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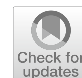
REVIEW



Glyphosate uptake, translocation, resistance emergence in crops, analytical monitoring, toxicity and degradation: a review

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Abstract
The herbicide glyphosate is widely used to control weeds in grain crops. The overuse of glyphosate has induced issues such as contamination of surface water, decreased soils fertility, adverse effects on soil microbiota and possible incorporation in food chains. Here we review biochemical, agricultural, microbiological and analytical aspects of glyphosate. We discuss uptake, translocation, toxicity, degradation, complexation behaviour, analytical monitoring techniques and resistance emergence in crops. We provide data of glyphosate toxicity on different ecosystems. Experiments reveal that excessive glyphosate use induces stress on crops and on non-target plants, and is toxic for mammalians, microorganisms and invertebrates. The long half-life period of glyphosate and its metabolites under different environmental conditions is a major concern. Development of analytical methods for the detection of glyphosate is important because glyphosate has no chromophoric or fluorophoric groups.

Keywords Glyphosate · Genetically modified crops · Monitoring · Microbial degradation · Toxicity

Introduction

Glyphosate [*N*-(phosphonomethyl) glycine], CAS Number: 1071-83-6, is one of most widely used herbicide worldwide since 1971 (Morton and Edwards 2005; Myers et al. 2016; Conrad et al. 2017). Glyphosate is derived from phosphonic acid and glycine (Table 1). It controls and eradicates grasses and broad-leaved weeds in crops (Mazzei and Piccolo 2012; Williams et al. 2016; Tarazona et al. 2017; EFSA 2017). It was first synthesized and commercialized by a Pharmaceutical Company of Switzerland in 1950, but its herbicidal properties were studied by John. E. Franz of Monsanto Company under trade name Roundup (Dill et al. 2010; Gill et al. 2018). Glyphosate is a polyprotic molecule having three polar functional groups (phosphonate, carboxyl and amino group) and half-life ranges from 2 to 215 days in soil and 2–91 days in aquatic medium (Battaglin et al. 2014; Maqueda et al. 2017).

The major product formed during the glyphosate degradation is aminomethylphosphonic acid (AMPA). The half-life times of glyphosate and AMPA is variable in different systems (soil, water, air) and ranges between few days to one or two years. The half-life primarily depends on environmental and edaphic conditions, such as soil moisture and temperature (EFSA 2013, 2017; Bento et al. 2016;

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Silva et al. 2018). As per the data of European Food Safety Authority (EFSA), in soils, the half-life time for glyphosate and AMPA was 143.3 days and of 514.9 days, respectively (EFSA 2013). In sea water, the half-life for glyphosate at 25 °C in low light was 47 days, while in dark at 25 °C the half-life increases to 267 days, and in the dark at 31 °C the half-life was found to be 315 days. In dark at 31 °C, glyphosate is found to persist maximally. Detection of AMPA (the microbial transformation product of glyphosate) under all conditions confirmed that degradation was mediated by the native microbial community (Mercurio et al. 2014). The half-life period of glyphosate and AMPA were numerically assessed for a vineyard and a wheat field in the Po Valley, Italy by la Cecilia et al. (2018). The Calculation of the Hazard Quotient suggested that glyphosate and AMPA can pose a risk of aquifer contamination in the top 1.5 m depth within 50 years of GLP use. There is a long debate on the toxicity and carcinogenicity of glyphosate, and based upon the availability of authentic data, it was found suitable for agricultural use every time. As per literature data and experimental evidence provided by the glyphosate manufactures, it is not considered to be persistent organic pollutants (POPs), persistent, bioaccumulative and toxic (PBT), and very persistent and very bioaccumulative (vPvB) chemical (Link 1 and 2). Based on its physicochemical and structural properties, it does not fall under the category of POP, PBT and vPvB. Use of glyphosate at a recommended dose level has shown its proper utility and best applications. Only few studies have been reported on the long persistence of glyphosate, which is not enough evidence to declare it as a non-suitable herbicide for agricultural uses (EFSA 2013, 2017; Mercurio et al. 2014; Bento et al. 2016; Silva et al. 2018).

The maximum acceptable daily intake of glyphosate in drinking water is 0.9 mg/L (Schriks et al. 2010) and per kg body weight is 1.75 mg/kg (Myers et al. 2016). Few studies revealed the level of glyphosate as high as 1.42 µg/L in groundwater of Ich-EK and 0.47 µg/L in urine samples of the farmers of the Francisco J. Mujica communities (Rendón-Von Osten and Dzul-Caamal 2017). Cell manifestation and glyphosate accumulation declined the uptake (Kutman et al. 2013) and translocation proficiency (Ou et al. 2018), for which plants developed resistance either by inheritance or genetic modification (Coupe and Capel 2016). The International Agency for Research on Cancer (IARC) classified herbicide glyphosate in Category '2a' which specifies glyphosate to be carcinogenic to humans (McClellan 2016). The USEPA has classified glyphosate as a 'Group E' carcinogen, which means it has 'evidence of non-carcinogenicity for humans' (Temple 2016), whereas European Food Safety Authority (EFSA) also specified that glyphosate poses to be a carcinogenic hazard to humans. The evidence from experimental studies does not support this conclusion in relation to its carcinogenic potential (Portier et al. 2016).

Glyphosate accounts for the most consumed pesticide in the USA and accounts for approximately 72% of worldwide usage (Myers et al. 2016). In European countries, Germany and Denmark, 35–39% of the agriculture relies on glyphosate (Steinmann et al. 2012) and in Argentina, 180–200 million tonnes of glyphosate is consumed annually (Nedelkoska and Low 2004). In India, 960 tonnes of glyphosate is consumed annually with an annual increase of 38.5% (Ministry of Chemicals and Fertilizers (Department of Chemicals and Petrochemicals) 2014–2015). Sabero Organics Ltd. (Gujarat) is the leading manufacturer of glyphosate with 21.45% of total production in India (Ministry of Chemicals and Fertilizers (Department of Chemicals and Petrochemicals) 2012–2013). The production of glyphosate in India decreased from 1700 metric tonnes to 960 tonnes

Table 1 Chemical and physical characteristics of glyphosate and its metabolites

General Name	IUPAC name	Chemical formula	MW (g/mol)	Solubility in water (g/L)	Log P (at 25 °C)	Density (g/cm^3)	Henry's law constant (Pa m^3 mol^{-1})
Glyphosate	2-(phosphonomethylamino)acetic acid;propan-2-amine	$C_6H_{17}N_2O_5P$	228.185	12	−5.4	1.7	2×10^{-12}
Aminomethylphosphonic acid	–	CH_6NO_3P	111.04	50	0.4	1.6	–
Sarcosine	*N*-methylglycine	$C_3H_7NO_2$	89.093	89.09	−2.8	1.093	2.47×10^{-9}
Glyoxylate	Glyoxylic acid	$C_2H_2O_3$	74.035	224	−0.07	1.384	3×10^{-9}
Formylphosphonate	Formylphosphonic acid	CH_3O_4P	110.005	24.8	−1.8	1.79	7.37×10^{-8}
Methylamine	Méthanamine	CH_5N	31.057	100	−0.57	0.693	–
Glycine	2-Aminoacetic acid	$C_2H_5NO_2$	75.066	249.9	−3.2	1.61	–
Formaldehyde	–	CH_2O	30.011	400	1.2	0.815	–

between the year 2009 and 2012 (Ministry of Chemicals and Fertilizers (Department of Chemicals and Petrochemicals) 2012–2013). Globally, the share of total use of glyphosate among other herbicide during 1974–2014 was 1.5%, which increased to 71.6% from 2005 to 2015 (Benbrook 2016; Kaur et al. 2017). Similar trends were noticed for the applications of glyphosate in India and the USA. The global herbicide market was $23.97 billion in 2016 and is estimated to reach $34.10 billion by 2022, at a growth rate of 6.05% for the forecasted period (Benbrook 2016). It was partially banned in Sri Lanka (Copping 2014; Sirinathsinghji 2014), Argentina (Ho 2010; Arancibia 2013), Malta (Redbond 2016) Brazil, Colombia, France (Green and Owen 2011) and Netherlands (Sirinathsinghji 2014) because of its persistence in surface and soil sediments (Peres-Oliveira et al. 2016; Bento et al. 2016).

Glyphosate is used in two broad ways (i) direct use: used in agriculture under different formulations and various salt compositions (Benbrook 2016; Kaur et al. 2017). After its introduction to the world market (since 1974), a 15-fold increase has been noticed in the production and consumption of this herbicide (Benbrook 2016). The corresponding share globally is 72%. (ii) indirect use: used in genetically modified crops (Benbrook 2016; Kaur et al. 2017). Fifty-six percentage of global glyphosate use include genetically engineered herbicide-tolerant crops.

This review discusses various aspects of uptake, translocation, resistance emergence in crops, analytical monitoring, toxicity and degradation of glyphosate.

Uptake and translocation of glyphosate in plants

The efficacy of the herbicides depends upon its dosage, which gets translocated to the subsistence parts of the plant (Gomes et al. 2014; Sammons and Gaines 2014; Kvesitadze et al. 2016). Glyphosate is one such broadspectrum herbicide which aids in regulating the plants when dispensed in the appropriate amount (Baird 1971; Caseley and Coupland 1985; Monaco et al. 2002; Dill et al. 2010). For the last 40 years, translocation of the effective dose of glyphosate in 40 different weeds has been studied to determine the uptake efficiency and translocation extent of the herbicide. The first study provides insight about the mechanism, by which the phloem aids in the translocation of the glyphosate to the meristematic portion of the roots and other parts of the plant (Sprankle et al. 1973; Dill et al. 2010). This movement of glyphosate via phloem assisted in linking the role of environmental conditions with translocation efficiency and plant development. This information is well encompassed in a book entitled “The Herbicide Glyphosate” (Caseley and Coupland 1985). Shikimic acid accumulation was found to be the major cause of EPSPS inhibition (Steinrücken and Amrhein 1980), which also aids in assessing the toxicity of glyphosate (Singh and Shaner 1998). Translocation and uptake are two different mechanisms, but both are studied mutually. Translocation encompasses the assessment of dosage for evaluating the distribution ratio, whereas uptake focuses on the drop size plus concentration of solute (Dill et al. 2010). The major enigma of the uptake mechanism is to relate the concentration and volume during the delivering of the desired dose (Feng et al. 2000). During hand application, it is impracticable to sustain the desired dose, as drop size is too small and in abundance (Dill et al. 2010). Subsequently, during experimentation the drop volume is small/large which disfigures the ratio of herbicide/surfactant/carries volume and shatters the opportunity to comprehend the proficiency of spray solution penetration (Feng et al. 2000). Thus, understanding the penetration mechanism has enabled us to optimize the herbicide formulation, in which herbicide gets transported through cuticle towards the apoplast, which subsequently reaches the symplast, where phloem transfers it to rest of the plant (Dill et al. 2010). Several independent factors such as type of surfactant as well as its concentration, ionic strength and salt concentration, droplet size and droplet spread, cuticle composition plus the thickness, humidity, and most significantly, the concentration of glyphosate regulate the uptake mechanism (Dill et al. 2010). In assessing these decisive factors, extensive studies are conducted by employing the ideal nozzle as well as a carrier (Prasad and Cadogan 1992; Feng et al. 2000). Moreover, inconvenience is encountered during the delivery of precise dose to leaf intercept via spraying, which leads to the assessment of the proficiency of leaf intercept. The concentration of herbicide, drop size and the surfactant has no cytology impact over leaf surface which can be linked to uptake efficiency (Feng et al. 2000). The excessive accumulation of surfactant/large surface area of cuticle offers the macro-drops to cease the active site and hastily discontinues loading via the phloem. Droplet generator aids in establishing the link among the drop size and concentration/penetration (Prasad and Cadogan 1992). Herbicide in small drops has resolved the size factor, and further, it exhibited a very less deteriorating effect on the epidermal tissue (Ryerse et al. 2004) by evading the transport inhibition because of cell injury. To verify the concept of soaking of minute spray droplets, D_2O (deuterium oxide) was employed, in which surfactant forms a network which aids the herbicide to invade the cuticle as quantified by measuring the D_2O amount in leaf (Feng et al. 1999). The advent of genetic resistant corn permitted the assessment of local droplets, herbicide toxicity, surfactant damage associated with drop size, which is retained less, and more efficiently load the glyphosate which results in enhanced translocation. Further, ^{14}C-glyphosate experimentation creates the ideal field environment and concurrently aids in understanding

the uptake mechanism plus characteristics (Feng et al. 2000, 2003b; Feng and Chiu 2005). The efficiency of translocation considerably gets affected via glyphosate toxicity which initiates additional absurdity that initially optimizes the translocation but with time it increases its toxicity. Negative effects of minute dosage can be visualized on meristems, as different tissues have a discrete cytological effect (Feng et al. 2003b). Toxicity regulates glyphosate efficiency as well as the distribution pattern. Various studies preferred the movement from the source towards sink confirmed by the sugar-beet model (Dewey 1981; Gougler and Geiger 1981) which at the end downgrades the photosynthesis and limits the rate of translocation (Geiger et al. 1986; Geiger and Bestman 1990). These analysed conundrums indicate that measuring the over-sprayed glyphosate translocation value is a hazardous practice. As it will primarily depend on sink strength, toxicity and indefinite amount of glyphosate which as a result restrain its translocation within the plant (Dill et al. 2010). As translocation studies promptly focus on the amount, one can use the specific dosage for a particular location (Feng and Chiu 2005). Moreover, the higher the uptake rate, superior is the process since its small amount will reach the sink and induce self-limitation route which eventually ceases the translocation revealing the relationship among sink and source (Dill et al. 2010). Comparing wild/sensitive-type of crops with GR (glyphosate-resistant) crops, it is delineated that GR facilitates in the parting of physical barriers such as cuticle, cell wall/membrane (Feng et al. 2003b; Feng and Chiu 2005). When the GR crops were unavailable, the ultra-low dosage is used which does not affect the uptake as well as translocation, which is demonstrated by resistant-horseweed (Feng et al. 2004). Studying the sensitive and resistant crops below the toxic level unravels the impact the physical activity incurs on translocation and partitioning process, affirmed by ryegrass and horseweed (Lorraine-Colwill et al. 2002; Feng et al. 2004; Powles and Preston 2006), whereas equal translocation is observed in Palmer amaranth (Culpepper et al. 2006; Sammons et al. 2007). Equal translocation works on a different principle which makes the crop self-sustainable, which is demonstrated by GR soybean which limits translocation towards apical meristem but equally translocate the herbicide in leaves and other tissues, implying apoplast unloading. In order to remove the source perception, there is a need for the cessation of source–sink linkage (Sammons et al. 2007). Apoplastic unloading is a new concept which changes the perception of source–sink linkage; the superficial movement from the source towards sink impersonates numerous prospects to illuminate symplastic regulation in addition to apoplastic movement.

Mechanistic action of glyphosate in plants

Glyphosate and aminomethylphosphonic acid (AMPA), which is a metabolite of glyphosate, is translocated to the leaves by two processes, in which first they penetrate through the cuticle and subsequent uptake via symplast (Monquero et al. 2004). Generally, symplast allows the entry either by endogenous carrier system (Burton and Balke 1988) or passive diffusion (Gougler and Geiger 1981), which depends on the attributes like the amount of herbicide, environmental factors and plant species (Fig. 1).

