	Significant growth Sensitive to glyphosate at this concentration	Krzysko-Lupicka and Sudol (2008)

use glyphosate as a source of phosphate (Hove-Jensen et al. 2014), *Penicillium chromogenum* does not use nitrate, but uses glyphosate as its sole source of nitrogen (Karpouzias and Singh 2006) and *Achromobacter* sp. kg16 converts glyphosate to acetylglyphosate (Zhan et al. 2018) (Table 2).

Some bacteria degrade glyphosate using both these mechanisms, like *Bacillus cereus* CB4, *Ochrobactrum anthropi* GPK3 1 and *Pseudomonas* sp. LBr and *Bacillus subtilis* uses another enzyme, glycine oxidase to metabolize glyphosate (Zhan et al. 2018).

Mineralisation in soil occurs in two phases, the first is rapid and attributed to direct microbial action followed by a slow phase, which may be due to microbial metabolism after adsorption of glyphosate (Villarreal-Chiu et al. 2017) (Table 1). Adsorption of glyphosate in soil slows down its degradation by soil microorganisms,

leading to accumulation over time (Van Bruggen et al. 2018). Glyphosate degrades rapidly in soil, with more than 20 to 70% of the glyphosate mineralised into CO₂ in about 5 weeks and up to 79 to 86% over a period of six months (Dill et al. 2010), depending on the type of soil. The AMPA metabolite can accumulate in soil corresponding to 10–20% of the glyphosate initially applied (Reddy et al. 2008). AMPA is toxic to bacteria and can be released into the environment (Villarreal-Chiu et al. 2017). Adsorption of glyphosate in soil slows down degradation by soil micro-organisms and causes it to accumulate over time (Van Bruggen et al. 2018). Intracellular metabolism of AMPA does not occur and it is released into the environment resulting in the contamination of several bacteria, such as, *Bacillus megaterium* 2BLW, *Pseudomonas* sp. 4 ASW, *Pseudomonas* sp. 7B and *Pseudomonas* sp. LBr (Zhan et al. 2018).

Glyphosate and AMPA residues in agricultural products

Glyphosate residues are frequently found in the food chain, as they are sprayed on cereals to accelerate ripening and more uniform drying of the grain (Mesnage and Antoniou 2020). Traces of this herbicide have been found in breast milk, honey, cereals and soybeans (Rueda-Ruzafa et al. 2019), with 95% of the levels of glyphosate in most human beverages, such as beer and wine being between 51 and 3.5 ppb (Rueda-Ruzafa et al. 2019). Concentrations of glyphosate and AMPA varies considerably in agricultural products, ranging from 0.1–100 mg kg⁻¹ in legumes (including soybeans), 0.1–25 mg kg⁻¹ in cereals and rice, 0.1–28 mg kg⁻¹ in oil seed and 1–344 mg kg⁻¹ in various types of forage (Van Bruggen et al. 2018). In Europe, MRLs are defined separately for each type of product. For barley and oats (cereals) it is 30 mg kg⁻¹, whereas the ADI is 0.5 mg/kg body weight per day (EFSA 2015).

Glyphosate and AMPA residues in soil, water, air, and humans

Glyphosate residues in humans

Humans may be exposed to glyphosate residues by consuming fruit, vegetables, and other agricultural products, as well as by drinking water (Nielsen et al. 2018). Glyphosate and AMPA residues are absorbed by animals and humans from water and plant products and then excreted in their faeces and urine (Van Bruggen et al. 2018), where they are reported in the urine of farmers and public, including children, with an incidence of 60–80% in the USA and in 44% of the public in Europe (Krüger et al. 2014; Niemann et al. 2015). The concentration is generally low but much higher in people in the United States (average of 2–3 µg l⁻¹ and maximum of 233 µg l⁻¹) than in Europe (average of 1 µg l⁻¹ and maximum of 5 µg l⁻¹) (Niemann et al. 2015). Studies report high levels of glyphosate in the breast milk of women in the United States; of 10 samples sent in by mothers; 3 women had detectable levels of glyphosate, with 166 µg l⁻¹ for a mother in Florida, 76 µg l⁻¹ for one in Virginia and 99 µg l⁻¹ for one in Oregon (Honeycutt and Rowlands 2014). The glyphosate level in 182 samples of urine from 18 European countries ranged from 0.16 µg l⁻¹ in Switzerland to 1.82 µg l⁻¹ in Latvia (Honeycutt and Rowlands 2014).

