Journal of Environmental Health and Sustainable Development

Toxicity, Biodegradability and Detection Methods of Glyphosate; the Most Used Herbicide: A Systematic Review

Mohsen Ansari [1, 2], Behnam Hatami [1], Samaneh Sedighi Khavidak [3*]

[1] *Environmental Science and Technology Research Center, Department of Environmental Health Engineering, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.*
[2] *Student Research Committee, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.*
[3] *Department of Biology, Khorramabad Branch. Islamic Azad University, Khorramabad, Iran.*

ARTICLE INFO

SYSTEMATIC REVIEW

Article History:
Received: 28 January 2019
Accepted: 20 April 2019

***Corresponding Author:**
Samaneh Sedighi Khavidak
Email:
sedighi.samaneh@yahoo.com
Tel:
+989133584815

Keywords:
Herbicide,
Toxicity,
Environmental Pollution,
Biodegradation,
Glyphosate.

ABSTRACT

Introduction: Glyphosate is known as the most used world's herbicides and contradictions exist over its classification as a probably carcinogenic for the human. This study aimed to review the newest evidences in toxicity, biodegradability and detection methods of glyphosate.

Materials and Methods: To conduct this systematic review, databases such as Scopus, Web of Science, PubMed, and Google Scholar were searched to extract studies on the non-target toxicity, biodegradability and detection methods of glyphosate from 2000 to 2018. The applied key words included glyphosate, herbicide, biodegradation, and bio decomposition. The number of articles retrieved and reviewed was 84 and 23, respectively.

Results: Glyphosate could cause endocrine disrupting effects, dermal irritation, embryo toxicity, electrolyte abnormalities, apoptosis, cardiovascular collapse, teratogenicity, and mutagenic effects. High-performance liquid chromatography, UV-visible spectroscopy, gas chromatography/ mass spectrometry, and ion-exchange liquid chromatography were techniques used for detecting glyphosate in soil and water. The biodegradation of glyphosate was performed by various bacteria and fungi microorganisms.

Conclusions: Given the high consumption and low rates of biodegradation of glyphosate, more attention should be paid to its toxicity potential in the human's environment and health.

Citation: Ansari M, Hatami B, Sedighi Khavidak S. ***Toxicity, Biodegradability and Detection Methods of Glyphosate as the Most Used Herbicide: A Systematic Review***. J Environ Health Sustain Dev. 2019; 4(2): 731-43.

Introduction

Annually, two million tons of pesticides are consumed only in 10 top pesticide consuming countries in the world [1]. Worldwide, 40 percent of pesticides are used as herbicides. Glyphosate is known as the most concerned herbicide in some countries such as Iran. Glyphosate has the chemical name of Glyphosate; N-(phosphonomethyl) glycine; 1071-83-6; Glyphosphate; Pondmaster; Roundup with the molecular formula of $C_3H_8NO_5P$, vapor pressure of 0.01 mPa at 25 ^{0}C, and the water solubility of 12000 mg/L at 25 ^{0}C.

Glyphosate is a systemic, non-selective, and acidophilic herbicide used to control weeds [2]. Glyphosate was widely used to control agricultural weeds in many areas such as the north of Iran [3]. Some important properties of glyphosate are known as an enzyme inhibitor , 5-

enolpyruvylshikimate-3-phosphate (EPSP) synthase [4, 5], antifungal agents, [6] and as an uncoupling agent . In terms of health aspects, the U.S. Environmental Protection Agency (USEPA) classified glyphosate originally as a carcinogen (Class C, possible human carcinogen) because of the increased incidence of renal tumours in the studied mice. Furthermore, the International Agency for Research on Cancer (IARC) announced that glyphosate was a plausible agent for human cancer. From the perspective of environmental issues, continued extensive use of glyphosate components in agricultural activities is a cause of fundamental risks such as bioaccumulation, biomagnification, and toxicity for the environment [7, 8]. These risks potentially effect soil biological cycles [9], non-target organisms , subsequent pollution of groundwater [10, 11], runoff, [12] and the residues on agricultural crops . Recently, researchers showed an increased interest in related issues such as toxicity, degradation, biodegradation, fate, pathways, and health risks of glyphosate herbicides. However, toxicity, biodegradability, and detection method of glyphosate has been discussed rarely.

The aim of this paper was to review the newest evidences in toxicity, biodegradability, and detection methods of glyphosate.

Materials and Methods

This review was conducted using key terms of toxicity, biodegradation, and detection methods of glyphosate. In this regard, databases including Scopus, Web of Science, PubMed, and Google Scholar along with related published books in this filed were investigated. Considering the study aims, more detailed references with technical explanation and clarification on glyphosate toxicity, biodegradability, and detection method in soil and water were included; whereas, the unrelated articles and references were excluded. Some of the excluded articles were on other aspects of glyphosate, such as its removal or were published before year 2000. In addition, the articles published in languages other than Persian or English were excluded. Finally, in the biodegradation section, 14 articles were included for further investigation.

Results

Figure 1 shows the clinical features of glyphosate mentioned in the literature. As Figure 1 represents, human health risks caused by glyphosate exposure ranged from skin irritation to death. On the other hand, in the absence of human data, studies on experimental animals can provide the most reliable tools for detecting the important toxic properties of chemical compounds and for estimating the risks for human and environmental health. In addition, the experimental animals that received glyphosate through a variety of ways were at the risks of glyphosate toxicity [13]. In the literature, many animal toxicity studies were conducted to survey the toxicity of glyphosate. The results of animal toxicity studies are summarized in Table 1. Previous glyphosate biodegradation studies identified different species of microbial. Table 2 represents the microbial species and their isolation environments. These microbial species are isolated based on the morphology differences from a various glyphosate-contaminated environment. Moreover, Table 3 illustrates some of the main characteristics of glyphosate biodegradation. So far, different methods have been applied to measure glyphosate in different environments. Table 4 shows the detection methods and techniques of glyphosate in several environments.