This uptake process is hindered by various environmental factors such as humidity and moisture of soil, cuticular wax synthesis, hydration and mineral assimilation (Franz et al. 1997; Sharma and Singh 2001). Glyphosate in the form of

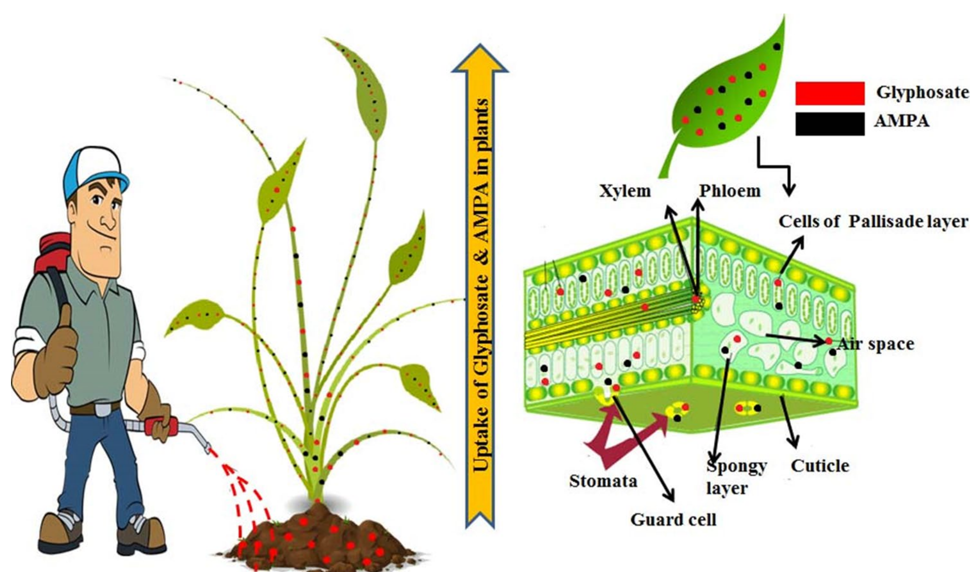


Fig. 1 Metabolism and adsorption of glyphosate and aminomethylphosphonic acid (AMPA) in plants

roundup formulation once penetrated and translocated accumulates at meristematic as well as actively dividing sites like root and shoot apices, tubers, rhizomes and young leaves, which act as a sink and amend normal life cycle of plants (Satchivi et al. 2000; Monquero et al. 2004; Cakmak et al. 2009). This was validated by ^{14}C glyphosate absorption in *Abutilon theoprasti* (Feng et al. 2003a). Moreover, exudation of translocated glyphosate from roots is a major problem as it constrains the progression of adjoining plants and seeds as observed in GR *Glycine max*, i.e. soybean (Kremer et al. 2005). Some studies reveal the glyphosate functions by capturing the active sites of the enzyme phosphoenolpyruvate by imitating the intermediate enzyme–substrate complete by using X-ray crystallographic techniques (Schönbrunn et al. 2001). Other studies also reported about inhibition of non-targeted plants like *Chenopodium quinoa* (Laitinen et al. 2007; Gravena et al. 2012).

Further, it was proposed that glyphosate gets disintegrated to AMPA, which is also taken up from the soil and translocated to the active site from the xylem passage to shoot apices. Moreover, extensive research needs to be done to know about AMPA and its phytotoxic influence on GR crops (Reddy et al. 2004). Glyphosate affects normal plant growth by debilitating the Shikimate process (Corrêa et al. 2016). It hampers the production of 5-enolpyruvylshikimate-3-phosphate synthase, an enzyme which supports the synthesis of essential amino acids (Gomes et al. 2014), Fig. 2.

5-Enolpyruvylshikimate-3-phosphate synthase is responsible for the biogenesis of chorismate, which is an important intermediate in the synthesis of aromatic amino acids, phenylalanine, tyrosine and tryptophan (Salman et al. 2016). Deficiency of this enzyme leads to senescence and death by affecting the metabolic functions of the plant (Mahendrakar et al. 2014). Glyphosate strongly binds on soil mineral impeding the availability of micro- and macronutrients uptake in plants (Mertens et al. 2018). Another method of glyphosate translocation in plants and other tissues is desiccation. A cyclic disorder of photosynthesis causes drying of plants. This process commences with closing stomatal part following limited respiration process. For better understanding the mechanism of glyphosate better, it is important to throw light on the translocation route of glyphosate in the plant (Helander et al. 2012). Glyphosate enters the plants through the cuticles of leaves (Gravena et al. 2012). It moves through the phloem to the tissues like bulbs, tubers and roots, ultimately affecting the meristems, storage organs, young roots, leaves and other growing tissues of the plant (Nguyen et al. 2016). The efficient action of glyphosate is attributed to its excellent uptake by the plant, brilliant

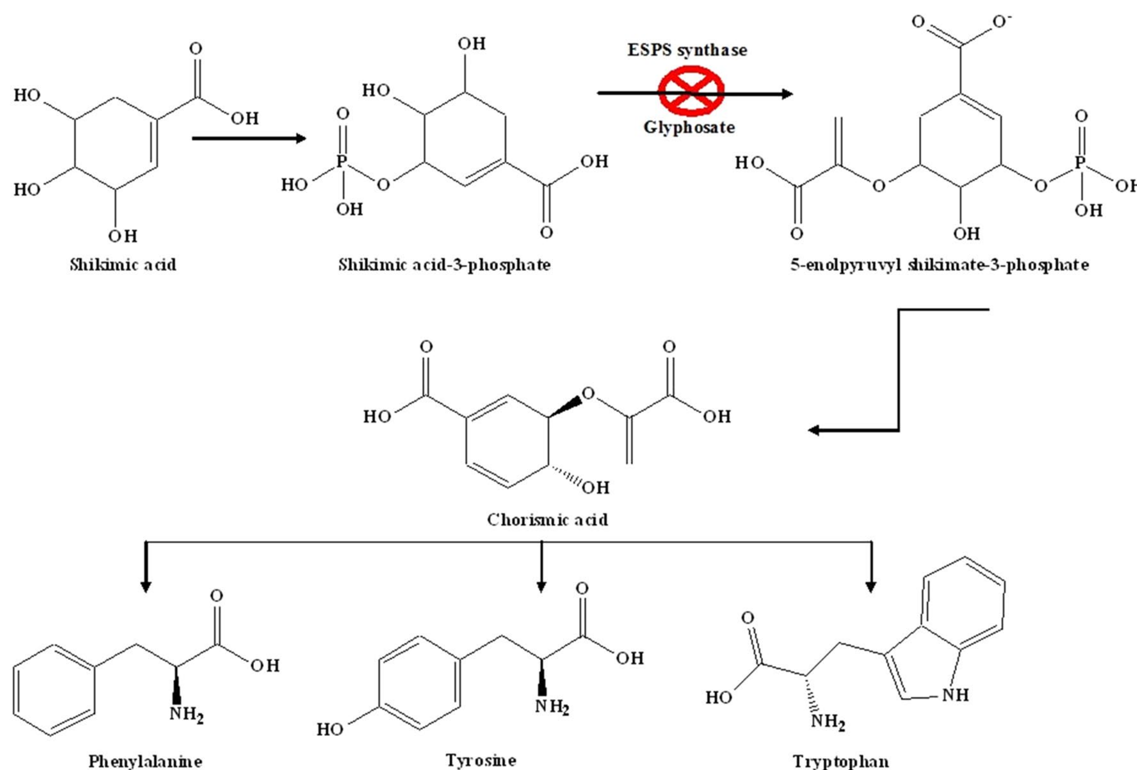


Fig. 2 Mechanistic action of glyphosate

translocation to meristems, partial degradation and slow mode of action (Helander et al. 2012; Nguyen et al. 2016).

The emergence of glyphosate-resistant (GR) crops

The swift implementation of glyphosate-resistant (GR), or "Roundup Ready", cropping systems has had a histrionic effect on agriculture to utilize glyphosate as a post-emergent, broadcast herbicide worldwide (Battaglin et al. 2014; Myers et al. 2016). Few resistant crops cultivated worldwide are *Brassica napus* (canola), *Glycine max* (soybean), *Gossypium hirsutum* (cotton) and *Zea mays* (maize) (Cerdeira and Duke 2006; Beckie and Owen 2007), which have influenced the economy by increasing the seed cost, reduced herbicide cost, enhanced crop yield and better profitability (Green 2011; Schütte et al. 2017). The few advantages such as low cost and limited erosion of topsoil prompted the sustainability and increased the GR technology (Duke and Powles 2009). Recent studies reveal that there was little or no risk or direct impact when transgenes of glyphosate resistance were introduced into wild-type populations.

The mechanism involved in the evolution of GR crops

The mechanism deduced for generating resistance involves five mechanisms: (i) alteration/mutation at the targeted site which induces complete/partial inhibition, (ii) deactivation of metabolic pathway, (iii) reduce uptake/translocation ability, (iv) compartmentation/sequestration and (v) overexpression/amplification of the targeted gene (Nandula et al. 2017). The extensive research permitted us to acquire better insight into the functioning of the plant and its retort to environmental stimuli under stress (Sammons and Gaines 2014). Development of GR crops was induced because of different traits like cross-pollination, genetic diversity, prolific production of seeds and dispersal of seeds over an extended area (DeVore et al. 2012). Plants were transformed (i) by incorporating the 5-enolpyruvylshikimate-3-phosphate synthase gene to attain resistant plant as its over-expression aids in enzyme stability (Lorentz et al. 2014). *Agrobacterium* sp. strain CP4, from which glyphosate-resistant EPSPS enzyme is isolated, has shown the high success rate in generating resistant plant (Imran et al. 2017). Generation of resistance in weeds provides more insight for understanding the physiological mechanism related to glyphosate resistance. The elevated level of 3-deoxy-d-arbino-heptulosonate 7-phosphate synthase, which is the first enzyme involved in the shikimate pathway, proposed to be responsible for enhanced carbon flow which further assisted is imparting the glyphosate resistance (Pline-Srnic 2006). (ii) Glyphosate oxidoreductase (GOX) is produced by soil microbes breaks the N–C bond of glyphosate and yields aminomethylphosphonic acid which is acetylated by glyphosate *N*-acetyl transferase (gat) producing gene which deactivates the action of glyphosate (Hadi et al. 2013). The third mechanism to generate the glyphosate-resistant plants, used commercially, involves the insertion of the amended EPSPS gene (Fig. 3).

Alteration of EPSPS gene can be done either by an amino acid substitution or site-directed mutagenesis which imparts resistance to crops (Pline-Srnic2006). CP4 genes of *Agrobacterium* sp. were utilized to disguise glyphosate-resistant 5-enolpyruvylshikimate-3-phosphate synthase. Similarly genes of Ochrobactrum anthropi were used to evaluate glyphosate resistance in Canola plants (Padgette et al. 1996). Also, to introduce glyphosate resistance in maize plants, genetic mutations in maize genes were performed (Vande Berg et al. 2008). With the introduction of these customized transgenic plants in agriculture, the usage of glyphosate has expanded multitudinous. The prolonged exposure to glyphosate directed the development of resistant weeds like Buckhorn Plantain, Common Ragweed, Common Waterhemp, Giant Ragweed, Goose-grass, Hairy Fleabane, Horseweed, Italian Ryegrass, Johnson-grass, Jungle Rice, Kochia, Liverseed Grass, Palmer Amaranth, Ragweed Parthenium, Rigid Ryegrass, Sour-grass, Sumatran Fleabane and Wild Poinsettia among the crop, by adapting to a fatal dosage for wild-type (Nandula et al. 2005).

Toxicity of glyphosate

Indiscriminate use of glyphosate not only adversely affects the non-target crops but also presents health risks to non-target animal species found in terrestrial and aquatic ecosystems. United States Environmental Protection Agency (USEPA) classifies glyphosate in toxicity class of IV for inhalation and oral exposure (Qaim and Traxler 2005; Gill et al. 2017). It causes irritation, vomiting, nausea and photo-contact dermatitis in humans (Reddenna and Krishna 2013) and is known to be slightly toxic for amphibians (Babalola and Van Wyk 2018) and fishes (Blann et al. 2009; Alcántara de la Cruz et al. 2016). Based on data available on toxicological area, glyphosate doesn't disrupt endocrine function through steroidogenesis, androgen or oestrogen mode of action (EFSA 2017). It is excreted in urine and faeces and does not bio-accumulate in animals. However, some reports cite the bioaccumulation of glyphosate in breast milk. But glyphosate concentration was found to be inconsistent with the animal toxicokinetic data which demonstrated that glyphosate has low distribution and is rapidly cleared from the body and does not cause any bioaccumulation in breast milk (Bus 2015).

Toxicity profiles of glyphosate against non-target plant species, microorganisms, lower invertebrates, higher vertebrates and humans are presented in Fig. 4 and Table 2.

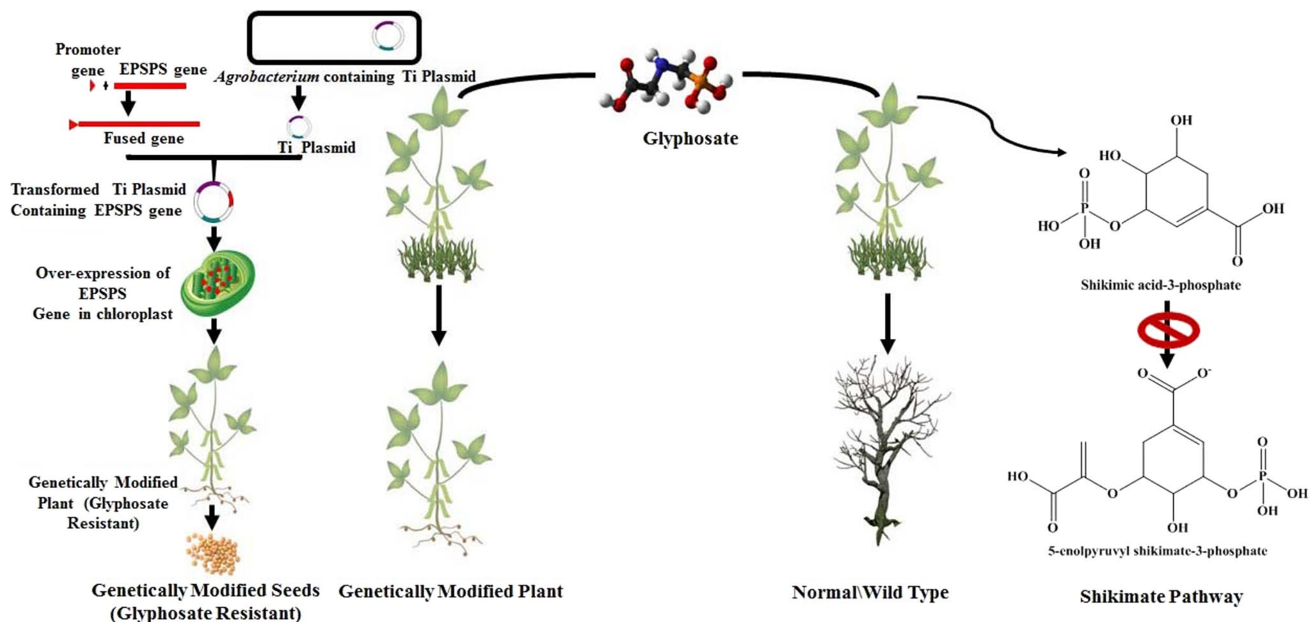


Fig. 3 Overview for the incorporation of the glyphosate-resistant gene (EPSPS) in plants via Ti plasmid