These levels were compared with those in breast milk, which are higher and can therefore influence the health and development of infants. In 21 samples of drinking water from the USA 13 had concentrations between 0.085 µg l⁻¹ and 0.33 µg l⁻¹, which is much lower than in urine and breast milk (Honeycutt and Rowlands 2014). The study of Conrad et al. (2017) shows that concentration of glyphosate in urine collected over the course of a day were significantly higher in 2013 (1.12 µg l⁻¹) and in 2014 (0.80 µg l⁻¹) than in other years. In addition,

glyphosate and AMPA concentrations are generally higher in male than female urine (Conrad et al. 2017).

Glyphosate residues in soil

Glyphosate and AMPA residues recorded in soil using GC-MS are both 0.05 mg kg⁻¹. In drinking water, groundwater, and surface water the concentration of glyphosate and AMPA is 0.03 µg l⁻¹ measured using LC-MS/MS and glyphosate in air using GC-MA with LOQ is 5 µg m⁻³ (EFSA 2015).

Glyphosate residues in air

There are very few studies on the atmospheric transport of glyphosate. In one study, glyphosate concentrations in air are reported to be less than 15.7 mg m⁻³ during silvicultural spraying (Chang et al. 2016). The frequency of detection of glyphosate in air and rain samples ranges from 60% to 100% and deposition rates from 0.01 to 1.51 µg m⁻² per day measured at 7-day intervals during the growing season at three sites in Alberta and Canada (Humphries et al. 2005).

Glyphosate residues in water

Glyphosate can reach aquatic ecosystems through uncontrolled runoff, aerial drift, accidental overexploitation or when sprayed directly on aquatic weeds. All these substances influence aquatic organisms (Cuhra 2015). In general, there are several ways in which herbicide can be degraded, such as photodegradation, oxidation (with chlorine, permanganate, air, or ozone), filtration and flocculation, adsorption and by using membranes, but these are costly and difficult to use for treating wastewater (Manogaran et al. 2017). Glyphosate has been detected in seawater at 0.1–2.5 µg l⁻¹ in surface waters in Germany, Switzerland, and Hungary and 165 µg l⁻¹ in Spain (Van Bruggen et al. 2018).

In European surface waters, glyphosate and AMPA occur at up to 370 and 200 µg l⁻¹, respectively, while in groundwater the concentration is 0.1 µg l⁻¹ (Mertens et al. 2018). Glyphosate has an aquatic half-life of 2–14 days (Howe et al. 2004).

Effects of glyphosate on microorganisms, plants, animals, and humans

Effect of glyphosate on soil microorganisms

Soil microorganisms play a central role in the degradation of herbicides and the maintenance of the functions of soil ecosystems, including nutrient cycling and bioremediation. For example, if the concentration of glyphosate is above 200 mg kg⁻¹, microbial biomass increases in less than 10 days at a pH below 5.5 and decreases in more than 100 days at a neutral pH (Liu et al. 2018).

Glyphosate can cause structural changes in local soil microbial communities by inhibiting the growth of soil microorganisms and facilitating the growth of soil fungal path-

ogens of plants that form the basis of ecosystem services such as pollutant transformation and nutrient cycling (Zabaloy et al. 2012; Zhan et al. 2018). Thus, the presence of free glyphosate in the soil profile changes the composition of microbial communities, resulting in a marked increase in the population of the phytopathogenic fungi *Fusarium* and *Phytophthora* (Kryuchkova et al. 2014).

Glyphosate application can change the balance between pathogenic *Fusarium* sp. and antagonistic microorganisms such as *Pseudomonas fluorescens* in favour of root pathogens, similarly, the human and animal pathogen *Staphylococcus aureus* is insensitive to glyphosate and can become more dominant in glyphosate-treated soil (Van Bruggen et al. 2018). This organophosphorus herbicide is the only one capable of inhibiting the mycelial growth and sexual reproduction of *Pythium* and *Fusarium* (Azouaoui-Ait Kettout et al. 2007) (Table 2).

The application of Roundup (glyphosate) (50 and 100 mg l⁻¹) results in an increase in *Aeromonas* compared to controls (Amoros et al. 2007). These microorganisms are tolerant of concentrations above 100 mg l⁻¹. The highest growth of *Acetobacter* sp. and *Pseudomonas fluorescens* was recorded in the control, which had the lowest concentration of glyphosate (7.2 mg l⁻¹).