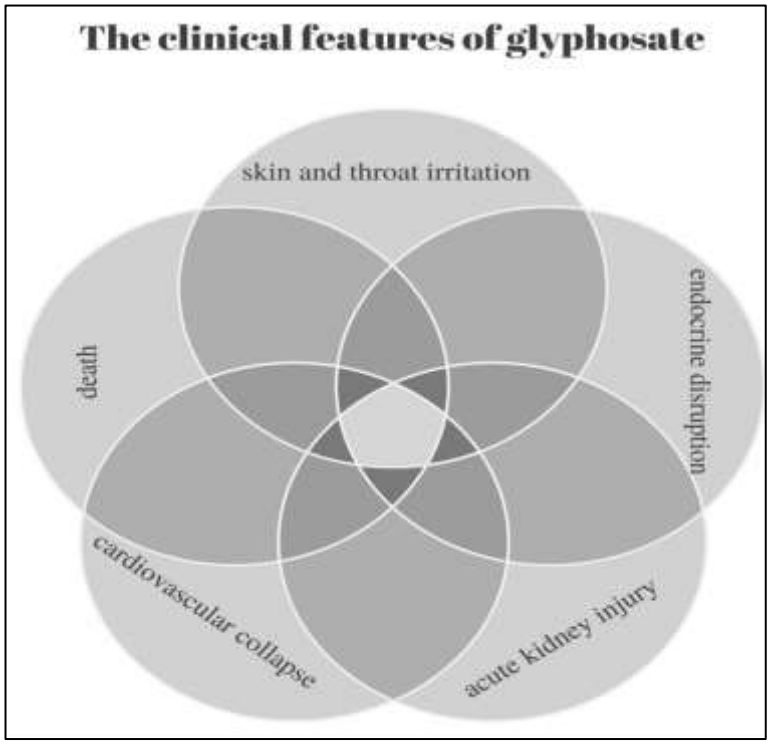

Figure 1: The clinical features of glyphosate

Table 1: The newest toxicity profiles of glyphosate against different animals

Host	Duration of exposure	Concentrations of glyphosate	Biochemical test	Observed disorders	Ref.
Adult offspring	1-5 Day	1% in drinking water	Glutamate excitotoxicity / oxidative stress	Oxidative stress, affects cholinergic and glutamatergic neurotransmission	14
Immature rat	Pregnancy and lactation	0.38% orally	$^{45}Ca^{2+}$ uptake, oxidative stress parameters, (14) C-α-methyl-amino-isobutyric acid ((14) C-MeAIB) accumulation, as well as glutamate uptake, release and metabolism	Oxidative stress and neural cell death	15
Odontesthes humensis	48-96 h	0.36-5.43 mg/L	Embryonic development and the number of somite pairs	Produce morphological alterations in fish embryos	16
Guppies	96 h	35 mg/L	The histopathological assessment	Tissue and gender-specific histopathological response	17
Zebrafish	96 h	1, 5, 10 and 100 mg/L	Enzyme activity, Reactive oxygen species, Apoptosis,	Body malformations with cellular apoptosis caused by ROS and inhibition of carbonic anhydrase,	18
Anuran	48 h	100, 1000, and 10,000 µg/g	The histopathological assessment	Increased the melanin area in MMCs, hepatic metabolism	19

Table 2: Microorganisms involved in the biodegradation of glyphosate Microbial Species

Microorganisms	Isolation environment	Region	Year	Ref.
Trichoderma viride strain FRP3	Agriculture land	Indonesia	2016	20
Pseudomonas sp. GA07, GA09 and GC04	Herbicide manufacturer	China	2015	21
Bacillussubtilis Bs-15	Pepper plant	China	2015	22
Actinomycetes	Apple orchards	Brazil	2014	23
Trichoderma viride strain FRP3	Malt extract agar	Japan	2013	24
O. anthropi GPK 3 and *Achromobacter sp.* Kg 16	Contaminated soil	Russia	2012	25
Stenotrophomonas maltophilia, Providencia alcalifaciens, Pseudomonas asplenii.	Oil palm plantation	Malesia	2012	26
Pseudomonas (Aeruginosa)	Citrus garden	Iran	2012	27
Penicillium oxalicum ZHJ6	Abandoned pesticide factories	China	2010	28
Escherichia sp, *Azotobacter* sp., *Alcaligenes* sp., *Acetobacter* sp. *Pseudomonas fluorescens)*	Rice fields	Nigeria	2010	29
Nocardioides sp.	Synthetic	Russia	2008	30
Filamentous fungi (91148 and 55.1)	Sugar cane	Brazil	2007	31

Table 3: Biodegradation characteristics of glyphosate

Study No.	Optimum pH	Temperature (^{0}C)	Initial concentration (mg/L)	Degradation rate (%)		Degradation media		Time (d)	Ref.
				Minimum	Maximum	Soil	Medium		
1	5.5	25	70	21.42	78	*		28	20
2	7	19-26	50	22.8	82	*		18	21
3	8	35	3800	19	71.57	*		4	22
4	6-8	60	1940	98.5	98.5	*		32	23
5	6.8-7.2	28	100	10	99		*	0.62	26
6	5	25	500	NA	52		*	4	28
7	7-8	NA	NA	NA	85	*		44	32
8	6	30	22	31.8	40	*		5	31

Table 4: Analytical techniques applied for detection and quantitative estimation of glyphosate residues