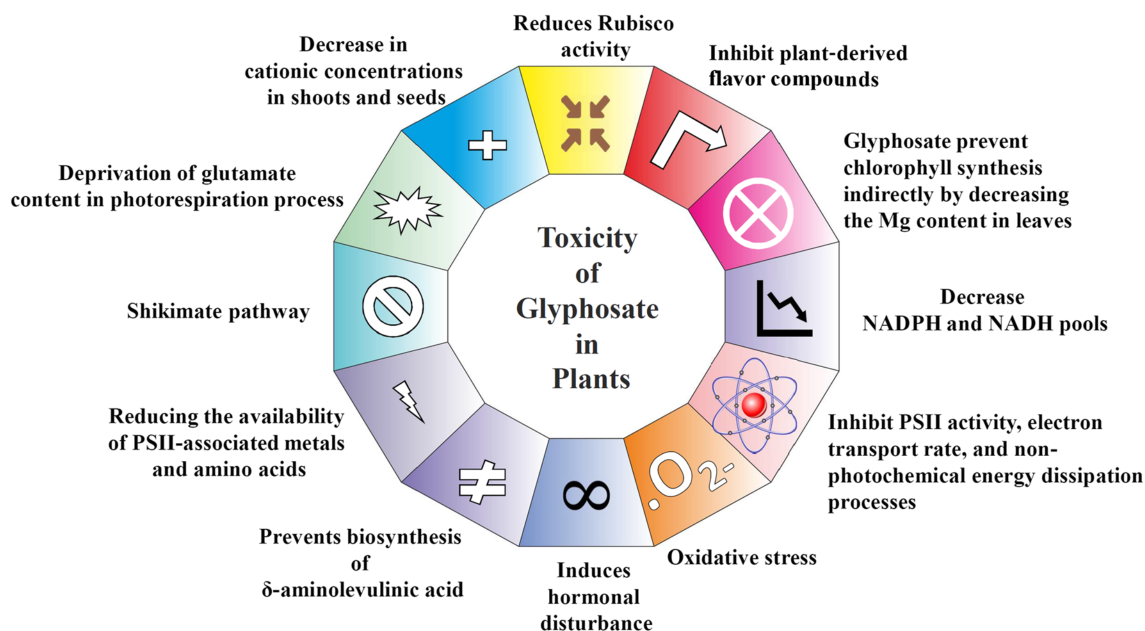


Fig. 4 Different aspects of the toxicity of glyphosate in plants

(a) Effect on non-target plant species

Impact of glyphosate has been studied on following non-target plant species viz. *Pisum sativum* (Orcaray et al. 2012; Zabalza et al. 2017), *Oryza sativa* (Ahsan et al. 2008), *B. Japonicum* (Hernandez et al. 1999), *Tritium aestivum* (Miteva et al. 2010), *Zea Mays* (Zablotowicz and Reddy 2007). Glyphosate has been shown to influence photosynthesis (Kremer and Means 2009; Kielak et al. 2011; Zobiole et al. 2012) chlorophyll biosynthesis (Reddy et al. 2004; Serra et al. 2013), photochemical reactions (Vivancos et al. 2011), carbon metabolism (Mateos-Naranjo et al. 2009; Zobiole et al. 2011b; Ding et al. 2011), nitrogen metabolism (Zobiole et al. 2010), plant mineral nutrition (Cakmak

Table 2 Toxicity and adverse effects of glyphosate on invertebrates and vertebrates

Category	Glyphosate used	Scientific name	Effects	Response	References
Amphibia	Technical-grade glyphosate acid Glyphosate isopropylamine Roundup MON 2139, Touchdown® Herbicide (4 LC-E) Roundup® Biactive (MON 77920)	*Crinia insignifera, Heleioporus eyrei, Limnodynastes dorsalis, Litoria moorei*	(1) LC_{50} values for technical glyphosate range from 81.2 to 121 mg/L in all the four species (2) LC_{50} values for glyphosate isopropylamine after 48 h ranges from 503 and 684 mg/L (3) LC_{50} values for Roundup® Herbicide (MON 2139) after 48 h from 8.1 to 32.2 mg/L (4) LC_{50} values for Touchdown® Herbicide after 48 h from 27.3 to 48.7 mg/L (5) LC_{50} values for Roundup® Biactive (MON 77920) after 48 h is 911 mg/L for *L. moorei* and > 1000 mg/L for *C. insignifera, H. eyrei,* and *L. dorsalis*	Roundup formulation (MON 2139) most toxic followed by touchdown isopropylamine, technical and roundup active (MON 77920)	Mann and Bidwell (1999)
	Glyphosate technical and polyethoxylated tallowamine surfactant (POEA)	*Rana clamitans,* *R. pipiens,* *R. sylvatica*, *Bufo americanus*	(1) Acute toxicity values in the order of decreasing toxicity were POEA > Roundup Original > Roundup Transorb® > Glyfos AU® (2) No significant acute toxicity was observed with glyphosate technical material or the glyphosate formulations Roundup Biactive®, Touchdown®, or Glyfos BIO®	The formulation was toxic than glyphosate	Howe et al. (2004)
Annelida	(1) Technical glyphosate (2) Roundup ultra	*Lumbriculus variegates*	Elevation of biotransformation enzyme-soluble glutathione S-transferase at non-toxic concentrations	Antioxidant enzyme activity significantly increased	Contardo-Jara et al. (2009)
Arthropoda	(1) Technical glyphosate (2) Roundup	*Daphnia magna*	EC values for technical glyphosate ranges of 3.7–10.6 mg a.i./l slightly higher than roundup formulations 1.4–7.2 mg a.i./l	Reduction of juvenile size; growth, fecundity and abortion rate negatively affected	Cuhra et al. (2013)
	(1) Roundup bioactive	*Lepthyphantes tenuis*	No detrimental effect on three concentrations 360, 720 and 1440 mg/L	Mortality rate less than 10% in all treatments	Haughton et al. (2001)
	(1) Herbolex	*D. magna*	Increased levels of lipid peroxidation	Feeding inhibition and oxidative stress-related responses	Puértolas et al. (2010)

Table 2 (continued)

Category	Glyphosate used	Scientific name	Effects	Response	References
	(1) Technical Glyphosate (2) Faena®	*D.magna* *Lecane quadridentata*	Inhibition of esterase activity in *L. quadridentata* EC_{50} was 1500-fold smaller than the LC_{50}	Faena (formulation of glyphosate) found more toxic to *D.magna* and around 11-fold more toxic to *L.quadridentata* than pure glyphosate	Domínguez-Cortinas et al. (2008)
Aves	(1) Technical glyphosate (2) Roundup	Human placental cells and aromatase	Disrupts aromatase activity and mRNA levels	Alternations in microsomes. Glyphosate is also reported to be toxic to human placental JEG3 cells; disruption of mammalian cytochrome P450 aromatase activity	Richard et al. (2005)
Mammal	(1) Agpro glyphosate 360 (2) Yates Roundup	*Oligosoma polychroma*	Mean daily percentages of skinks from each group that selected warmer temperatures were 61.2% for the control group, 65.1% and 78.8% for the agpro glyphosate 360 group Yates roundup weedkiller group, respectively	Physiological stresses were observed	Carpenter et al. (2016)
	(1) Technical glyphosate	*Rat jejunum strips*	Motility disturbances are also observed	Glyphosate affects the spontaneous motoric activity of rat isolated jejunum strips at very low concentrations	Chłopecka et al. (2014)
	(1) Roundup	*Rattus novergicus*	(1) 50% mortality rate for dams (2) Skeletal alterations were observed in 15.4, 33.1, 42.0 and 57.3% of fetuses from the control, 500, 750 and 1000 mg/kg glyphosate groups	It is toxic to the dams and induces developmental retardation of the foetal skeleton	Dallegrave et al. (2003)
	(1) Technical glyphosate (2) Roundup	*Rattus novergicus*	(1) At 0.5 mM concentration roundup significantly depresses RCR and ADP/O ratio while technical grade not (2) Roundup depresses the efficiency of the electron transport chain	Excessive lipid peroxidation leading to overload on maternal and foetal antioxidant defence system in rats	Peixoto (2005)

Table 2 (continued)

Category	Glyphosate used	Scientific name	Effects	Response	References
	(1) Herbicygon	*Rattus novergicus*	High lipid peroxidation induced with glyphosate ingestion leads to an overload of maternal and foetal antioxidant defence systems	Irreversible damage in hepatocytes. Increase in number of Kupffer cells, large deposition of reticulin fibres, leakage of hepatic intracellular enzymes, alanine aminotransferase (ALT) and aspartate aminotransferase (AST)	Beuret et al. (2005)
	(1) Biocarb®	*Homo sapiens (Placental cells)*	(1) Leakage of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and hepatic intracellular enzymes (2) Large deposition of reticulin fibres	Hepatic histological changes as well as AST and ALT leaking from the liver to serum	Benedetti et al. (2004)
Mollusca	(1) Roundup	*Pseudosuccinea columella*	(1) Inhibition of egg hatching 10 mg/L (2) Abnormalities and polyembryony were observed in snails exposed to 0.1 and 10 mg/L	Affected reproduction and development. Effect on the population dynamics	Tate et al. (1997)
Pisces	Roundup	*Prochilodus lineatus*	(1) LC_{50} of Roundup after 96 h was 13.69 mg/L (2) Increase in catalase liver activity	Activation of antioxidant defence increased. Biochemical, physiological and histological altered	Langiano and Martinez (2008)
	Roundup	*Leporinus obtusidens*	Levels of ammonia in both tissues increase in fish at all glyphosate concentrations	Acetylcholinesterase (AChE) activity significantly decreased in the brain; significant reduction in muscle glycogen and glucose	Glusczak et al. (2006)
	Technical Glyphosate	*Cyprinus carpio*	(1) LC-50 value at 48 h exposure was 645 and 620 mg/L (as the active ingredient) after 96 h (2) Histopathological changes observed	Leucocyte infiltration, hypertrophy of chloride cells, lifting and rupture of the respiratory epithelium on secondary lamellae	Nešković et al. (1996)
	Roundup	*Piaractus mesopotamicus*	Severe damage in the liver	Liver showed cytoplasmic vacuolization, lipid accumulation, nuclear and cellular membrane alterations and glycogen depletion further hampering the detoxification and tissue repair process	Shiogiri et al. (2012)

Table 2 (continued)

Category	Glyphosate used	Scientific name	Effects	Response	References
	Gigurlyphosate	*Oreochromis niloticus*	LC_{50} value was 1.05 mg/L for 96 h of exposure	Major significant alterations in kidney, gills, liver and brain. Epithelial lifting, hyperplasia, lamellar fusion in gills	Ayoola (2008a)
	Gigurlyphosate	*Clarias gariepinus*	The LC_{50} value was found to be 0.063 mg/L for 96 h	Liver showed fatty acid degeneration, severe fat vacuolation, necrosis. Kidney showed haemopoietic necrosis and severe pyknotic nuclei. In the brain, neuronal degeneration, spongiosis, mononuclear infiltration was observed	Ayoola (2008b)
	Roundup	*Prochilodus lineatus*	(1) AChE activity was repressed in brain and muscle after 24 and 96 h of exposure (2) Increased glutathione-S-transferase (GST) activity and lipid peroxidation	Reduction in superoxide dismutase (SOD) and an increase in glutathione peroxidase (GPx) was observed	Modesto and Martinez (2010)
	Roundup	*P. Lineatus*	(1) Genotoxic damage in gill cells and erythrocytes (2) The comet scores obtained for erythrocytes after 6 and 96 h were higher than respective negative controls	Myelin-like structures in carp hepatocytes and other ultrastructural changes in mitochondria were observed	Cavalcante et al. (2008)
	Roundup	*Rhamdia quelen*	(1) Appearance of myelin-like structures in carp hepatocytes (2) Disappearance of the internal membrane of mitochondria at both exposure concentrations (205 and 410 mg/L)	Ammonia was found to increase in both tissue types while protein level increased in liver and decreased in white muscle	Szarek et al. (2000)
Reptilia	Roundup	*Caiman latirostris*	LC_{50} ranges from 0.55 to 2.52 mg of active ingredient (AI)/L after 4 days of exposure	A significant increase in DNA damage in treated groups	Relyea (2005)
	Roundup	*Salvator merianae*	Increase in DNA damage at a concentration of 500 µg/egg was observed	Increase in DNA damage as observed via comet assay	Poletta et al. (2009)
	Roundup	*Caiman latirostris*	Significant increase in DNA damage was observed in 100 µg/egg treated groups	Decreased complement system activity and suppresses immune system leading to increased risk of diseases	Schaumburg et al. (2016)

Table 2 (continued)

Category	Glyphosate used	Scientific name	Effects	Response	References
	Roundup	*Caiman latirostris*	Low complement system activity	The decrease in WBCs, a higher percentage of heterophils, a low percentage of F2 protein and negative effect on growth	Siroski et al. (2016)
	Roundup	*Trachemys scripta elegans*	Exposed to two different concentrations (11 or 21 mg/L) resulting in alterations in the plasma proteins growth of caimans and selected immune parameters	Higher percentage of heterophils. Decrease in WBC counts. Higher TPC (with a low percentage of F2 protein fraction).	Latorre et al. (2013)
	(1) Glypro® (2) LI700	*Oligosoma polychrome*	(1) Genetic damage at concentrations ranging from 0 to 11,206 ppm of Glypro® and 0 to 678 ppm of the surfactant (2) Low hatching success	Showed heat-seeking behaviour could be related as a fever response to increase metabolism and thereby counteracting physiological stress	Sparling et al. (2006)

et al. 2009; Senem et al. 2009; Zobiole et al. 2010, 2011b, 2012), oxidative stress (Ahsan et al. 2008), disruption of lignin, phytohormones, etc. (Sergiev et al. 2006; Miteva et al. 2010). Glyphosate inhibits the synthesis of chlorophyll, fatty acids, amino acids (Gomes et al. 2017a), and secondary metabolites such as quinones (Dewick 1995) which forms an important component in the physiological processes of the plants (Mateos-Naranjo et al. 2009; Zobiole et al. 2012; Yanniccari et al. 2012). Glyphosate decreases the Mg content in leaves (Cakmak et al. 2009) which leads to reduced photosynthetic rate and chlorophyll content (Zobiole et al. 2012). Glyphosate-based herbicides also cause change in the activity of ascorbate peroxidase (APX), catalase (CAT) and polyamine (PA) in *L. minor* tissues (Mkandawire et al. 2014). It also prevents the biosynthesis of catalase, peroxidase and δ-aminolevulinic acids which are the major component of chlorophyll biosynthetic pathway by inducing Fe deficiency in plants (Marsh et al. 1963). However, it affects ALA production by competing with the major product of the ALA synthetase active site or leading to deprivation of glutamate content by competing with glycine in the photorespiration process (Vivancos et al. 2011). Another study evaluated the foliar uptake, spray retention and translocation of glyphosate in *Ambrosia artemisiifolia* and found glyphosate to be translocated in developing apical tissues as well as roots within 3 h (Hussain et al. 2009). Glyphosate causes a reduction in the availability of amino acids and metal ions which are associated with PSI and PSII to transfer photon (light energy) into the electron transport chain system (Cakmak et al. 2009). Foliar spray of glyphosate and its metabolites reduces the CO_2 assimilation capacity by decreasing the net carbon exchange and stomatal conductance in plants (Mateos-Naranjo et al. 2009; Zobiole et al. 2011a; Ding et al. 2011). Exposure of glyphosate also affects ribulose 1,5-biphosphate carboxylase oxygenase (Rubisco) activity in plants by reducing the levels of ribulose-1,5-biphosphate (RuBP) and 3-phosphoglyceric acid (PGA) (Servaites et al. 1987; Siehl 1997; De María et al. 2006).

Glyphosate affects the physiology of the host plant indirectly by influencing the nitrogen metabolism or directly by effecting rhizobial symbionts (Zobiole et al. 2011a) thus leading to growth inhibition and finally death (De María et al. 2006). Glyphosate has also been reported to decrease nitrogen fixation activity and nodulation in plants (Zobiole et al. 2012). Some studies reveal that glyphosate induces nutritional disturbances by interfering with their location mechanism. Blockage of the shikimate pathway leads to the oxidative stress by inhibiting specific target sites of the plants was also reported in which changes were observed in oxidative stress markers (Ahsan et al. 2008). Glyphosate also reduces lignin content which is associated with functional and morphological quality of plants (Gaspar and Coumans 1987). It reduces the synthesis of lignin by inhibiting the

EPSPS and by minimizing the supply of cinnamate precursors (Marchiosi et al. 2009). Glyphosate also induces a hormonal disturbance in soybean, which could affect development and growth characteristics (Cakmak et al. 2009; Sugano et al. 2013). Glyphosate prevents the biosynthesis of auxin which is synthesized from the indolic tryptophan precursor by inhibition of the Shikimate pathway. Guo et al. (2015) also confirmed the negative aspects of glyphosate on algal species, as they measured environment concentrations (MEC) and the EC 50 value of glyphosate in *Scenedesmus quadricauda* to be 0.1 µg/L and 4.4 mg/L, respectively.