A recent meta-analysis indicated that the effect of glyphosate on soil microbial communities is very variable and depends on many different factors, including the concentration and formulation of glyphosate, number of applications, soil pH and exposure. For example, glyphosate concentrations > 200 mg kg⁻¹ induce a short-term increase (100 days) in soil microbial biomass in soils with a pH of 5.5, whereas lower concentrations of glyphosate reduce the long-term (> 100 days) increase in microbial biomass in soils with a neutral pH (Liu et al. 2018), *Bacillus subtilis* strain Bs-15 degraded 67% of 5000 mg glyphosate l⁻¹ in sterile soil after 96 h, and the degradation up to 72% greater in unsterilised soil, probably due to the stimulation of endogenous microorganisms (Shehata et al. 2013; Yu et al. 2015; Villarreal-Chiu et al. 2017). Significant decrease in Xanthomonada-substituted gamma-proteotic acid and limbs (Villarreal-Chiu et al. 2017).

Glyphosate can disrupt freshwater microbial communities and reduce species biodiversity in aquatic communities, as *Vibrio fischeri*, a marine bacterium, is sensitive to glyphosate at a concentration of EC50 5.4 to 7.6 mg l⁻¹ (Van Bruggen et al. 2018). The concentration of glyphosate required to inhibit the growth of *Escherichia coli*, *Bacillus subtilis*, *Bacillus jaboricum* and *Pseudomonas aeruginosa* by 50% is estimated to be 75 µM, 174 µM, 1.1 mM and 1.1 mM, respectively (Duke et al. 2012). Specifically, at 4 kg ha⁻¹ of glyphosate, nitrogenase activity decreased by 22% in *Azotobacter vinelandii*, but only by 2% in *Azotobacter chroococcum*. A higher application of glyphosate (12 kg ha⁻¹) resulted in nitrogenase activity of 45% and 13%, respectively, in *Azotobacter vinelandii* and *Azotobacter chroococcum* (Aristilde et al. 2017).

Release of AMPA into the environment as a result of intracellular metabolism leads to contamination of *Bacillus megaterum* 2BLW, *Pseudomonas* sp. 4ASW, *Pseudomonas* sp. 7B, *Pseudomonas* sp. LBr that use glyphosate as a source of phosphorus (Zhan et al. 2018).

Effect of glyphosate on plants

Glyphosate is transported throughout a plant in 4 hours via the phloem (Mesnage and Antoniou 2020), is toxic to monocotyledons (such as grasses) and dicotyledons (broadleaved plants) (Gomes et al. 2014), affects photosynthesis by degrading chlorophyll and AMPA disrupts the biosynthesis of chlorophyll resulting in yellowing and necrosis of foliage (Gomes et al. 2016).

Glyphosate affects the metabolism of carbon, nutrition, and oxidative events, and disrupts interactions between plants and microorganisms (Kremer and Means 2009; Zobiolo et al. 2012). This adversely effects nitrogen fixation and inhibits PSII activity and undiluted photochemical energy dissipation processes (Gomes et al. 2014). Low Mg content in leaves, results in a decrease in chlorophyll content and photosynthesis (Gomes et al. 2014).

In susceptible plants, it inhibits CO₂ uptake and depletes photosynthetic intermediates (Gomes et al. 2017). For example, glyphosate reduces the ability of bean plants to defend themselves against anthracnose (Johal and Rahe 1988). Plants treated with glyphosate do not produce secondary aromatics, including antimicrobial phytoalexins that defend them against pathogens, which can lead to changes in the endophytic microbiome and rhizosphere (Van Bruggen et al. 2018). Glyphosate and its breakdown product AMPA inhibit the activities of antioxidant enzymes and induce the accumulation of species oxygen reactants (ROS) that cause physiological dysfunction and cell damage (Gomes et al. 2016).

Effect of glyphosate on animals

Glyphosate in animal feed affects not only intestinal bacteria but also fungi, such as mucorales, which are fast-growing fungi that often form ball spores on fungal threads and are therefore sometimes called mussel pins (Van Bruggen et al. 2018). The absence of the shikimate pathway in animals is the reason why glyphosate is not toxic for animals such as mammals, amphibians and reptiles even when exposed to relatively high doses (Van Bruggen et al. 2018), but animals can ingest glyphosate and AMPA by drinking water and eating contaminated plants, which may damage or reduce the survival of many animals, including benthic insects, fish, birds and earthworms (Tsui and Chu 2003). It can also damage the DNA and chromosomes of fish (Zhan et al. 2018).