Study	Detection method	Detection technique	Environment	Ref.
1	Derivatization with fluorenylmethyl chloroformate	(LC-MS/MS)	Water	33
2	Stable isotope co-labeled 13C3 15N-glyphosate	UPLC-MS i-Class system	Water	34
3	Direct detect	HPLC	Soil	35
4	Derivatization with Fluorenylmethyl chloroformate (FMOC-Cl)	UV-visible spectroscopy (265 nm)	Soil	36
5	Vanadate-molybdate	UV-visible spectroscopy (880 nm)	Soil	37
6	Derivatization reaction with Acetic Acid/TMOA	GC/MS	Soil	26
7	Methamidophos assay	GC	Soil	38
8	Determination of turbidity	UV-visible spectroscopy (660 nm)	Soil	39
9	NA cylated derivatives	Ion-exchange liquid chromatography	Soil	40

NA: Not Available

Discussion

Toxicity of glyphosate against living organisms human health effects

evidence for carcinogenicity

The evidences over carcinogenicity of glyphosate in humans were reported by several national and international agencies [41]. The IARC's study showed a limited evidence on carcinogenicity of glyphosate in humans [42]. However, in some case-control studies, a positive evidence association was observed between occupational exposure to glyphosate and non-hodgkin lymphoma [43, 44]. Therefore, IARC interpreted all the evidences in order to justify the theory of glyphosate carcinogenicity [45]. The theory of

glyphosate carcinogenicity was confirmed, although it has limited evidences in humans. In fact, IARC relied on the evidences of carcinogenicity in animals and strong mechanistic evidences of genotoxicity and oxidative stress as a reasonable reason to accept carcinogenicity in humans. In another study, the Environmental Protection Agency (EPA) conducted a systematic review study over the carcinogenicity of glyphosate based on the Agency's own Cancer Guidelines and other related papers. It finally reported that glyphosate was not carcinogenic to humans [46].

Human toxicity

The most glyphosate toxicity studies were conducted on patients who ingested the commercial product "Round-up" consisting of a mixture of glyphosate (as an isopropylamine salt) and a surfactant (polyoxyethyleneamine). The U.S. Environmental Protection Agency (USEPA) reported that the chronic Reference Dose (cRfD) of glyphosate was 1.75 mg of glyphosate in mg/kg/day [47]. However, several studies showed potential adverse health effects on humans. According to Figure 1, glyphosate is known as an endocrine disruptor [48, 49]. Considering this reason, the level of testosterone, 17β-estradiol, and total protein, as indexes of endocrine disreputability, significantly decreased ($p \leq 0.05$) by exposure to glyphosate [50]. In addition, the concentrated solutions of glyphosate can also cause dermal irritation [51]. Most human cases were intoxicated through ingestion, inhalation, and skin contact in the previous studies. Ingestion of glyphosate can result in acute kidney injury, electrolyte abnormalities, acidosis [52], and cardiovascular collapse [53]. Human lymphocytes, with or without metabolic activation, were proved by negative genotoxicity of glyphosate [54]. A number of modern diseases are associated with exposure to the glyphosate toxicity. Gluten sensitivity or intolerance, as a known Celiac disease, is a complex disorder affected by a variety of risk factors. Exposure to glyphosate can be considered as an environmental factor [55]. The mechanism of glyphosate toxicity appears intricate and complicated. In this regard, Zhan et al. reported that presence of surfactants in the glyphosate compound aggravated this complexity [56]. Weng et al. showed that the surfactant component of glyphosate was contributed by rhabdomyolysis (a serious syndrome can lead to serious complications such as renal (kidney failure) and compartment syndrome [57]. In addition, Sribanditmongkol et al. described that the toxic effects of the surfactant polyoxyethylene amine (POEA) and glyphosate were caused by their capability to erode tissues [58]. Although glyphosate toxicity related to the central nervous system is still unknown, Malhotra et al. showed that its probability was a reversible encephalopathy to the direct neuronal toxic effects of glyphosate [59]. The toxicokinetics properties of glyphosate are also complicated. Respiratory failure, metabolic acidosis, tachycardia, elevated creatinine level, and hyperkalemia are known as sings of the refractory cardiopulmonary failure [60]. Moon et al.'s pathological findings in glyphosate fatality indicated that the gastric mucosa of anterior fundus showed hemorrhage and the small intestines identified the bowel obstruction [61]. The ingestion of glyphosate can result in acute kidney injury. Garlich et al. showed that hemodialysis should be considered because ingestion of glyphosate is associated with severe acidosis and acute kidney injury [62]. The results of Mink et al.'s epidemiologic review showed no significant positive correlation and causal relation between exposure to glyphosate and diseases of non-cancer respiratory debases, diabetes, myocardial infarction, reproductive and developmental outcomes, rheumatoid arthritis, thyroid, and Parkinson's disease (PD) [63]. Chen, et al.'s surveillance study indicated that Paraquat (one of the most widely used herbicides) and glyphosate are known as mild caustic agents that can injure the oesophagus. Injuries of the oesophagus caused by glyphosate have only grades 1, 2a, and 2b. The glyphosate commercial formulation was more cytotoxic than the only active component; this condition implies that the additive plays the main role in the glyphosate toxicity when the additive was added to the glyphosate commercial formulation [64]. However, glyphosate induces some adverse formations in the structure of micronucleus and some risky modification in the chemical

structure of DNA in a buccal epithelial cell line (TR146). In addition, glyphosate can alter some functional activity of human placental JEG3 cells[65]. The glyphosate exposure and risk of lymph hematopoietic cancer (LHC) including non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), multiple myeloma (MM), and leukemia were assessed by Chang and Delzell [66]. They found that Meta-relative risks (meta-RRs) were statistically positive for the association between the contrast without facing and risk of NHL and MM. These associations were statistically null for HL, leukemia, and NHL subtypes except B-cell lymphoma. Sorahan conducted a re-analysis of US Agricultural Health Study (AHS) data to find the relation between multiple myeloma and glyphosate use. According to Sorahan's study, positive association confirmed in some previous can be rejected due to their limited data. In this regard, their results showed no statistically significant trends for multiple myeloma risks in relation to application of the glyphosate [67].