(b) Effect of glyphosate on plant growth-promoting rhizobacterial (PGPR) microorganisms

Several workers have studied the adverse impacts of glyphosate on soil microorganisms. Residual glyphosate in soil and aquatic ecosystems is reported to adversely affect the population, community structure and activities of soil microorganisms (Newman et al. 2016). Most of the studies have found negligible impact of glyphosate on microbial communities and their composition (Busse et al. 2001; Liphadzi et al. 2005; Ratcliff et al. 2006; Weaver et al. 2007; Cherni et al. 2015). It exhibited adverse effects on the growth rate of beneficial microorganisms, resulting in decreased nitrogenase activity lower indole-3-acetic acid and gibberellin production and inferior phosphate and zinc solubilizing activities (Madhaiyan et al. 2006). Glyphosate also hinders the growth of beneficial rhizospheric communities by reducing the profusion of indole acetic acid-producing rhizobacteria, Mn-reducing bacteria, indole acetic acid-producing bacteria, etc. (Zobiole et al. 2011a). Glyphosate also reduces root mycorrhization in *Trifolium repens* L inoculated with arbuscular mycorrhizal fungi by reducing soil AMF spore biomass, propagules and vesicles formation (Zaller et al. 2014).

Negative effects of glyphosate on Mn-transforming bacteria, indole acetic acid-synthesizing bacteria and fluorescent-pseudomonads were also reported (Zobiole et al. 2011a). Glyphosate lowers the respiration and photosynthetic levels by 20% in *Euglena* species (Richardson et al. 1979). Glyphosate is also known to hinder the radial growth of hyphae in the endophytes by influencing their root colonization ability, propagule density and spore viability (Druille et al. 2013).

(c) Effect on invertebrates

Impact of glyphosate formulation (Roundup) was also considered in *Lumbriculus variegates* for four days at a concentration between 0.05 and 5 mg/L. Antioxidant enzyme superoxide dismutase and membrane-bound glutathione S-transferase activity were found to be significantly increased (Contardo-Jara et al. 2009). Glyphosate toxicity also exerts negative effects on aquatic invertebrates like *Daphnia magna*. Reduction in size of juveniles significantly was observed even at the lowest dose of 0.05 mg active ingredient/L for both glyphosate and roundup. Growth, fecundity and abortion rate were found to be affected at 0.45 mg active ingredient/L of the roundup. Hundred percentage abortion rate of eggs and the embryonic stage was observed at 1.35 mg active ingredient/L of roundup (Cuhra et al. 2013). The toxic effects of glyphosate on *Lepthyphantes tenuis* (Araneae, Linyphiidae), a common spider was also studied in which mortality was found to be less than 10% in all treatments after 24 and 48 h and increased only marginally (to 13%) after 72 h of spray application (Cuhra et al. 2013). From the results, it could be inferred that glyphosate is harmless to non-target arthropods.

Feeding inhibition and stress-related response like increase in lipid peroxidation and antioxidant enzyme activities was observed in *D. magna* (Puértolas et al. 2010). The effect of glyphosate on *Pseudosuccinea columella* (intermediate snail host of *Fasciola hepatica*) was also studied. Glyphosate was found to affect population dynamics of *F. hepatica* by affecting their reproduction and development. The resultant could be increased infections in animals including humans (Tate et al. 1997). In a comparative study, the order of toxicity was found to be chlorpyrifos formulation > chlorpyrifos active ingredient > cypermethrin formulation > cypermethrin active ingredient > glyphosate formulation > glyphosate active ingredient in *Daphnia Magna*. This indicated the relatively less toxic nature of glyphosate (Demetrio et al. 2014). Comparison of toxicity of glyphosate with its formulation Faena® was evaluated on cladoceran *D. magna* and rotifer *Lecane quadridentata*. Faena® was found to be slightly more toxic to *D. magna* and around 11 fold more toxic to *L. quadridentata* than technical glyphosate (Domínguez-Cortinas et al. 2008).

Effect on vertebrates

Effect on amphibians and fishes

The toxicity of roundup (formulation of glyphosate) on neotropical fish *Prochilodus lineatus* was studied, and the LC_{50} after 96 h was found to be 13.69 mg/L. An increase in plasma glucose in the exposure of 10 mg/L depicted the induction of stress. Activation of antioxidant defence was found to increase as the catalase liver activity showed an increase. Other biochemical, physiological and histological alterations were also found (Langiano and Martinez 2008). Another teleost fish, *Leporinus obtusidens* (Paiva), was exposed to various concentration of roundup (formulated glyphosate). Acetylcholinesterase (AChE) activity significantly decreased in the brain of fish; significant reduction

in muscle glycogen and glucose was observed in glyphosate-exposed fish. Glyphosate concentration of 5 mg/L causes epithelial hyperplasia and subepithelial oedema. At 10 mg/L, more pronounced changes including infiltration of leucocytes, chloride cells hypertrophy, rupture and lifting of respiratory epithelium on secondary lamellae were observed (Nešković et al. 1996). *Oreochromis niloticus* was exposed to roundup formulation at a concentration of 15 ppm for 3 months. Cell proliferation in the gills, hyperplasia of the lamellar cell, lamellar fusion, lifting of epithelium and aneurysm, vacuolation of the hepatocyte, kidney lesions and pyknosis of nucleus cells were observed as histopathological alterations in *Oreochromis niloticus* after exposure of commercial formulation roundup (Jiraungkoorskul et al. 2003). Three formulations of glyphosate (Roundup, Touchdown and Roundup Bioactive) were compared for toxicity on four species of southwestern Australian frogs (*Crinia insignifera, Heleioporus eyrei, Limnodynastes dorsalis,* and *Litoria moorei*). Roundup was the most toxic of all the three thereafter touchdown and roundup active in order (Mann and Bidwell 1999). Roundup-ready, another formulation of glyphosate was used to evaluate the toxicity on *Piaractus mesopotamicus*. The gill histopathology was unaltered, but the liver showed nuclear and cellular membrane alterations, cytoplasmic vacuolization, glycogen depletion and lipid accumulation. This may hamper the detoxification and tissue repair process and may prove to be lethal (Shiogiri et al. 2012). An elevated level of GST and LPO in the liver, DNA damage and erythrocyte nuclear abnormalities were observed due to glyphosate in *Prochilodus lineatus.* The toxicity of glyphosate on Nile tilapias (*Oreochromis niloticus*) was evaluated. Significant changes in liver, kidney, gills and brain were observed. Epithelial lifting, lamellar fusion and hyperplasia were noticed in gills. Vacuolation of hepatocytes and necrosis was observed in liver. The kidney was characterized by hyaline droplets in the tubular epithelial cells and pyknosis. Erratic swimming, respiratory stress and instant death of fish were also reported. The mortality was directly correlated with the dosage of pesticide (Ayoola 2008a). Significant increases in glutathione peroxidase and catalase enzymes were observed in rainbow trout when exposed to glyphosate concentration 2.5, 5 and 10 mg/L (Topal et al. 2015). In another study, African catfish *C. gariepinus* was exposed to acute concentrations of glyphosate. Cellular infiltration was observed in the gills. Liver showed fatty acid degeneration, severe fat vacuolation, necrosis. Kidney showed haemopoietic necrosis and severe pyknotic nuclei. In the brain, neuronal degeneration, spongiosis, mononuclear infiltration was observed. The juvenile was found to be more affected than adults (Ayoola 2008b). It is very interesting to note that fish have evolved to alleviate the reactive oxygen species in their system by converting superoxide anions with the help of antioxidant enzymes to hydrogen peroxide and further to H_2O and O_2 (Xing et al. 2012). Toxicity of glyphosate and its formulation, the roundup was compared for four amphibian species (*Rana clamitans, R. pipiens, R. sylvatica*, and *Bufo americanus*). The formulation was found to be toxic than glyphosate (Howe et al. 2004). *Prochilodus lineatus* was also studied for roundup toxicity. Increase in glutathione peroxidase (GPx) and reduction of superoxide dismutase (SOD) was observed. Inhibition of AChE in the brain and muscles after 96 h and 24 h of exposure was observed (Modesto and Martinez 2010). Roundup is genotoxic to erythrocytes and gill cells of *P. Lineatus* (Cavalcante et al. 2008). Formulation of glyphosate affects the growth, acetylcholinesterase activity, metabolic and haematological parameters in Paiva (*Leporinus obtusidens*). An elevated level of plasma alanine aminotransferase (ALT) was observed in hybrid fish, in Surubim, after glyphosate action. Increase in ventilator frequency level was observed for the initial 5 min, and declined level was observed on the exposure of 96 h (Glusczak et al. 2006). Hepatocytes of carp (*Cyprinus carpio*) were also found to be affected by roundup. Observations include swelling of mitochondria, myelin-like structures in carp hepatocytes and disappearance of the internal membrane of mitochondria and other ultrastructural alterations (Szarek et al. 2000). Sobjak et al. (2017) studied the toxicity of glyphosate in larvae of *Rhamdia quelen* at 6.5 mg/L of glyphosate concentration. Neurotoxicity and antioxidant system using catalase, glutathione transferase, glutathione reductase, cholinesterases and lipoperoxidation were found to be affected. Lactate levels in liver and white muscles were found to be increased after exposure to glyphosate. Ammonia was found to increase in both tissue types while protein level increased in liver and decreased in white muscle in silver catfish (*Rhamdia quelen*). Roundup is also reported to kill 96–100% of larval amphibians after three weeks of exposure (Relyea 2005).

Effect on higher vertebrates

The genotoxic potential of roundup was evaluated in *Caiman latirostris*. The comet assay and micronucleus assay were performed on the erythrocytes to evaluate genotoxicity. Treated groups were characterized by significant elevation in DNA damage when compared to control (Poletta et al. 2009). Roundup is also reported to cause an increase in DNA damage as observed via comet assay tegu lizard (*Salvator merianae*) embryos (Schaumburg et al. 2016). Commercial glyphosate, the roundup was found to decrease complement system activity and suppress the immune system leading to increased risk of diseases in broad-snouted caiman (*Caiman latirostris*) (Siroski et al. 2016). The decrease in WBCs, a higher percentage of heterophils, adverse growth effects in juveniles and a low percentage of F2 protein exposed to roundup were also reported (Latorre et al. 2013). An

increase in the levels of ALT (alanine aminotransferase), AST (aspartate aminotransferase), γ-GT (*gamma*-glutamyl transpeptidase), MCV (*mean corpuscular volume*), lipid peroxidation, whereas declination in erythrocytes, haematocrit and haemoglobin were observed in Swiss albino mice after glyphosate evaluation after 15 days (Jasper et al. 2012). Eggs of red-eared sliders (*Trachemys scripta elegans*) were exposed to the single application of commercial glyphosate, Glypro, in the concentration of 0 to 11206 ppm wet weight of glyphosate along with 0 to 678 ppm of surfactant, LI700. The hatching success was significantly reduced in the highest concentration of herbicide in comparison to other treatments. Glyphosate in addition to LI700 poses a low-level risk to embryos in comparison to glyphosate alone (Sparling et al. 2006). Dermal exposure of two different formulations of glyphosate (144 mg/L) was introduced on New Zealand common skink (*Oligosoma polychrome*).

Agpro glyphosate 360 did not have any significant impact while skinks in Yates roundup showed heat-seeking behaviour which could be related as a fever response to increase metabolism and thereby counteract physiological stress (Carpenter et al. 2016). Haematological parameters like aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), lactate dehydrogenase (LDH), amount of serum lipoprotein (LDL, HDL), total cholesterol and creatinine were also found to be altered in rat after the exposure of glyphosate formulation, roundup at 56 mg/Kg and 560 mg/kg each day for 13 weeks (Çağlar and Kolankaya 2008). The toxicity of glyphosate was also studied on the rat for its effect on the spontaneous motoric activity of the intestine. Biphasic response (miorelaxation accompanied by contraction) was observed in muscles. Overall, glyphosate was detected to impair the motility of gastrointestinal muscles (Chłopecka et al. 2014). Glyphosate toxicity in rats causes leakage of ALT, AST and ALP which depicted damage in the hepatocytes. Increase in creatinine and urea level also depicted kidney damage (El-Shenawy 2009). Female Wistar rats were treated with 500, 750, 1000 mg/Kg of roundup formulation of glyphosate from 6 to 15 days of pregnancy. Fifty percentage mortality in female rats was observed at 1000 mg/Kg. Skeletal alterations up to 57% in foetuses were recorded, and it was concluded that roundup formulation is teratogenic and induced developmental retardation in the foetal skeleton (Dallegrave et al. 2003). Exposure of sub-lethal concentrations of glyphosate to rats also increases glutathione transferase enzyme and reduction in glutathione and lipid peroxidation in liver, small intestine and kidneys (Larsen et al. 2012). Glyphosate toxicity is also related to the uncoupling of oxidative phosphorylation in mitochondria (Peixoto 2005). Excessive lipid peroxidation as a result of glyphosate also leads to an overload on maternal and foetal antioxidant defence system in rats (Beuret et al. 2005). Glyphosate-biocarb, a formulation of glyphosate, also leads to irreversible damage in hepatocytes, increase in the number of Kupffer cells, large deposition of reticulin fibres, leakage of hepatic intracellular enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (Benedetti et al. 2004). The application of glyphosate is also reported to modify the density and habitat use of birds (Morrison and Meslow 1984). Zebra finches (*Poephila guttata*) died after ingestion of seeds containing glyphosate (5000 µg/g) (Evans and Batty 1986). The World Health Organisation (WHO) and the Food and Agriculture Organisation (FAO) in its latest report (2016) provide positive evidence for non-Hodgkin's lymphoma in some case–control studies. But, large sample size studies depict no correlation between glyphosate and cancer at any exposure level (Gill et al. 2017).