It directly affects the morphology, behaviour and reproduction of several species and adversely affects the long-term survival of arthropods in the soil (Villarreal-Chiu et al. 2017). Glyphosate concentrations above 400 µg l⁻¹ are potentially toxic to certain aquatic species,

including amphibians and fish (Mesnage and Antoniou 2020). Exposure of zebrafish embryos to 50 mg l⁻¹ Roundup® results in developmental defects in the fore-brain, midbrain, and eye lesions (Roy et al. 2016). A concentration of Roundup® of 3.6 mg l⁻¹ for 4 h causes DNA damage in the blood, gills and liver of the European eel, *Anguilla anguilla* (Van Bruggen et al. 2018). Changes in liver cells and mitochondria occur in freshwater carp (*Cyprinus carpio*) exposed to Roundup® at 205 or 410 mg l⁻¹ (Van Bruggen et al. 2018).

The International Organisation for Biological Control found that exposure to freshly dried Roundup® killed more than 50% of three species of beneficial insects: a parasitoid wasp, a nymph, and a ladybird beetle (Hassan et al. 1988) and more than 80% of a predatory beetle. Glyphosate is extremely toxic to birds, but only in large quantities.

Effect of glyphosate on humans

Acute use of glyphosate is correlated with a wide variety of human diseases, including various forms of cancer, mental problems, and disorders such as ADHD, Autism, Alzheimer's and Parkinson's (Hadi et al. 2013; Fu et al. 2017; Namratha et al. 2019). Inhalation of droplets of spray is a minor route of exposure to glyphosate, whereas contact with skin is the main route of exposure (Acquavella et al. 2004). The use of soybeans (as a dietary supplement) contaminated with glyphosate may pose a risk of breast cancer due to its potential for additive estrogenicity. They hypothesize that glyphosate may behave as a xenoestrogen (Thongprakaisang et al. 2013).

Indeed, glyphosate can also kill human cells, by disrupting mitochondrial succinate dehydrogenase, 3/7 caspases and adenylate kinase, and is even responsible for oxidative damage to human epidermal cells (Clair et al. 2012). Richard et al. (2005) report that glyphosate inhibits aromatase Cyp 450, an enzyme crucial for the synthesis of the sex steroid hormone (Krüger et al. 2014).

At the genomic and cellular level, it affects the regulation of the cell cycle (Santovito et al. 2018). In 2001, Barbosa proposed that glyphosate may contribute to parkinsonism because of its chemical similarity to glycine, which is a necessary cofactor for the activation of the N-methyl-d-aspartate receptor (NMDA), which controls the excitatory actions of the central nervous system and is also involved in memory and learning, however, clinical studies have shown no evidence of NMDA activity in relation to glyphosate toxicity (Krüger et al. 2014). Thongprakaisang et al. (2013) and Cattani et al. (2014) report that it is teratogenic and cytotoxic to the human placenta by inhibiting the aromatase effect of cytochrome P450 (Shehata et al. 2013). Studies on Ecuadorians have shown that aerial spraying of glyphosate on coca crops damages the DNA of erythrocytes and induces an increase in haemolysis and metahaemoglobin, at moderate to high concentrations (85 to 1690 mg l⁻¹) and decreased DNA methylation at 42 mg l⁻¹ glyphosate *in vitro* leading to

DNA damage, cancer and apoptosis in human cell lines (Honeycutt and Rowlands 2014; Villarreal-Chiu et al. 2017; Van Bruggen et al. 2018). In 2015, the International Agency for Research on Cancer (IARC) classified glyphosate as a "known human carcinogen" (Group 2A) (Chang and Delzell 2016; Drašar and Poc 2017; Tarone 2018). AMPA inhibits the activities of antioxidant enzymes that induce the accumulation of ROS, causing physiological dysfunction and cell damage. It is a glutamic acid receptor in the CNS, so the activity of acetylcholine esterase in the body can be affected by exposure to 70 mg/kg/day (Van Bruggen et al. 2018).

Conclusion

This study summarizes the literature on environmental pollution due to the excessive use of glyphosate. This herbicide persists in the environment for long periods of time due to its adsorption properties, can also occur in groundwater, changes the composition of bacterial and fungal communities, which in turn adversely affects the functions of the soil ecosystem and animal and plant health. Microorganisms have a crucial role in the transformation of toxic organic compounds such as pesticides into harmless products, which allows them to be used in bioremediation. For this reason, it is suggested that the harmful effects of glyphosate could be due to the adjuvants in the GBH formulations.

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