Animal toxicity studies

Rats and mice

Rats and mice are the most studied experimental animals in glyphosate toxicology. So far, many types of the immunological, biochemical, genetic, and histopathology examinations have been carried out on rats and mice. The results reported that exposure to glyphosate did not affect the uterine weight, but could modulate the expression of estrogen-sensitive genes [68]. The EPA screening assay results (in the Endocrine Disruptor Screening Program) for 52 pesticide chemicals showed no detectable evidence of disruption in the thyroid pathway. In contrary, de Souza et al.'s showed that by glyphosate exposure to thyroid-stimulating hormone (TSH), expression of genes associated with thyroid hormone was disrupted during the perinatal period in male rats. Oxidative stress is one of the most frequently used biochemical examinations in analysing the potential cytotoxicity of chemical compounds and refers to the difference between existence of free radicals and body ability in detoxifying the risky effects of free radicals [69]. In rats, the lipid peroxidation (LPO) level is considered as an oxidative stress response [70]. In rats, roundup is probably a better antioxidant disruptor than an active ingredient glyphosate. Hence, a typical response to stress and inflammation is increased by exposure to a sub-lethal concentration of glyphosate [71]. Consequently, the antioxidant defence system is activated due to the increase in hydrogen peroxide generation. Therefore, the glyphosate-contained herbicides disrupts the normal biochemical function of liver and kidney [72]. Enzyme assay measures either the consumption of substrate or by-product for the whole time of cell's life. Therefore, this assay can help to have a better understanding of the chemicals' toxic effects. The results of enzymatic activity in the pregnant rats and their foetuses who were exposed to glyphosate showed that maternal exposure to glyphosate during pregnancy caused some functional abnormalities. The abnormalities were observed in isocitrate dehydrogenase-NADP dependent glucose-6-phosphate dehydrogenase and malic dehydrogenase affected liver, heart, and brain of the pregnant rats and their foetuses [73]. In a study by Ait Bali et al., mice were subjected to behavioural and immunohistochemical tests to investigate their sub-chronic and chronic exposure to glyphosate. The results showed that unlike acute exposure, both sub-chronic and chronic exposure to glyphosate induced a decrease in body weight gain and locomotors activity, while they increased anxiety and depression-like behaviour levels. In addition, the immunohistochemically findings showed that the chronic treatment induced only a reduction of TH-immunoreactivity. However, both sub-chronic and chronic exposure reduced serotonin -immunoreactivity in the dorsal raphe nucleus, basolateral amygdala, and ventral medial prefrontal cortex [74]. Cattani et al. studied exposure to glyphosate herbicide and depressive-like behaviour by developed the glutamate excitotoxicity and oxidative stress tests in adult offspring. The results of Cattani et al.'s study showed that glyphosate exposure caused oxidative stress and affected cholinergic and glutamatergic neurotransmission in offspring hippocampus from immature and adult rats [14].

Rabbits

A few glyphosate toxicity studies were conducted on rabbits. However, some results indicated that glyphosate toxicity had some effects on sperm quality. The adverse effects may be caused due to the cytotoxic effects of glyphosate on spermatogenesis directly and/or via hypothalami-pituitary-testis axis indirectly, which controls the reproductive efficiency [75]. Prenatal development of rabbits' cardiovascular status was affected when glyphosate posed a risk for cardiovascular malformations [76].

Fishes

The glyphosate embryotoxicity was not well known as its oxidative stress effects. Therefore, Zebral et al. estimated the effect of exposure to glyphosate on the odontesthes humanises embryonic development. They found that exposure to concentration for 96 h (0.36-0.54 mg/L) reduced the eye diameter and the distance between eyes of odontesthes humanises. In addition, main result of Zebral et al.'s study indicated that exposure to glyphosate (0.54mg/L) caused high mortality rates of fish embryos [16]. Sulukan et al. assessed body malformations during embryonic development on zebra fishes. Their results determined that glyphosate decreased CO_2 extraction and subsequently led to developing respiratory acidosis condition. In this condition, reactive oxygen species (ROS) level, as a carbonic anhydrase (CA) inhibitor increased. Finally, embryonic malformations were caused by ROS and inhibition of CA [18].

Other animals

McVey et al. conducted an exposure study to find the adult nervous system disorder in relation to Caenorhabditis elegans eggs exposed to glyphosate-containing herbicide. McVey et al.'s study showed that eggs from Caenorhabditis elegans exposed to glyphosate resulted in larva with abnormal neuronal cell bodies [77].

Glyphosate biodegradation

Table 2 shows that bacterial species were used in most glyphosate degradation studies. These microbial species had the ability to grow on media containing glyphosate as carbon, nitrogen, or phosphorus sources. Furthermore, Table 3 indicates that the minimum value of pH for optimum glyphosate degrading is 5 and Penicillium oxalicum is responsible for it. Table 3 also indicates that the minimum and maximum required temperature for optimal glyphosate biodegradation were recorded at 19 and 60 ^{0}C, respectively. In addition, the highest and lowest removal rates of glyphosate were 58.8 and 33.92 percent, respectively. The time required for maximum glyphosate removal was calculated between 0.62 and 32 days with a mean of 16.9 days. The strain could grow well in a wide range of pH (4 to 6.5) and the optimum growth was observed at pH range of 5-5.5. The results of kinetic investigation showed that the kinetic data of the glyphosate biodegradation process were characterized by the rate constants (k) of 0.0740, 0.0434, and 0.0946/day for strains GA07, GA09, and GC04, respectively [21]. Nourouzi et al. observed that with increase in initial glyphosate concentration, the percentage of glyphosate degradation decreased from 100 to 98 percent and from 20 to 10 percent when the pH and initial inoculums size were constant, respectively. Nourouzi et al. suggested that the Haldane model was more suitable for prediction of the growth inhibition kinetic of glyphosate [26]. Bacteria and fungus microorganisms were studied in glyphosate biodegradation due to their ability to degrade glyphosate as carbon or phosphorus or nitrogen sources. Accessibility to carbon, phosphorous, and nitrogen (CNP) sources is a significant issue in determining the biodegradation capability of pesticides in the soils. Moreover, due to high requirement of nutrients, microorganisms have to adapt themselves to the alternative nutrient sources when certain nutrients are deficient in the medium [78]. In the biodegradation studies, glyphosate was added to the cultivation medium as carbon, phosphorous, or nitrogen sources by bacteria and fungi [79]. Arfarita et al. reported a continuous tense increase in the growth of utilizing bacterial species when glyphosate was used as a phosphorus source and glucose was applied as the carbon source [24]. Castro et al. reported the glyphosate biodegradation as a sole source of phosphorous by fungal strains. Castro et al.'s study elaborated that the filamentous fungi belonging to the