Effect on humans

Glyphosate has no threat to a human life. Several regulatory agencies concluded that generally there are fewer glyphosate exposures than the reference dose and the acceptable daily intakes, thus supporting a conclusion that even for these highly exposed populations the exposures were within regulatory limits (Solomon 2016). Initial reports of Roundup Ultra 360 SL along with glyphosate on the human erythrocytes were found to be less harmful as it showed the elevation in the level of methaemoglobin and haemolysis, but no significant change in GSH (glutathione) level (Pieniżek et al. 2004). Its formulation (Roundup)-induced problems during pregnancy affirmed by exposing the JEG3 (human placental cell line) to low concentration for 18 h displayed its role in hindering the functionality of aromatase enzyme as well as fluctuated the mRNA level by amending the active site (Richard et al. 2005). Microarray analysis on mammalian cell line, MCF-17 showed its competence to amend the gene expression of the dysregulated CXCL12, EGR1 (early-growth response 1) and HIF1 (hypoxia-inducible factor 1) gene. Glyphosate is also reported for its severe consequences on the adult as well as foetal cells. In vivo xenobiotic toxicity assessment of its four formulations over HepG2 (hepatic cell line) revealed the disruption of MDA-MB453-kb2 (androgen receptor) at 0.5 ppm concentration, whereas the formulation R400 terminated the transcription cycle of oestrogen receptor of HepG2. The 10 ppm concentration exhibited a cytotoxic effect, whereas 5 ppm lead to the DNA damage (Gasnier et al. 2009). Glyphosate intoxication leads to the complications like arrhythmia, hypotension, mental relapse, renal and respiratory failure, where surfactant volume is claimed to be a critical element for inducing toxicity among the humans (Seok et al. 2011). Buccal epithelial cell line TR146 exposed to glyphosate and roundup developed cancer to the dosage of less than 40 mg/L testified by the cytotoxic effect like membrane damage as well as impaired mitochondrial function. The dosage of > 80 mg/L elevated LDH

(lactate dehydrogenase) leads to membrane and DNA damage to the epithelial cells (Koller et al. 2012). Intoxication by glyphosate is assessed by various assays like Alamar Blue, MTT, ToxiLight and comet and techniques like HPLC–MS, mass Spectrometry. The common intoxication symptom comprises cardiovascular shock, haemodynamic hinderance, intravascular coagulation, myocardial infarction and failure of multiple organs (Zouaoui et al. 2013). A different formulation of glyphosate was exposed to HEK293 (Embryonic), HepG2 (Hepatic) and JEG3 (Placental) cell lines for 24 h showed the alteration on the caspase 3/7 enzyme, membrane degradation and mitochondrial functionality. POE-15 (polyethoxylated tallow amine) formulation of glyphosate was tested on hepatic (HepG2), embryonic (HEK293) and placental (JEG3) cell lines. It was found that the formulation was highly toxic even at 1–3 ppm concentration and intruded the cell integrity, necrosis during micellization, stimulated the disruption of the endocrine system and respiratory system. JEG3 was found to be 2 times more sensitive to treatment than HEK293 and HepG2 (Mesnage et al. 2013). Similar results were seen on T47D cell line as the amendment in oestrogen response element activity resulted via antagonistic oestrogen which alters the ERα and ERβ expression up to 5-13 fold (Thongprakaisang et al. 2013). GlyBH (glyphosate-based herbicides) have been reviewed and realized to have an enduring chronic effect such as hepatorenal, teratogenic and tumourigenic, which can be corroborated via oxidative stress as well as disruption of endocrine functionality. Its role in trans-generational, reproductive and neurological disorder is under investigation (Mesnage et al. 2015)

Analytical detection and quantification of glyphosate

Detection of glyphosate has always been an issue of major concern, subjected to its poor solubility, high polarity and evaporation issues (Gomes et al. 2017b). Several authors have reported difficulties in detection and estimation of glyphosate due to non-availability of fluorophores and chromophores groups in its molecular structure (Gill et al. 2018). Due to good efficiency, multiple uses, high toxicity, long lifetime and high stability, researchers have made efforts towards its derivatization. Different methods have been reported till date for the quantification and detection of glyphosate and its metabolites in diverse environmental matrixes (soils, sludges, sediments, juices, plant material, groundwater, surface water and biological fluids, etc. (Balderacchi et al. 2013; Koskinen et al. 2016). Different techniques such as ultraviolet (UV) (Lee et al. 2010), electrochemical detection (ECD) (Songa et al. 2009), HPLC coupled to mass spectrometry (MS) (Guo et al. 2005), high-performance liquid chromatography (HPLC) coupled with tandem MS (MS/MS) (Sanchís et al. 2012), fluorescence (FLD), inductively coupled plasma MS (ICP-MS) (Chen et al. 2009), time-of-flight MS (TOF–MS) (Koskinen et al. 2016), ion chromatography (IC) coupled to conductivity detection (CD) (Guo et al. 2007), condensation nucleation light scattering detection (CNLSD) (You et al. 2003), ICP-MS capillary electrophoresis (CE) with capacity couple contactless conductivity detection (C4D) (Guo et al. 2007), UV capillary zone electrophoresis (CZE) with CD and UV detection (Goodwin et al. 2002), gas chromatography (GC) coupled to MS (Krüger et al. 2014), a flow injection (FI) system with electrochemiluminescence (ECL) detection (Chuang et al. 2013), enzyme-linked immunosorbent assay (ELISA) (Mörtl et al. 2013; Krüger et al. 2014; Chang et al. 2016; Wang et al. 2016) solution spectrophotometry and solution electrochemical detection (ECD) are employed for the quantification of glyphosate and its major metabolite AMPA in environmental samples. Derivatization (using various derivatizing agents) is an additional preparatory step often required in glyphosate and AMPA analysis. Methods for extraction, derivatization, pre-concentration and different detection methods with their methods are gas chromatography (GC), gas chromatography-mass spectrometry (GC/MS), ion chromatography (IC), high-performance liquid chromatography (HPLC), liquid chromatography-mass spectrometry (LC/MS), capillary electrophoresis (CE), enzyme-linked immunosorbent assay (ELISA) and spectrophotometric techniques and use of nanosensors.

The detection and estimation of glyphosate in water has been reported in (Börjesson and Torstensson 2000) guava fruit extract, soil (Peruzzo et al. 2008), sediments (Aparicio et al. 2013), animal and human tissues (Krüger et al. 2014), plants tissues (Nedelkoska and Low 2004), wheat grains (Jan et al. 2009), urine samples, organs of dairy cow (Krüger et al. 2014), soybean extracts (Arregui et al. 2004), in carrots (Kataoka et al. 1996), etc.

The detection of glyphosate in different matrices is quantified using GC coupled with mass spectroscopy (Krüger et al. 2014), including different detectors like electron capture detector. The estimation of glyphosate and its residues in river soil, water and carrot samples were quantified by using gas chromatography coupled with flame photometric detection using a DB-1701 capillary column (Kataoka et al. 1996). The range of percentage recovery varied from 91 to 106%. The detection limit was 8 picogram. The determination of glyphosate in water and soil samples is performed by GC–MS method. This method involves ligand exchange, anion exchange and derivatization and final identification and quantification by GC–MS and exhibit limit of detection was 0.1 μgL^{-1}, 0.006 μg/g in water and soil samples (Börjesson and Torstensson 2000). The complicated procedures involved in the derivation of glyphosate before analysis reduce its applicability and practical aspects such as ECD, nitrogen phosphorous detector (NPD) (Hu et al. 2011), flame

photometric detector (FPD) (Kataoka et al. 1996) and flame ionization detector (FID) (Kudzin et al. 2002). The presence of hydrogen bonding between hydrogen atoms and an amino group in glyphosate attributes to high boiling point and high polarity of the molecule (Kumar et al. 2017). Such physicochemical properties of glyphosate make its detection difficult through GC. To solve this problem, the polar groups are deactivated by carrying out derivatization of glyphosate and its residues. Table 3 shows different reports on the detection and estimation of glyphosate. A recovery of glyphosate from water and soil samples up to 90% has been reported by many authors.

High-performance liquid chromatography

HPLC is also a rapid analytical technique with high precision and high reproducibility for the quantification of glyphosate. But the complexity in the derivatization procedures limits its practical applications. The absence of chromophores and fluorophores make derivatization an indispensable step during the analysis (Wang et al. 2016). The derivatization procedures may include pre-column or post-column derivatization step. Different pre-derivatizing reagent commonly used for HPLC analysis are 2,5- dimethyl benzene sulfonyl chloride, p-toluenesulphonyl chloride, o-nitrobenzenesulfonyl chloride, ophthalaldehyde, 9-fluorenylmethylchoroformate (FMOC) (Kawai et al. 1991; Sancho et al. 1996b; Nedelkoska and Low 2004; Fang et al. 2014). Detectors used in the HPLC detection of glyphosate are UV detector and fluorescence detector (FLD). Post-column derivatization procedures involve the use of fluorescence detector (FLD) and sodium hypochlorite and a mixture of o-phthalaldehyde and mercaptoethanol as derivatizing agent (Ding et al. 2015). According to reports procedures involving post-column derivatization lead to more precision compared to pre-column derivatization. Determination of glyphosate in water and plants by HPLC method after pre-column derivatization with 9-fluorenylmethyl chloroformate (FMOC-Cl) using single and coupled polymeric amino columns was also studied. This approach exhibits a detection limit of 0.16 g/L in rainwater samples and 0.3 mg/Kg in plant tissues, with recovery values of 94% and 82.4%, respectively. The HPLC–UV detection of glyphosate in water, soil and sediments from soybean cultivation area was studied which involves the derivatization by 9-fluorenylmethylchloroformate (FMOC-Cl), and the methods have detection limits of 0.04 mg/L for water samples and 0.10 mg/Kg for soil samples. Glyphosate residues in transgenic glyphosate-resistant soybean with the help of HPLC–UV detection, with recovery values of 83–113% and the detection limit of 0.02 mg $Kg^{-}1$, were also studied (Arregui et al. 2004).

Ion chromatography

Ion chromatography is another analytical technique based on the ion-exchange. IC-ICP is an element-specific and highly sensitive detection technique. The detection of glyphosate molecule by IC involves the use of anion exchange column and alkaline buffer as an eluent due to the ionic nature of glyphosate. The detection of glyphosate in water samples has been reported using self-fabricated IC-ICP IC-CNLSD (You et al. 2003) and IC-CNLSD*178* IC-ICP (Guo et al. 2007) detectors. Quantitative determination of trace glyphosate and its residue water samples have been reported by Guo et al. (2005) by IC-ICP/MS using polymer anion exchange column (Dionex IonPac AS16, 4.0 mm × 250 mm) and citric acid as eluent. This method has high recovery values of 97.1–107.0%. The detection of glyphosate residues by suppressed conductivity detection (DX-100) and Na_2CO_3 and NaOH as eluent (LOD ~ 0.042 µg/mL) was also reported (Zhu et al. 1999). Detection of glyphosate in analysed surface, well, potable and ultrapure water samples for glyphosate residues was studied and the analysis was carried by Dionex Model ICS-3000 ion chromatograph fitted with a 25-µL loop, IonPac AG19 guard and AS19 analytical columns, ASRS-300 (2 mm) suppressor, and conductivity detector, and detection limit of 0.05 mg/L and recovery in the range of 90–105% have been achieved (Marques et al. 2009).

The technique is advantageous over the other chromatographic analytical techniques due to simple procedures involved. IC procedure does not involve pre-concentration, derivatization, and mobile phase conductivity inhibition (Guo et al. 2005; Ding and Yang 2013). It is simple, rapid, reliable and inexpensive technique. But suffers from low sensitivity and high detection limits hence has limited practical applications compared to other chromatographic techniques. Its applicability only to water and soil samples is another limitation to this approach.

Chromatographic techniques coupled with mass spectrometry

The conventional chromatographic techniques suffer from certain limitations for the detection of analysis of glyphosate. Coupling the existing chromatographic technique to mass spectrometry not only eliminates the most indispensable step of derivatization but also improves the sensitivity of glyphosate detection. The common modes used in mass spectrometry are multiple reaction monitoring (MRM) and selection reaction monitoring (SRM) which analysed glyphosate residues in surface water, particulate matter, sediment and soil samples from sixteen agricultural sites and forty-four streams in the agricultural basin by UPLC-MS/MS ESI(±). The process involved extraction by potassium

Table 3 Analytical techniques used in the qualitative and quantitative analyses of glyphosate and its derivatives under different geo-climatic and experimental conditions

Analytical technique	Detector	Method	Source	Sample detection	Percentage Recovery	References
Gas chromatography (GC/GC–MS)	GC–MS	GC–MS system, with oven temperature starting at 80°C and after 2 min, at a rate of 28.8°C min^{-1}	Water	For GP = 0.67 (LOD) and 2.02 μg L^{-1} (LOQ) For AMPA = 0.15 (LOD) and 0.45 μg L^{-1} (LOQ)	70–120%	Silva et al. (2015)
			Soil	For GP = 0.0027 and AMPA 0.006 mg/kg		
			Sediment	For GP = 0.0081 and AMPA 0.0018 mg/kg		
	FID	N-methyl-N-tert.-butyl-dimethylsilicontrifluoro acetamide and dimeth-ylformate	Water	–	> 90%	Tsunoda (1993)
	FID	trifluoroacetic acid-trif-luoroacetic anhydride and trimethyl orthofor-mate	Water	–	> 95%	Kudzin et al. (2002)
	GC–MS (EI mode)	Oven temperature 70 °C. Helium was used as the carrier gas flow rate—0.7 mL min	Water and soil	0.1(water) and 0.006 (soil) $\mu g L^{-1}$	–	Börjesson and Torstensson (2000)
	FPD	Isopropyl chloroformate and diazomethane	Soil	–	> 91%	(Kataoka et al. 1996)
	NPD	Trifluoroacetic anhydride and 4,4,4-trifluoro-1 -butanol	Soil	0.02 mg/kg	> 84%	(Hu et al. 2011)
	FPD	Solid–liquid extraction	River water, soil and car-rot samples	12 pg	91–160%	(Kataoka et al. 1996)
	MS	Dilution for urine sam-ples Tissue samples were minced homogenized, freezed and thawed	Residues in animals and humans (urine and tissues)	1 μg/mL (human urine) 3.17 μg/mL rabbit urine 4.7 μg/mL (organs)	91%	(Krüger et al. 2014)
Capillary electrophoresis	ECL detector	Indirect detection	Wheat sample	0.8/μg mL-~	–	(Cikalo et al. 1996)
		Electrochemilumines-cence detection	Soybeans	0.6 μg/L (water) glypho-sate 4.04 μg/L (water) AMPA 0.6 μg/L (Soya) glypho-sate		(Chiu et al. 2008)
		Indirect detection	Water	5 μM	–	(Cikalo et al. 1996)

Table 3 (continued)

Analytical technique	Detector	Method	Source	Sample detection	Percentage Recovery	References
		Pre-concentrate by using anion exchange resin.	Water	5 g mL^{-1} for glyphosate and 4 g mL^{-1} for AMPA	84 to 87% for glyphosate (R.S.D. < 6%) and from 85 to 98% for AMPA	(Khrolenko et al. 2003)
		Electrospray condensation nucleation light scattering detection (ESI-CNLSD)		0.2 mg/mL	–	(You et al. 2003)
	MRM	Acclaim® Mix-mode WAX-1 column (RP and weak anion) A methanol/water = 50:50 (v/v), B 300 mM ammonium acetate in A phase (gradient elution)	Groundwater	1 µg/L	–	(Hao et al. 2011)
	MRM	CAPCELL PAK ST column (1 50 mm × 2.1 mm) 10 mM ammonium acetate aqueous solution (PH10.1): acetonitrile = 72:28 (v/v)	Drinking water	4 µg/L	–	(Zheng et al. 2013)
	MRM	Hypersil gold aQ column (100 mm × 2.1 mm, 3 µm) A ammonium acetate aqueous solution (containing 0.4% formic acid), B acetonitrile (gradient elution)	Drinking water	2 µg/L	–	(Guo et al. 2005)
	Electrospray tandem mass spectrometry (LC–ESI–MS/MS)	Solid-phase extraction using fluorenylmethylchloroformate (FMOC-Cl)		0.2 ng/L (glyphosate) 0.2 ng/L (AMPA) 0.6 ng/L (glufosinate)	91–107%	(Hanke et al. 2008)
	Fluorescence detection	Pre-column derivatization with 9-fluorenylmethyl chloroformate		0.5 mg/kg	80–99%	(Hogendoorn et al. 1999)
	Pre-column fluorogenic labelling (fluorescence detection)	Coupled-column liquid chromatography (FMOC)		0.2/µL/1	48–54%	(Sancho et al. 1996a)

Table 3 (continued)

Analytical technique	Detector	Method	Source	Sample detection	Percentage Recovery	References
High-performance liquid chromatography (HPLC/HPLC-MS/UPLC-MS)	HPLC–UV	–		LOD 9.93 and LOQ 30.1 μg L^{-1} (water) 0.04 mg/kg (soil) and 0.120 mg/kg (sediments)	70% to 120%	Silva et al. (2015)
		2,5-Dimethylbenzenesulfonylchloride		67 μg/L		(Fang et al. 2014)
		p-Toluenesulphonyl chloride	Water	10 μg/L	10	(Kawai et al. 1991)
		FMOC	Water	0.02 μg/L		(Hidalgo et al. 2004)
		FMOC	Water	0.1 μg/L		(Sancho et al. 1996a)
	Polymeric amino column	FMOC	Water	0.16 μg/L (water) 0.3 mg/kg (Grass)		(Nedelkoska and Low 2004)
		UV detector	Soil water, stream water	35–1502 μg/kg (soil) glyphosate 299–2256 μg/kg (Soil) AMPA 15% (water) glyphosate 12% (water) AMPA 66% (stream) glyphosate 88.5% (stream) AMPA		(Aparicio et al. 2013)
	SH + PM	Water SAX anion exchange column Mobile phase: Citrate buffer	Water	2 μg/L		Abdullah et al. (1995)
	HPLC/UV	Liquid–liquid extraction with 4-chloro-3,5-dinitrobenzotrifluoride	Environmental water samples	0.009 mg L^{-1}	91.80–100.20%	Qian et al. (2009)
	HPLC with UV detection (fluorescence detector)	Calcium hypochlorite and then coupled with the *o*-phthalaldehyde-2-mercaptoethanol complex	Soyabean	1.9–4.4 mg/kg Leaves 0.1–1.8 mg/kg Seeds	87–113%	Arregui et al. (2004)
		LIGAND-exchange, anion exchange and derivatization	Water and soil	0.05 μg L^{-1} in groundwater and 0.003 μg g^{-1} in soil	78% in soil 104% in water samples	Börjesson and Torstensson (2000)
	HPLC–UV detection	9-Fluorenylmethylchloroformate (FMOC-Cl)	Soil and Sediment	0.5/5.0 mg/kg Soil and sediments 0.10–0.70 mg/L water	82.4%	Peruzzo et al. (2008)
Ion chromatography	Fluorimetric	Anion exchange method (− 0.005 M KH_2PO_4 mobile phase)	Groundwater	2 μg L^{-1}	25%	Mallat and Barceló (1998)

Table 3 (continued)

Analytical technique	Detector	Method	Source	Sample detection	Percentage Recovery	References
	Conductivity detection (DX-100)	Liquid–liquid extraction using dichloromethane	Aquatic environment West Lake	0.042 mg mL^{-1}	96.4 ~ 103.2%.	Zhu et al. (1999)
	Conductivity detector	Dionex model ICS 3000	Water	0.05–0.75 mg/L	90–105	Marques et al. (2009)
	SPE	Laser-induced fluorescence detection	Water	0.4 mM		Jiang and Lucy (2007)
	Coupled column	Liquid chromatography	Water	0.5–10 µg/L	–	Sancho et al. (1996b)
	Coupled column	Liquid chromatography with fluorescence detection	Cereal	0.5 mg/kg	74%	Hogendoorn et al. (1999)
	–	Dionex AS18 column 33 mM KOH solution	Natural water	38 µg/L		Coutinho et al. (2008)
		IonPac AS19 column 35 mM KOH solution	Drinking water	4.8 µg/L		Qiu et al. (2013)
		IonPac AS19 column (250 mm × 0.4 mm) KOH solution (gradient elution)	Drinking water	2.0×10^5 µg/L		Ye et al. (2011)
Nanosensors	Cysteamine-stabilized gold nanoparticles	Liquid–liquid extraction	Water sample	0.01 mg/L	90–105%	Marques et al. (2009)
	Capillary electrophoresis and electrochemiluminescence detection	Colorimetric probe (glyphosate, 1.2 mL of the CS-AuNPs solution and 1.5 mL of HAc–NaAc buffer (20 mM, pH 4.0)	Environmental water samples	5.88×10^{-8} M	92.76–110.10%	Zheng et al. (2013)
	Carbon disulphide to form dithiocarbamic acid (UV detector)	Alumina-coated iron oxide nanoparticles	Water and guava fruit extract	0.3 ng mL^{-1} in a water sample 0.01 g^{-1} in guava fruit	46%	Hsu and Whang (2009)
Spectrophotometric		Solid-phase extraction of glyphosate from water samples	Wheat grains and water samples	1.1 ± 0.173 µg mL^{-1}	80.0–87.0%, (Soil) 95.0–102% (Wheat grains) 85.0–92.0%, Water samples	Jan et al. (2009)
Immunogenic techniques	ELISA	Polyclonal antisera	Water	7.6 µg/mL		Clegg et al. (1999)
	ELISA	Highly sensitive linker-assisted enzyme-linked immunosorbent assay	Groundwater and water	0.1 µg/L		Lee et al. (2002)
	ELISA	Competitive ELISA technique	Tap, glyphosate spiked and river waters			Rubio et al. (2003)
	ELISA	Automated immunosensor	Immunocomplex capture assay protocol	0.021 µg/L		González-Martínez et al. (2005)

Table 3 (continued)

Analytical technique	Detector	Method	Source	Sample detection	Percentage Recovery	References
	ELISA	The conjunction of ELISA technique with traditional methods	Water	0.1 µg/L		Byer et al. (2008)
	ELISA	The functionalized oligo-peptide-based surface plasmon biosensor		0.58 µM		Ding and Yang (2013)
	Enzyme conjugation	Microtitre plate	Ground and surface water	0.05–0.12 ng/mL		Mörtl et al. (2013)
	ELISA	Glyphosate-specific antibodies	Meat			Krüger et al. (2014)
	ELISA	Label-free and simple colorimetric method		1 µM		Chang et al. (2016)
	ELISA	Fluorescence method	Plant tissues	8 ng/mL	87.4–103.7%	Wang et al. (2016)

SH + PM stands for sodium hypochlorite + o-phthalaldehyde and mercaptoethanol, *SRM* selected reaction monitoring, *MRM* multiple reaction monitoring, *SPE* solid-phase extraction, *ELISA* enzyme linked immune sorbent assay, *NPD* nitrogen phosphate detector, *FPD* flame photometric detector, *ECD* electron capture detector, *FID* flame ionization detector, *NPD* nitrogen phosphate detector, *ECL* electron enhanced chemiluminescence

dihydrogen phosphate, followed by derivatization with 9-fluorenylmethyl chloroformate (FMOC-CL) in acetonitrile (Aparicio et al. 2013). The estimation of glyphosate in water and soil samples with a limit of detection 0.1 µg/L and 0.006 µg/L, respectively, by GS/MS technique was also studied (Börjesson and Torstensson 2000). Despite the simplicity in the process, this technique is not widely used for glyphosate detection due to the high cost and interface technology problems.

Capillary electrophoresis (CE)

Indirect detection is a good alternative because it reduces the time of analysis for analytes with little or no absorbance. Few CE methods have been reported for glyphosate (Abdullah et al. 1995; Royer et al. 2000; Chen et al. 2007). To achieve a LOD of 0.06 g/L for glyphosate, online sample stacking and indirect UV detection was used for the detection of glyphosate which was later on improved by using off-line ion-exchange pre-concentration (Corbera et al. 2005). The detection of glyphosate in water by CE approach via indirect detection was also reported in which detection was made using glyphosate phthalate background electrolyte with 0.5 mM tetradecyl trimethyl ammonium bromide (TTAB) as an electro-osmotic flow modifier, followed by separation under reverse polarity conditions and indirect detection (Cikalo et al. 1996). CE-laser-induced fluorescence detection of glyphosate in river water samples have been reported using ion-exchange solid-phase extraction (SPE) technique with detection limits of 0.04 nM. Bio-Rad AG1-X8 anion exchanger beads were used for off-line extraction, and fluorescent labelling was carried out using naphthalene-2,3-dicarboxaldehyde (NDA)–cyanide allowing micellar electrokinetic chromatography (MEKC) separation followed by laser-induced fluorescence detection (LIF) with a violet diode laser (Jiang and Lucy 2007).

A CE-electrospray ionization mass spectrometry (CE-ESI–MS) method for rapid and selective detection of glyphosate with a LOD of 10 ng/mL and minimal sample handling was also reported (Börjesson and Torstensson 2000). Use of improved technique of electrospray condensation nucleation light scattering detection (ESI-CNLSD) in combination with CE has been demonstrated for determination of glyphosate in environmental water directly (You et al. 2003). It should be pointed out, however, that CE seems to be a method of choice since it is much cheaper and less time-consuming if comparing HPLC.

Spectrophotometric analysis technique

The direct spectrophotometric and fluorometric method for determination of glyphosate has not been reported due to the absence of chromophore or fluorophore groups in the

structure of glyphosate. Reports are available for glyphosate estimation by forming coloured complexes with suitable reagents and then analysing the complexes by UV–Vis or fluorometric techniques. It is a simple selective spectrophotometric method for the determination of glyphosate herbicide in the environmental and biological samples. The analysis involved the complex formation of glyphosate present in the soil, wheat grains and water samples with carbon disulphide and copper in ammonia. The yellow complex formed was analysed for its absorbance at 435 nm with a molar absorptivity of 1.864 × 103 L mol^{-1} cm^{-1}. The recovery reported for different samples ranges from 80 to 102%. This method is simple with high sensitivity and can be easily applied to environmental samples (Jan et al. 2009).

Immunogenic techniques

ELISA is a cost-effective technique which enhances the temporal and spatial resolution to study the monitoring of glyphosate in water samples. It is a technique based on polyclonal antiserum for detection of glyphosate and its metabolites in water samples. In this method, polyclonal antiserum reacts with the metabolite of glyphosate (AMPA). The detection limit is good with a value of 7.6 µg/mL having IC_{50} value of 154 mL^{-1}. A highly sensitive linker-assisted enzyme-linked immunosorbent assay for the analysis of glyphosate in groundwater and water samples was also reported which involves the derivatization of glyphosate using succinic anhydride which emits the binding of glyphosate to hapten molecule which effectively recognizes by linker-assisted enzyme-linked immunosorbent with high detection limit up to 0.1 µg/L (Lee et al. 2002). A new methodology for detection of glyphosate based on competitive ELISA technique detects glyphosate and its metabolites in tap, glyphosate spiked and river waters. It is swift and extremely sensitive technique having a coefficient of variation between 10 and 19% in tap water (Rubio et al. 2003). An automated immunosensor based on immunocomplex capture assay protocol was devised in which the sensor is based on analyte derivatization which uses selective peroxidase enzyme tracer of glyphosate and antiserum of glyphosate. Its shows selectivity towards the glyphosate and its residues and shows a high range of detection up to 0.021 µg/L (González-Martínez et al. 2005). Detection of glyphosate in water has also been carried out using a conjunction of ELISA technique with traditional methods with a detection limit of 0.1 µg/L which shows a bimodal distribution of the samples (Byer et al. 2008). A functionalized oligopeptide-based surface plasmon biosensor was also developed for the detection of glyphosate. An SPR gold sensor chip is coated with TPFDLRPSSDTR, and an oligopeptide was modified with a limit of detection up to 0.58 µM with a sensitivity of 1.02 RU/µM having high specificity against glyphosate derivatives (Ding and Yang 2013). Alternative approach based on ELISA for glyphosate detection in ground and surface water was developed. This method includes enzyme conjugate of glyphosate and a specified antibody mixture of glyphosate in a microtitre plate. This technique has high specificity, no laborious extraction and LOD ranges from 0.05 to 0.12 ng/mL (Mörtl et al. 2013). Krüger et al. (2014) constructed a method to recover the glyphosate from meat samples using ELISA technique by homogenising the samples followed by centrifugation, and samples were tested by glyphosate-specific antibodies (Krüger et al. 2014). A label-free and simple colorimetric process for the detection of glyphosate and its metabolites was developed by Chang et al. (2016) which inhibits the activity of copper in peroxidase which catalyses the oxidation of 3,3′,5,5′-tetramethylbenzidine (TMB) to oxidized TMB (oxTMB) in the presence of hydrogen peroxide with detection limit up to 1 µM with linear range 2–200 µM (Chang et al. 2016). For the detection of glyphosate, a sensitive fluorescence method was established based on immune reaction. Carbon dot labelled antibodies (I_gG-CDs) which have the ability for identification of glyphosate were prepared by using environmentally friendly carbon dots (CDs) and glyphosate antibody (I_gG), I_gG-CDs. To visualize the in situ distribution of glyphosate in plant tissues, these I_gG-CDs could be used. The detection limit was of 8 ng/mL. The recovery ratio was found to be in the range between 87.4 and 103.7% (Wang et al. 2016).

Nanotechnology-based biosensors

Considering the use of various nano-compounds, methods for quantification of glyphosate and its residues were also applied.

Cysteamine-stabilized gold nanoparticles (CS-AuNPs) were put to use for the detection of glyphosate in water by electrostatic interaction in acidic medium by observing peak shift in surface Plasmon band with a detection limit of 5.88×10^{-8} M, with the linear range of 0.500–7.00 µM (Zheng et al. 2013). An additional experiment was performed that resulted in the development of gold DNA-coated nanoparticles biosensor which could effectuate the quantitative analysis of sDNA on the basis of glyphosate concentration (Lee et al. 2010).

Chemical degradation of glyphosate

The chemical, photochemical and chemical with photochemical methods have been reported for the degradation of glyphosate. Both glyphosate and AMPA degraded at 20 °C in dilute aqueous suspensions of birnessite {$(Na_{0.3}Ca_{0.1}K_{0.1})(Mn^{4+}, Mn^{3+})_2O_4$ $1.5H_2O$}, as over several days there was an accumulation of orthophosphate in solution. Here the abiotic degradation involved C–P bond cleavage at the Mn

oxide surface in case of AMPA (degradation product of glyphosate) and C–N bond cleavage in case of glyphosate and sarcosine. The degradation of glyphosate was faster than that of AMPA, and addition of Cu^{2+} inhibited degradation. Researchers were not able to detect glyphosate degradation in an equimolar solution of $MnCl_2$ (0.5 mM) in a similar experimental design. However, it was illustrated that the oxidation of Mn^{2+} is better both in solution and on an inert surface, in the presence of glyphosate (4:1 Mn-glyphosate molar ratio), which suggests the oxidative breakdown of glyphosate in the presence of Mn^{2+} through the spontaneous oxygen-mediated oxidation of manganese (Barrett and McBride 2005). The electrochemical oxidation of glyphosate on RuO_2 and IrO_2 (dimensionally stable anode electrodes) have also been applied for its degradation. Electrolysis was completed under galvanostatic control as a function of pH, glyphosate concentration, supporting electrolyte and current density. Oxide composition effect on glyphosate degradation was significant in the absence of chloride, and the use of chloride medium increases the oxidizing power. $Ti/Ir_{0.30}Sn_{0.70}O_2$ was the best electrode material to oxidize glyphosate, and the influence of the oxide composition was meaningless. The oxidation of glyphosate was favoured at low pH values (Polubesova and Chefetz 2014). Complete glyphosate removal from the electrolyzed solution was obtained at 30 mA cm^{-2} and 4 h of electrolysis in the absence of chloride medium and 50 mA cm^{-2} in the presence of chloride medium (Aquino Neto and de Andrade 2009). In another study, density functional calculations to identify the vibrational bands of glyphosate and AMPA in surface-enhanced Raman spectroscopy (SERS) and attenuated total reflectance Fourier transform infrared (ATR–FTIR) spectra experiments, to provide the abiotic degradation process of glyphosate into AMPA with an important role of metals. SERS confirms the presence of AMPA after glyphosate is deposited from aqueous solution on different metallic surfaces. In ATR–FTIR experiments, AMPA is also detected when glyphosate interacts with metallic ions in aqueous solution (Ascolani Yael et al. 2014).

According to early studies, in contrast to microbial metabolism photodegradation plays a very insubstantial role in the environmental decomposition of glyphosate (Rueppel et al. 1977). However, the effect of artificial as well as sunlight on glyphosate in the water of varying qualities made some different findings. The results indicate that AMPA is the main breakdown product in the photolytic process and that AMPA is far more stable to photodegradation than the parent compound (Lund-HØie and Friestad 1986). The photoinduced degradation of glyphosate in ferrioxalate system was also investigated under irradiation with a 250 W metal halide lamp ($\lambda \geq 365$ nm). Photodegradation efficiency of glyphosate (represented by orthophosphates release) increased with decreasing the initial concentrations of glyphosate and Fe(III)/oxalate ratios. At acidic pH (3.5–5.0), 60.6% orthophosphate release was achieved, whereas efficiency dropped to 42.1% at pH 6.0. The photochemical process includes the predominant species of Fe(III), namely Fe $(C_2O_4)^{2-}$ and Fe $(C_2O_4)_3^{3-}$, which leads to the formation of hydroxyl radicals in the presence of dissolved oxygen under UV–Vis irradiation.