Fusarium genre consumed glyphosate effectively as the source of phosphorous by increasing the biomass observed during the assay; even at a high concentration this compound supported the growth of Fusarium [31]. Shushkova et al. added the glyphosate to MS1 medium, instead of NH_4Cl, as a source of nitrogen and phosphorus. Shushkova et al. provided a further support for the hypothesis that changing the type of phosphorus source in the inoculum medium affected both the growth of culture and the decrease of glyphosate concentration. Furthermore, the highest level of biomass production and the maximum amount of utilized glyphosate were observed when the glyphosate was used as a phosphorus source [25]. Moneke et al. explained the effect of adding glyphosate, as a carbon and phosphorous sources in sole or combined forms on the glyphosate biodegradability. Moneke et al.'s study showed that glyphosate degradation by *Pseudomonas fluorescens* was significantly more than *Acetobacter* sp., while glyphosate was used as carbon and phosphorus sources . The isolated *Acetobacter* sp., *Azotobacter* sp., and *Alcaligenes* sp. bacteria were grown on the salt medium containing glyphosate as a sole phosphorus source. However, *Escherichia* sp. did not have any noticeable growth on the medium [29]. Finally, biodegradation was categorized under the two terms of bio-mineralization and biotransformation. In the bio-mineralization process, the organic compounds are completely degraded and converted to an inorganic material such as water and carbon dioxide [80]. However, in biotransformation, a part of the organic compounds is degraded and the remaining is converted into other simple organic compounds [81]. By reviewing related studies, it can be concluded that the glyphosate biodegradation is not classified in the bio-mineralization process.

Environmental detection of glyphosate

Depending on soil composition, glyphosate persists in soil for a long time (a few days to several months, or even one year) [82]. However, the average of glyphosate's half-life in water may differ from a few days to 91 days [83]. The mentioned half-life indicates that glyphosate has a good detection capability. Therefore, different methods were used to measure glyphosate in different environments. Table 4 represents analytical techniques applied for detection and quantitative estimation of glyphosate residues include derivatization with fluorenylmethyl chloroformate, stable isotope co-labeled 13C3 15N-glyphosate, direct detect, derivatization with fluorenylmethyl chloroformate (FMOC-Cl), vanadate-molybdate, derivatization reaction with acetic acid/TMOA, methamidophos assay, determination of turbidity, N -acylated derivatives. Glyphosate detection in various media was performed through complex analytical procedures. As shown in Table 4, liquid chromatography-tandem mass spectrometry (LC-MS/MS), UPLC-MS i-Class system, high-performance liquid chromatography (HPLC), UV-visible spectroscopy (in 265 nm), UV-visible spectroscopy (in 880 nm), gas chromatography mass spectrometry, gas chromatography, UV-visible spectroscopy (in 660 nm), and Ion-exchange liquid chromatography are techniques coupled with the above methods. Table 4 highlights that the spectroscopy measures were the major instrumental methods for detecting residue glyphosate. Another detection method was the separation processes such as chromatography. Application of appropriate methods in pesticide detection can provide more precision for the analyser and saves time, cost, and energy to improve the performance of integrated pesticide management [84]. Sun et al. and Al-Rajab et al. used high-performance liquid chromatography to separate, identify, and quantify glyphosate and its product amino methyl phosphoric acid (AMPA) in a mixture form [35, 85]. Moreover, Zhao et al. detected the glyphosate in the culture liquid and soil by HPLC [21]. Nourouzi et al. and Zhao et al. used chromatography technique for detecting the glyphosate in soil environment [26, 86]. Further research is required to develop ultrasensitive, real-time, and robust detection methods to detect and measure glyphosate and its production.

Conclusion

Environmental pollution, bioaccumulation, bio-magnification, and hazard effects on living organisms are the inevitable results of glyphosate

increased use. A crucial need exists to restrict the global use of herbicides and their impacts on the living organisms, water, and soil should be equally recognized. The expected glyphosate biodegradation depends on several key factors such as pH, temperature, and CNP values. The optimum condition of glyphosate biodegradation was obtained when pH was at 5 and temperature was from 19 to 60 ^{0}C. Accessibility to carbon, phosphorous, and nitrogen (CNP) is considered as a life crucial factor for microorganisms' growing. Therefore, glyphosate surfactant herbicides, which contains CNP in its composition can be degraded easily by microorganisms. The field and concentration monitoring of glyphosate and its derivatives are facilitated mainly by high-performance liquid chromatography, UV-visible spectroscopy, gas chromatography/ mass spectrometry, and ion-exchange liquid chromatography techniques.

Acknowledgements

This work was not possible without the support of Environmental Science and Technology Research Center, Department of Environmental Health Engineering, Shahid Sadoughi University of Medical Sciences.

Conflict of Interest

Authors declare no conflict of interests.

Funding

Authors declare no financial and material support in this work.