The light absorption of glyphosate increased and accelerated its degradation (by direct photolysis) upon its complexation with Fe(III). It was shown by the ninhydrin test for primary amines that the glyphosate was attacked by hydroxyl radicals with C–N cleavage to yield AMPA and C–P cleavage to yield sarcosine. The decomposition of reactive radicals produced through ligand-to-metal charge transfer of ferric–glyphosate complexes may increase the photodegradation (Chen et al. 2007). The photocatalytic degradation of a glyphosate derivative had been analysed in aqueous suspensions of TiO_2 at different pH values. However, Zn^{2+} has not shown to affect the photodegradation of glyphosate (Katz et al. 2015). Degradation was much efficient in alkaline pH, whereas no adsorption occurs on the surface of the catalyst in the dark. Main degradation path involves the cleavage of the C–P bond producing sarcosine and glycine as intermediate products (Muneer and Boxall 2008). The photocatalytic degradation of glyphosate increases in alkaline medium and also in acidic medium. The photodegradation efficiency of glyphosate was found to be 66.9% at pH 2, 36.2% at pH 6 and 49.4% at pH 12 (Chen and Liu 2007). UV light with TiO_2 immobilized on silica gel as photocatalyst has also been used for the degradation of glyphosate along with acephate and dimethoate. Within 60 min of photocatalytic treatment, 100% decomposition of dimethoate and glyphosate was achieved, while total degradation of acephate was observed after 105 min of treatment. Following the Langmuir–Hinshelwood apparent first-order degradation kinetics, acephate and dimethoate decomposition showed only the photocatalytic nature of pesticide disappearance, whereas glyphosate decomposition followed both adsorption and photocatalytic reactions. Production of heteroatoms at their highest oxidized states (SO_4^{2-}, NO_3^-, and PO_4^{3-}) made to conclude that pesticide degradation occurred primarily through photocatalytic oxidation reactions. Unlike other degradation treatments, unavailability of toxic intermediates reveals swift destruction of the pesticides into harmless by-products using this system (Echavia et al. 2009).

The combination of H_2O_2 and UV radiation was also used for glyphosate degradation. Three factors, namely effects of initial pH, H_2O_2 initial concentration and incident radiation, were studied. Degradation increases significantly from pH 3–7, and increase becomes much less noticeable above this pH. The reaction rate was dependent on initial herbicide concentration, had an optimum plateau of H_2O_2 to glyphosate molar concentration ratio between 7 and 19 and was

nonlinearly dependent on irradiation rate. It was also possible to identify the critical reaction intermediaries and to quantify the main end products (Manassero et al. 2010). In an attempt to study the degradation of glyphosate in water, various advanced oxidation processes that included ozonation at pH 6.5 and 10, photolysis and heterogeneous photocatalysis (where TiO_2 was used as a semiconductor and dissolved oxygen as an electron acceptor) were used. Analysis of three required factors, viz. the degree of glyphosate degradation, the reactions kinetics and the formation of the major metabolite, AMPA, was performed. Ozonation at pH 10 leads to the maximum degradation of glyphosate which followed the first-order kinetics with a half-life of 1.8 min (Assalin et al. 2010).

To explore the C–P bond cleavage mechanism, generation of phosphonates by UV photo-oxidation and to trace their sources in the environment, the stable oxygen isotope analysis was applied. Glyphosate and phosphonoacetic acid were used as model compounds and effectively degraded after exposure to UV irradiation. In corroboration with previous suggested mechanisms of UV-photon excitation reactions, it was found out that both ambient water and atmospheric oxygen were responsible for the C–P bond cleavage. Both the phosphonates used are having markedly lower values when compared to naturally derived organophosphorus compounds as indicated by the calculation of oxygen isotopic composition of the original phosphonate P^-moiety (Sandy et al. 2013). In an attempt to study the role of Fe^{3+} as a natural photosensitizer towards the decomposition of organic phosphorus to release phosphate, glyphosate was used as the organic phosphorus model in deionized and natural waters under UV and sunlight irradiation. Degradation by Fe^{3+} was confirmed by the decrease in glyphosate concentration and total organic contents in both Fe^{3+}/UV and Fe^{3+}/sunlight systems. The released amount of phosphate was higher in the presence of Fe^{3+} than control, and the rate of generation of phosphate increased with increasing Fe^{3+} concentrations (Jiang et al. 2016).

With a step ahead, some photocatalysts were prepared and applied for the degradation of glyphosate. In a similar advancement, manganese dioxide/graphite (MnO_2/C) composite was used as a photocatalyst for the degradation of glyphosate, through high energy electron beam irradiation. This type of radiation is effectively helpful in reducing MnO_4^- to MnO_2 nanospheres via the reducing nature of e^-, e^-_{aq} and $^{\cdot}H$, as well as make graphite possess rough surface by an electron beam having thermal and sputtering effects. Moreover, numerous hydroxyl groups are introduced on the surface of MnO_2 nanospheres by the process of fabrication, thereby promoting the adhesion of MnO_2 nanospheres on the rough surface of graphite via hydrogen bonding. Therefore, the resultant MnO_2/C composite has large specific surface area and a high dispersion and therefore forms to be an excellent adsorbent having greater catalytic degradation performance on glyphosate (Wang et al. 2016). Similarly, visible-light-driven bismuth vanadate ($BiVO_4$) photocatalysts, prepared by the co-precipitation method and characterized by using X-ray diffraction, UV–visible diffuse reflectance, electrochemical impedance spectroscopy, photocurrent, as well as electron microscopy (SEM, TEM), were used for the degradation of glyphosate. The photocatalytic activity of the as-prepared $BiVO_4$ samples was tested through the photocatalytic oxidation of glyphosate under visible light irradiation. The $BiVO_4$ sample calcined at 400 °C showed the highest photocatalytic activity for glyphosate degradation under visible light irradiation because of its high charge separation efficiency is proven by electrochemical impedance spectroscopy and photocurrent (Huo et al. 2017). In another attempt to use a chemical with photochemical phenomena for the degradation of glyphosate, electrolysis and photoelectrolysis with diamond anodes were applied. Results showed that photolysis used singly is not as efficient technique as coupled with electrolysis for the removal of the pesticide. The use of a combined technique leads to the production of higher concentrations of free radicals from the photoactivation of the oxidants electrogenerated. As a result of the generation of different oxidant species (peroxocarbonates, peroxosulfates and hypochlorite), the supporting electrolyte plays an important role in the removal of glyphosate, as these species also contribute to its degradation. Because of the strong relationship between current density and the oxidants produced on the anode surface, the removal of glyphosate is also influenced by the former (current density) (Rubí-Juárez et al. 2016).

Possible degradation pathways of glyphosate

Glyphosate is a frequently used herbicide worldwide which has the capability of rapid degradation in soils, particularly by microbial processes. AMPA forms to be the most commonly found degraded product of glyphosate in water and soil (Barrett and McBride 2005; Grandcoin et al. 2017) (Fig. 5).

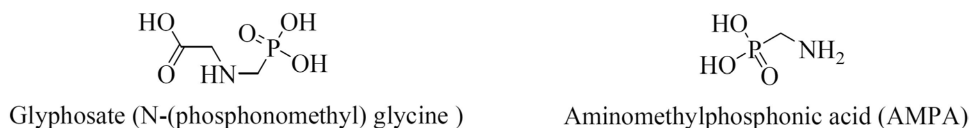


Fig. 5 Structure of glyphosate and AMPA

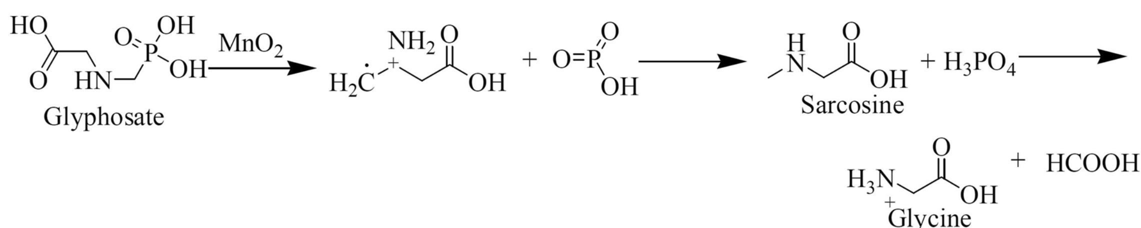


Fig. 6 Photodegradation pathway of glyphosate in the presence of manganese oxide

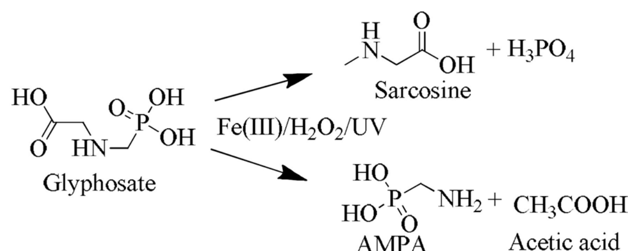


Fig. 7 Photodegradation pathway of glyphosate in the presence of Fe(III)/H_2O_2

Several possible reaction pathways have been proposed for the degradation of glyphosate. According to Barrett and McBride (2005), the degradation is accomplished by using manganese oxide with the intermediate sarcosine, which finally produces glycine and formic acid (Fig. 6).

Chen et al. (2007) employed the Fe(III)/H_2O_2/UV process for degradation, proposed the cleavage of C–N and C–P bonds and attributed the process to the existence of hydroxyl radicals (Fig. 7).

The degradation in aqueous suspensions of titanium dioxide at low and high pH values proposed the formation of sarcosine from low pH and direct generation of glycine at high pH (Muneer and Boxall 2008) (Fig. 8).

There is a tentative pathway for the degradation of glyphosate by photocatalysis using TiO_2 as a catalyst (Echavia et al. 2009). The pathway is presented in Fig. 9.

The photodegradation pathway of glyphosate with the H_2O_2/UV system shows the glycine, formaldehyde, formic acid, nitric acid along with some radicals and ions as the main intermediates were also reported (Assalin et al. 2010) and the reaction pathway summarized in Fig. 10.

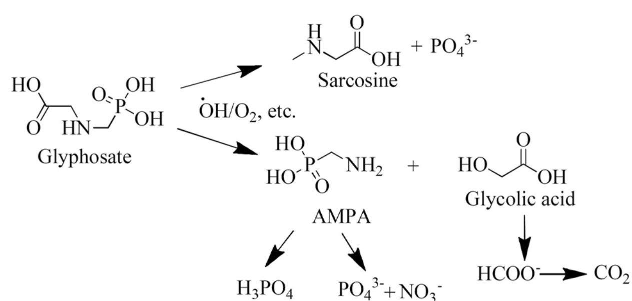
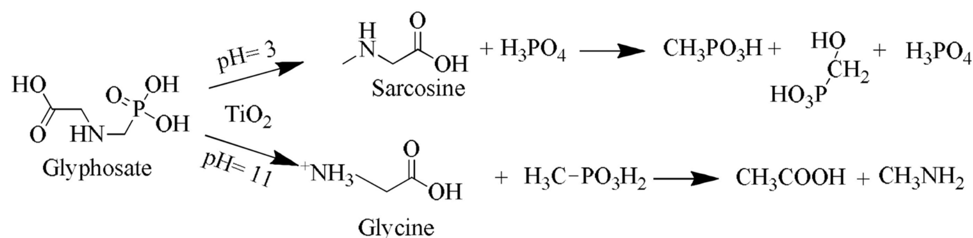


Fig. 9 Photocatalytic pathway of glyphosate in the presence of immobilized TiO_2

Fig. 10 Photodegradation pathway of glyphosate in the presence of the H_2O_2/UV system

Fig. 8 Photodegradation pathway of glyphosate in the presence of TiO_2 at low pH and high pH



Therefore, we can conclude that the degradation pathway of glyphosate, whether chemical, photochemical or chemical with photochemical, is dependent on the technique used.

Microbial degradation of glyphosate

Glyphosate hardly produce physicochemical effects (hydrolysis, photolysis), but there are microbial enzymatic systems that cleave the C–P bond and can lead to its degradation. Phosphorus present in glyphosate is a driving force for its microbial degradation, as the microorganisms use this phosphorus for their metabolic functions (Briceño et al. 2007). A number of microbial species and strains have been shown to exhibit glyphosate metabolism as listed in Table 4. Microbial degradation pathway involves the cleavage of glyphosate to glyoxylate and aminomethylphosphonic acid by the enzyme glyphosate oxidoreductase (Fan et al. 2012). An alternate pathway for its degradation involves its conversion to methylamine and inorganic phosphate in the presence of enzyme C–P lyase (Sviridov et al. 2012; Fu et al. 2017). Microorganisms later consume methylamine and glyoxylate (Shushkova et al. 2012). Glycine oxidase acts upon glyphosate leading to its conversion to aminomethylphosphonic acid and glyoxylate (Pollegioni et al. 2011). C–P lyase causes degradation of glyphosate to initially inorganic phosphate and sarcosine, then formaldehyde and glycine. Formaldehyde and glycine are consumed by the microorganism present in soil (Dick and Quinn 1995). The strong adsorption capacity of soil towards glyphosate slows down the process of its degradation by microorganisms. Hence, it has an average half-life of more than two months.

Further, the type of microbial community in the soil affects the rate of degradation (Tu et al. 2011). Microbes release enzymes that cleave the C–P bond of the glyphosate molecule. Similar metabolic processes have been reported in a *Pseudomonas* PG 2982 strain that breaks glyphosate into phosphorous (Moore et al. 1983; Jacob et al. 1985, Lane et al. 2012). Microbial species, viz. *Rhizobium meliloti, Arthrobacter* GLP-1, and *Agrobacterium radiobacter* exhibit analogous pathway for glyphosate degradation (Pipke et al. 1987; McAuliffe et al. 1990; Liu et al. 1991; Dick and Quinn 1995). According to Pipke and Amrhein (1988) and Obojska et al. (1999), bacterial strain *Arthrobacter* GLP-1/Nit-1 exploits glyphosate as nitrogen source while *Streptomyces* spp. consumes it for both phosphorus and nitrogen.

Enzymatic degradation for the breakdown of glyphosate results in the development of glyoxylate and aminomethyl phosphonic acid (AMPA) in which oxidoreductase aids the splitting of the C–N (Barry et al. 1992). The second pathway is through the initial C–P lyase activity which splits the C–P bond in the second pathway to give sarcosine, glycine and formaldehyde (Sviridov et al. 2012).

This metabolic pathway was first reported in 1983 in which *Pseudomonas* PG2982 strain was able to degrade glyphosate as a sole phosphorus source (Jacob et al. 1985). Consequently, the pathway was recognized in other microorganisms including an *Agrobacterium radiobacter, Arthrobacter* GLP-1 strain, *Rhizobium meliloti* and other *Rhizobium* strains (Pipke et al. 1987; McAuliffe et al. 1990; Liu et al. 1991; Dick and Quinn 1995). Altogether the above strains utilizes parent compound as a sole phosphorus source, but were unable to utilize the complex as either carbon or nitrogen source. This was accredited to the presence of an uptake regulation system for glyphosate in most phosphonate-degrading microorganisms which limits organophosphonate utilization since the phosphorus unconfined after breaking of the C–P bond represses the degradation system (Obojska et al. 1999). Conversely, a mutant of the *Arthrobacter strain* GLP-1, named *Arthrobacter* GLP-1/Nit-1, could use glyphosate as its sole nitrogen source as well (Pipke and Amrhein 1988). It was revealed that the incapability of *Arthrobacter* GLP-1 strain to utilize glyphosate as a nitrogen source is due to the rigorous control of glyphosate uptake by surplus phosphate released during the degradation of the herbicide. A similar skill to utilize glyphosate as both phosphorus and nitrogen source was described for two *Streptomyces spp.* (Obojska et al. 1999).