References

1. Uqab B, Mudasir S, Nazir R. Review on bioremediation of pesticides. J Bioremediat Biodegrad. 2016; 7(343): 2.
2. Wagner V, Antunes PM, Irvine M, et al. Herbicide usage for invasive non-native plant management in wildland areas of North America. J Appl Ecol. 2017; 54(1): 198-204.
3. Filizadeh Y, Rajabi Islami H. Toxicity determination of three sturgeon species exposed to glyphosate. Iran J Fish Sci. 2011; 10(3): 383-92.
4. Lu W, Li L, Chen M, et al. Genome-wide transcriptional responses of Escherichia coli to glyphosate, a potent inhibitor of the shikimate pathway enzyme 5-enolpyruvylshikimate-3-phosphate synthase. Mol Biosyst. 2013; 9(3): 522-30.
5. Ferreira MF, Franca EF, Leite FL. Unbinding pathway energy of glyphosate from the EPSPs enzyme binding site characterized by Steered Molecular Dynamics and Potential of Mean Force. J Mol Graph Model. 2017; 72: 43-9.
6. Zaller JG, Heigl F, Ruess L, et al. Glyphosate herbicide affects belowground interactions between earthworms and symbiotic mycorrhizal fungi in a model ecosystem. Sci Rep. 2014; 4: 8.
7. Myers JP, Antoniou MN, Blumberg B, et al. Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environ Health. 2016; 15: 13.
8. Pérez DJ, Okada E, Menone ML, et al. Can an aquatic macrophyte bioaccumulate glyphosate? Development of a new method of glyphosate extraction in Ludwigia peploides and watershed scale validation. Chemosphere. 2017; 185: 975-82.
9. Parfitt RL, Yeates GW, Ross DJ, et al. Effect of fertilizer, herbicide and grazing management of pastures on plant and soil communities. Appl Soil Ecol. 2010; 45(3): 175-86.
10. Guzzella L, Pozzoni F, Giuliano G. Herbicide contamination of surficial groundwater in Northern Italy. Environ Pollut. 2006; 142(2): 344-53.
11. Demonte LD, Michlig N, Gaggiotti M, et al. Determination of glyphosate, AMPA and glufosinate in dairy farm water from Argentina using a simplified UHPLC-MS/MS method. Sci Total Environ. 2018; 645: 34-43.

12. Krutz LJ, Senseman SA, Zablotowicz RM, et al. Reducing herbicide runoff from agricultural fields with vegetative filter strips: a review. Weed Sci. 2005; 53(3): 353-67.
13. Niemann L, Sieke C, Pfeil R, et al. A critical review of glyphosate findings in human urine samples and comparison with the exposure of operators and consumers. J Verbraucherschutz Lebensmittelsicherh. 2015; 10(1): 3-12.
14. Cattani D, Cesconetto PA, Tavares MK, et al. Developmental exposure to glyphosate-based herbicide and depressive-like behavior in adult offspring: Implication of glutamate excitotoxicity and oxidative stress. Toxicology. 2017; 387: 67-80.
15. Cattani D, de Liz Oliveira Cavalli VL, Heinz Rieg CE, et al. Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity. Toxicology. 2014; 320: 34-45.
16. Zebral YD, Costa PG, de Castro Knopp B, et al. Effects of a glyphosate-based herbicide in pejerrey Odontesthes humensis embryonic development. Chemosphere. 2017; 185: 860-7.
17. Antunes AM, Rocha TL, Pires FS, et al. Gender-specific histopathological response in guppies Poecilia reticulata exposed to glyphosate or its metabolite aminomethylphosphonic acid. J Appl Toxicol. 2017; 37(9): 1098-107.
18. Sulukan E, Kokturk M, Ceylan H, et al. An approach to clarify the effect mechanism of glyphosate on body malformations during embryonic development of zebrafish (Daino rerio). Chemosphere. 2017; 180: 77-85.
19. Pérez-Iglesias JM, Franco-Belussi L, Moreno L, et al. Effects of glyphosate on hepatic tissue evaluating melanomacrophages and erythrocytes responses in neotropical anuran Leptodactylus latinasus. Environ Sci Pollut Res Int. 2016; 23(10): 9852-61.
20. Arfarita N, Djuhari, Prasetya B, et al. The application of trichoderma viride strain frp 3 for biodegradation of glyphosate herbicide in contaminated land. Agrivita. 2016; 38(3): 275-281.
21. Zhao H, Tao K, Zhu J, et al. Bioremediation potential of glyphosate-degrading Pseudomonas spp. strains isolated from contaminated soil. J Gen Appl Microbiol. 2015; 61(5): 165-70.
22. Yu XM, Yu T, Yin GH, et al. Glyphosate biodegradation and potential soil bioremediation by Bacillus subtilis strain Bs-15. Genet Mol Res. 2015; 14(4): 14717-30.
23. Andrighetti MS, Nachtigall GR, de Queiroz SCN, et al. Biodegradation of glyphosate by microbiota of soils of apple tree fields. Rev Bras Cienc Solo. 2014; 38(5): 1643-53.
24. Arfarita N, Imai T, Kanno A, et al. The potential use of trichoderma viride strain FRP3 in biodegradation of the herbicide glyphosate. Biotechnol Biotechnol Equip. 2013; 27(1): 3518-21.
25. Shushkova TV, Ermakova IT, Sviridov AV, et al. Biodegradation of glyphosate by soil bacteria: Optimization of cultivation and the method for active biomass storage. Microbiology. 2012; 81(1): 44-50.
26. Nourouzi MM, Chuah TG, Choong TSY, et al. Modeling biodegradation and kinetics of glyphosate by artificial neural network. J Environ Sci Health B. 2012; 47(5): 455-65.
27. Hoodaji M, Tahmourespour A, Partoazar M. The efficiency of glyphosate biodegradation by Pseudomonas (Aeruginosa): World Scientific Publishing Co. 2012: 183-6.
28. Zhao R-B, Bao H-Y, Liu Y-X. Isolation and characterization of penicillium oxalicum ZHJ6 for biodegradation of methamidophos. Agric Sci China. 2010; 9(5): 695-703.
29. Moneke AN, Okpala GN, Anyanwu CU. Biodegradation of glyphosate herbicide in vitro using bacterial isolates from four rice fields. Afr J Biotechnol. 2010; 9(26): 4067-74.
30. Zelenkova NF, Vinokurova NG. Determination of glyphosate and its biodegradation products by chromatographic methods. J Anal Chem. 2008; 63(9): 871-4.
31. Castro JRV, Peralba MCR, Ayub MAZ. Biodegradation of the herbicide glyphosate by filamentous fungi in platform shaker and batch

bioreactor. J Environ Sci Health B. 2007; 42(8): 883-6.
32. Alexa E, Sumalan R, Negrea M, et al. Studies on the biodegradation capacity of14C-labelled glyphosate in vine plantation soils. J Food Agric Environ. 2010; 8(3-4): 1193-8.
33. Claude B, Berho C, Bayoudh S, et al. Preliminary recovery study of a commercial molecularly imprinted polymer for the extraction of glyphosate and AMPA in different environmental waters using MS. Environ Sci Pollut Res. 2017; 24(13): 12293-300.
34. Wang S, Seiwert B, Kästner M, et al. (Bio)degradation of glyphosate in water-sediment microcosms-A stable isotope co-labeling approach. Water Res. 2016; 99: 91-100.
35. Sun LS, Wang N, Kong DY, et al. Influence of soil physical and chemical properties on detection of glyphosate residue. J Ecol Rural Enviro. 2017; 33(9): 860-4.
36. Qian K, Tang T, Shi T, et al. Residue determination of glyphosate in environmental water samples with high-performance liquid chromatography and UV detection after derivatization with 4- chloro-3, 5-dinitrobenzotrifluoride. Anal Chim Acta. 2009; 635(2): 222-6.
37. Huo R, Yang XL, Liu YQ, et al. Visible-light photocatalytic degradation of glyphosate over BiVO4 prepared by different co-precipitation methods. Mater Res Bull. 2017; 88: 56-61.
38. Yu Y, Zhang H, Zhou Q. Using soil available P and activities of soil dehydrogenase and phosphatase as indicators for biodegradation of organophosphorus pesticide methamidophos and glyphosate. Soil Sediment Contam. 2011; 20(6): 688-701.
39. Liu CM, McLean PA, Sookdeo CC, et al. Degradation of the herbicide glyphosate by members of the family Rhizobiaceae. Appl Environ Microbiol. 1991; 57(6): 1799-804.
40. Sancho JV, Hernández F, López FJ, et al. Rapid determination of glufosinate, glyphosate and aminomethylphosphonic acid in environmental water samples using precolumn fluorogenic labeling and coupled-column liquid chromatography. J Chromatogr A. 1996; 737(1): 75-83.
41. Portier CJ, Armstrong BK, Baguley BC, et al. Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA). J Epidemiol Community Health. 2016; 70(80): 741-5.
42. Guyton KZ, Loomis D, Grosse Y, et al. Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. Lancet Oncol. 2015; 16(5): 490-1.
43. Williams GM, Aardema M, Acquavella J, et al. A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to the IARC assessment. Crit Rev Toxicol. 2016; 46(sup1): 3-20.
44. Acquavella J, Garabrant D, Marsh G, et al. Glyphosate epidemiology expert panel review: A weight of evidence systematic review of the relationship between glyphosate exposure and non-Hodgkin's lymphoma or multiple myeloma. Crit Rev Toxicol. 2016; 46(sup1): 28-43.
45. Williams GM, Aardema M, Acquavella J, et al. A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to the IARC assessment. Crit Rev Toxicol. 2016; 46: 3-20.
46. USEPA. Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. EPA's Office of Pesticide Programs; 2016.
47. Benbrook CM. Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur. 2016; 28(1): 3.
48. Thongprakaisang S, Thiantanawat A, Rangkadilok N, et al. Glyphosate induces human breast cancer cells growth via estrogen receptors. Food Chem Toxicol. 2013; 59: 129-36.
49. Gasnier C, Dumont C, Benachour N, et al. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. Toxicology. 2009; 262(3): 184-91.
50. Omran NE, Salama WM. The endocrine disruptor effect of the herbicides atrazine and glyphosate on Biomphalaria alexandrina snails.

Toxicology and Industrial Health. 2016; 32(4): 656-65.
51. Thakur DS, Khot R, Joshi PP, et al. Glyphosate poisoning with acute pulmonary edema. Toxicol Int. 2014; 21(3): 328-30.
52. Bradberry SM, Proudfoot AT, Vale JA. Glyphosate poisoning. Toxicol Rev. 2004; 23(3): 159-67.
53. Gress S, Lemoine S, Séralini GE, et al. Glyphosate-Based herbicides potently affect cardiovascular system in mammals: Review of the literature. Cardiovasc Toxicol. 2015; 15(2): 117-26.
54. Williams GM, Berry C, Burns M, et al. Glyphosate rodent carcinogenicity bioassay expert panel review. Crit Rev Toxicol. 2016; 46: 44-55.
55. Samsel A, Seneff S. Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance. Interdiscip Toxicol. 2013; 6(4): 159-84.
56. Zhang M, Wei Y, Zhao K, et al. Glyphosate degradation with industrial wastewater effluent by combined adsorption treatment and advanced oxidation processes. Advanced Materials Research. 2011; 233: 369-72.
57. Weng SF, Hung DZ, Hu SY, et al. Rhabdomyolysis from an intramuscular injection of glyphosate-surfactant herbicide. Clin Toxicol. 2008; 46(9): 890-1.
58. Sribanditmongkol P, Jutavijittum P, Pongraveevongsa P, et al. Pathological and toxicological findings in glyphosate-surfactant herbicide fatality: A case report. Am J Forensic Med Pathol. 2012; 33(3): 234-7.
59. Malhotra RC, Ghia DK, Cordato DJ, et al. Glyphosate-surfactant herbicide-induced reversible encephalopathy. J clin neurosci. 2010; 17(11): 1472-3.
60. Campbell AW. Glyphosate: Its effects on humans. Altern Ther Health Med. 2014; 20(3): 9-11.
61. Moon JM, Chun BJ, Cho YS, et al. Cardiovascular effects and fatality may differ according to the formulation of glyphosate salt herbicide. Cardiovasc Toxicol. 2018; 18(1): 99-107.
62. Garlich FM, Goldman M, Pepe J, et al. Hemodialysis clearance of glyphosate following a life-threatening ingestion of glyphosate-surfactant herbicide. Clin Toxicol. 2014; 52(1): 66-71.
63. Mink PJ, Mandel JS, Lundin JI, et al. Epidemiologic studies of glyphosate and non-cancer health outcomes: A review. Regul Toxicol Pharmacol. 2011; 61(2): 172-84.
64. Chen YCS, Hubmeier C, Tran M, et al. Expression of CP4 EPSPS in microspores and tapetum cells of cotton (Gossypium hirsutum) is critical for male reproductive development in response to late-stage glyphosate applications: Review article. Plant Biotechnol J. 2006; 4(5): 477-87.
65. Richard S, Moslemi S, Sipahutar H, et al. Differential effects of glyphosate and roundup on human placental cells and aromatase. Environ Health Perspect. 2005; 113(6): 716-720.
66. Chang ET, Delzell E. Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers. J Environ Sci Health B. 2016; 51(6): 402-34.
67. Sorahan T. Multiple myeloma and glyphosate use: a re-analysis of US Agricultural Health Study (AHS) data. Int J Environ Res Public Health. 2015; 12(2): 1548-59.
68. Varayoud J, Durando M, Ramos JG, et al. Effects of a glyphosate-based herbicide on the uterus of adult ovariectomized rats. Environ Toxicol. 2017; 32(4): 1191-1201.
69. de Souza JS, Kizys MML, da Conceição RR, et al. Perinatal exposure to glyphosate-based herbicide alters the thyrotrophic axis and causes thyroid hormone homeostasis imbalance in male rats. Toxicology. 2017; 377: 25-37.
70. Patra RC, Swarup D, Dwivedi SK. Antioxidant effects of alpha tocopherol, ascorbic acid and L-methionine on lead induced oxidative stress to the liver, kidney and brain in rats. Toxicology. 2001; 162(2): 81-8.

71. Gill JPK, Sethi N, Mohan A, et al. Glyphosate toxicity for animals. Environ Chem Lett. 2017; 16(2): 401–26.
72. El-Shenawy NS. Oxidative stress responses of rats exposed to roundup and its active ingredient glyphosate. Environ Toxicol Pharmacol. 2009; 28(3): 379-85.
73. Daruich J, Zirulnik F, Sofía Gimenez M. Effect of the herbicide glyphosate on enzymatic activity in pregnant rats and their fetuses. Environ Res. 2001; 85(3): 226-31.
74. Ait Bali Y, Ba-Mhamed S, Bennis M. Behavioral and immunohistochemical study of the effects of subchronic and chronic exposure to glyphosate in mice. Front Behav Neurosci. 2017; 11: 146.
75. Yousef MI, Ibrahim HZ, Helmi S, et al. Toxic effects of carbofuran and glyphosate on semen characteristics in rabbits. J Environ Sci Health B. 1995; 30(4): 513-34.
76. Kimmel GL, Kimmel CA, Williams AL, et al. Evaluation of developmental toxicity studies of glyphosate with attention to cardiovascular development. Crit Rev Toxicol. 2013; 43(2): 79-95.
77. Mcvey KA, Snapp IB, Johnson MB, et al. Exposure of C. elegans eggs to a glyphosate-containing herbicide leads to abnormal neuronal morphology. Neurotoxicol Teratol. 2016; 55: 23-31.
78. Zhan H, Feng Y, Fan X, et al. Recent advances in glyphosate biodegradation. Appl Microbiol Biotechnol. 2018; 102(12): 5033-43.
79. Uqab B, Mudasir S, Nazir R. Review on bioremediation of pesticides. J Bioremediat Biodegrad. 2016; 7(3): 2.
80. Yao SS, Jin BA, Liu ZM, et al. Biomineralization: from material tactics to biological strategy. Adv Mater. 2017; 29(14): 19.
81. Zhang SB, Yin LB, Liu Y, et al. Cometabolic biotransformation of fenpropathrin by Clostridium species strain ZP3. Biodegradation. 2011; 22(5): 869-75.
82. Borggaard OK, Gimsing AL. Fate of glyphosate in soil and the possibility of leaching to ground and surface waters: A review. Pest Manag Sci. 2008; 64(4): 441-56.
83. Giesy JP, Dobson S, Solomon KR. Ecotoxicological risk assessment for roundup herbicide. In: Ware GW, editor. Rev Environ Contam Toxicol. New York, NY: Springer New York; 2000. p. 35-120.
84. Xu M-L, Liu J-B, Lu J. Determination and control of pesticide residues in beverages: a review of extraction techniques, chromatography, and rapid detection methods. Appl Spectrosc Rev. 2014; 49(2): 97-120.
85. Al-Rajab AJ, Schiavon M. Degradation of 14C-glyphosate and aminomethylphosphonic acid (AMPA) in three agricultural soils. J Environ Sci. 2010; 22(9): 1374-80.
86. Zhao R-B, Bao H-Y, Liu Y-X. Isolation and characterization of penicillium oxalicum ZHJ6 for Biodegradation of Methamidophos. Agr Sci China. 2010; 9(5): 695-703.