In the second pathway, glyphosate is degraded to AMPA and glyoxylate by cleavage of the C–N bond. The previous metabolite is exposed to dephosphorylation by enzyme C–P lyases, leading to the formation of methylamine and formaldehyde and is finally mineralized to CO_2. Methylamine is produced by the alteration of several pesticides, including carbofuran and atrazine, and serves as a carbon and/or nitrogen source for microorganisms (Chapalamadugu and Chaudhry 1992). This pathway was initially reported to occur in a *Flavobacterium* sp., which was isolated from an industrial biosystem dispensation glyphosate wastes (Balthazor and Hallas 1986).

Flavobacterium sp. was able to take glyphosate as a sole source of phosphorus. After that, the same pathway was apparent in cultures of a *Pseudomonas* LBr strain, isolated from a glyphosate waste treatment which uses glyphosate as the sole energy of phosphorus (Jacob et al. 1988). While the AMPA pathway was recognized as the major degradation pathway of glyphosate by this strain, *Pseudomonas* LBr strain was also able to convert about 5% of the initially added glyphosate via formation of sarcosine and glycine. This was the first and solitary report of a glyphosate-degrading microorganism that could degrade the compound via both metabolic routes. *Arthrobacter atrocyaneus* and *Pseudomonas pseudomallei* were also reported to metabolize glyphosate via the same AMPA pathway ((Pipke and Amrhein 1988; Peñaloza-Vazquez et al. 1995). *Geobacillus caldoxylosilyticus* T20 strain being thermophilic isolated from a heating

Table 4 Microorganisms involved in the biodegradation of glyphosate under in situ and experimental conditions

Microbial species	Geographical location/region	Intermediate/end products	Source	References
Achromobacter sp. *Rhizobium radiobacter)*	USA	AMPA	Sludge	McAuliffe et al. (1990)
Achromobacter sp. MPS 12 A	Russia	Sacrosine	Soil	Sviridov et al. (2012)
Achromobacter sp. 16 kg	Russia	–	Soil	Shushkova et al. (2012)
Agrobacterium radiobacter	US	Putatively sarcosine	Wastewater	Wackett et al. (1987)
Alcaligenes sp. GL	Germany	AMPA (5%) and sarcosine (95%)	Selective medium	Lerbs et al. (1990)
Arthrobacter atrocyaneus ATCC 13752	Germany	AMPA	Microbial collection	Pipke and Amrhein (1988)
Arthrobacter sp GLP-1	USA	Sarcosine	Selective medium	Pipke et al. (1987)
Aspergillus niger	Poland	AMPA	Soil	Krzyśko-Łupicka and Orlik (1997)
Aspergillus niger	Nigeria	AMPA and sarcosine	Soil	Adelowo et al. (2014)
Aspergillus oryzae A-F02	China	AMPA and methylamine	Soil	Fu et al. (2017)
A. section Flavi and A. niger	Argentina	–	–	Carranza et al. (2017)
Bacillus subtilis	India	AMPA and methylamine	Soil	(Singh et al. 2019)
Bacillus cereus CB4	China	AMPA, glyoxylate, sarcosine, glycine and formaldehyde	Soil	Fan et al. (2012)
Comamonas odontotermitis P2	Pakistan	–	Soil	Firdous et al. (2017)
Flavobacterium sp GD1	Missouri	AMPA	Sludge	Balthazor and Hallas (1986)
Fusarium oxysporum	Nigeria	AMPA and sarcosine	Soil	Adelowo et al. (2014)
Geobacillus caldoxylosilyticus T20	UK	AMPA	–	Obojska et al. (2002)
Ochrobactrum anthropi GDOS	Iran	AMPA	Soil	Hadi et al. (2013)
Ochrobactrum anthropi GPK 3	Russia	–	Soil	Shushkova et (al. 2012)
O. anthropi GPK 3	Russia	AMPA	Soil	Sviridov et al. (2012)
O. anthropi LBAA	UK	AMPA	Soil	Obojska et al. (2002)
O. anthropi S5	USA	AMPA	Soil	Gard et al. (1997)
Pseudomonas pseudomallei	USA	AMPA	Soil	Peñaloza-Vazquez et (al. 1995)
Pseudomonas sp. 4ASW	UK	Sarcosine	Soil	Dick and Quinn (1995)
Pseudomonas sp. LBr	Missouri	AMPA (95%), sarcosine (5%)	Sludge	Jacob et al. (1988)
Pseudomonas sp. PG298231	Louisiana	Sarcosine	Mixed culture	Moore et al. (1983)
Rhizobium leguminosarum	India	AMPA and methylamine	Soil	Singh et al. (2019)
Rhizobium meliloti 1021	Massachusetts	Sarcosine	Mutation of the wild strain	Liu et al. (1991)
Streptomyces sp.	India	AMPA and methylamine	Soil	(Singh et al. 2019)
Streptomyces sp. StC	Poland	Sarcosine	Sludge	Obojska et al. (1999)
Penicillium notatum	Poland	AMPA	Mutation of the wild-type	Bujacz et al. (1995)
Salinicoccus spp	Iran	AMPA	Soil	Sharifi et al. (2015)
Scopulariopsis sp.	Poland	AMPA	Soil	Krzyśko-Łupicka and Orlik (1997)
Trichoderma harzianum	Poland	AMPA	Soil	Krzyśko-Łupicka and Orlik (1997)
Trichoderma viridae	Nigeria	AMPA and sarcosine	Soil	(Adelowo et al. 2014)
Trichoderma viride Strain FRP 3	Indonesia	–	Soil	Arfarita et al. (2016)
Ochrobactrum anthropi GPK 3 Achromobacter sp. 16 kg	Russia	–	Soil	Shushkova et al. (2012)

system was able to utilize glyphosate as an energy source of phosphorus (Obojska et al. 2002). Degradation of glyphosate by the thermophilic strain *Geobacillus caldoxylosilyticus* T20 led to the formation of glyoxylate and AMPA. *Bacillus cereus* CB4 is able to utilize glyphosate in an incubation period of 5 days via two concurrent pathways in which glyphosate is degraded into AMPA, glyoxylate, sarcosine, glycine and formaldehyde as a product (Fan et al. 2012). *Ochrobactrum anthropi* GPK 3 and *Achromobacter* sp. KG 16 utilize glyphosate as a source of carbon and phosphorous using batch fermentation technique (Shushkova et al. 2012). *Comamonas odontotermitis* P2 degrades glyphosate via CP lyase and GOX metabolic pathways using glyphosate as a sole source of carbon and phosphorus (Firdous et al. 2017). The generalized metabolic pathways of glyphosate biodegradation are mentioned in Fig. 11.

Apart from bacteria and actinomycetes, fungi have been revealed to degrade glyphosate. The isolation of a fungal strain, *Penicillium citrinum,* which could metabolize glyphosate were first reported by Zboińska et al. (1992). Later *P. notatum* was isolated in a study that metabolized glyphosate by using AMPA pathway (Bujacz et al. 1995). Fungal strains, including *Scopulariopsis* sp., *Trichoderma viride, T. harzianum, Alternaria* sp. and *A. niger* isolated from soil, showed an improved ability to grow on numerous organophosphates including glyphosate (Krzyśko-Łupicka

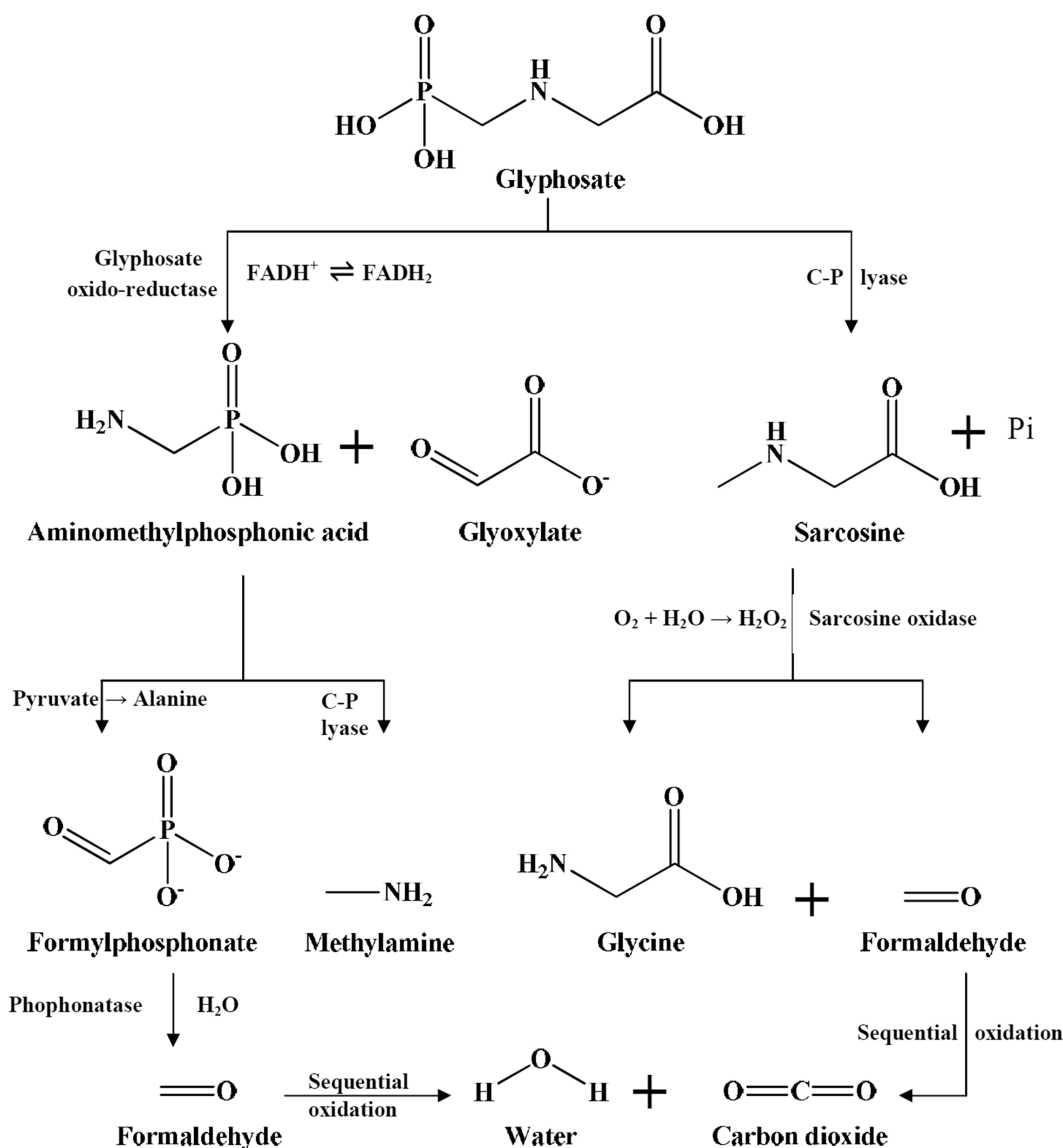


Fig. 11 Metabolism pathways of glyphosate biodegradation

and Orlik 1997). These fungal strains use glyphosate via the AMPA pathway. Other species of the *Aspergillus* genus such as *A. flavi* and *A. niger* utilize glyphosate as a single source of phosphorus or nitrogen and are potent to grow in glyphosate environmental conditions (Carranza et al. 2017). All the reported above fungal strains utilize glyphosate as a source of phosphorus. A number of fungal species have been isolated including *Penicillium simplicissimum, Mucor* sp., *Penicillium janthinellum* and *Alternaria alternata* from non-disinfected carrot seeds, which utilizes glyphosate as a phosphorus source, that have also been reported (Javaid et al. 2016).

Complexation chemistry of glyphosate with metal ions and humic acid

Glyphosate (world top-ranked herbicide) has three functional groups (P-OH, NH and COOH) for strong coordination chemistry with metal ions at variable pH values (Thelen et al. 1995; Sundaram and Sundaram 1997; Gimsing and dos Santos 2005; Duke et al. 2012; Kaur et al. 2017; Singh et al. 2017).

Glyphosate has the capability to get adsorbed on the soil surface and humic substances over a wide range of pH owing to strong interactions through OH (two P-OH and one of the COOH). These OH groups complex with metal ions and therefore aid in the adsorption onto the soil surface at agricultural pH range 3.5–9.0 (Sundaram and Sundaram 1997; Gimsing and dos Santos 2005; Kaur et al. 2017; Singh et al. 2017). Simultaneously, it should be noted that glyphosate forms stable complexes with metal ions present in the soil. Stable complexation causes the depletion of important metal ions of soils, and these metal ions are very important for the plant growth (Sundaram and Sundaram 1997; Gimsing and dos Santos 2005; Kumar et al. 2015a, b, c, d, 2016, 2017; Singh et al. 2016, 2017; Kaur et al. 2017). Glyphosate interacts with clay minerals as it forms complexes with interlayer metal ions. In literature, a study on 1:1 and 2:1 complexation of glyphosate with transition metal had shown stability order: Mn(II) > Zn(II) > Cu(II) > Fe(II) (Sundaram and Sundaram 1997; Gimsing and dos Santos 2005; Kaur et al. 2017; Singh et al. 2017). UV–visible-, FTIR- and NMR-based studies on glyphosate interactions with alkaline and first transition metal ions series have been reported by various authors. Glyphosate-to-metal ion binding occurred through the amino, carboxylic and phosphonic moieties that lead to the formation of thermodynamically and chemically stable five-membered rings (Sundaram and Sundaram 1997; Gimsing and dos Santos 2005; Duke et al. 2012; Kaur et al. 2017; Singh et al. 2017).

As humic substances form mixed metal and mixed ligand complexes of different stability, transport of the essential metal ions is significantly affected by variation in stability factors of these complexes. Humic acid is an important part of soils; recently, various authors have shown interest in the coordination behaviour of glyphosate in the presence of humic acid. Humic acid rich with phenoxyl, hydroxyl and carboxyl reactive groups forms the coordinate bond with metal ions and hydrogen bond with pesticides including the glyphosate (Undabeytia et al. 1996; Maqueda et al. 1998; Gimsing and dos Santos 2005; de Santana et al. 2006; Khoury et al. 2010; Mazzei and Piccolo 2012). Humic acid containing salicylate moiety, which generally forms the square planar complex with metal ions, and pesticides join axially or form a second bidentate chelate ring in the equatorial position. Axial bond formation with the metal–humic acid system in reaction mixture occurred through the most donating sites (P=O > N–H > C=O) of glyphosate. Glyphosate interacts with humic acid-to-metal ion complex (HA-M(II)) through inner-sphere complexes formation mechanism (Undabeytia et al. 1996; Maqueda et al. 1998; de Santana et al. 2006). The main mode of interaction of glyphosate with HA-M(II) complexes and adsorption on soil or clay minerals was through the phosphonic moieties of glyphosate. Few studies have shown that at low concentration level, glyphosate forms inner-sphere complexes with HA-M(II) through phosphonic moieties by ligand exchange mechanism, whereas at higher concentration, extra glyphosate binds by hydrogen bonding mechanism to humic acid and already bound glyphosate molecules (Undabeytia et al. 1996; Maqueda et al. 1998; Gimsing and dos Santos 2005; de Santana et al. 2006; Khoury et al. 2010; Mazzei and Piccolo 2012). The literature has shown that the correct order of stability of simple metal/glyphosate complexes ratios is 1:1 < 1:2 < 1:3 (Undabeytia et al. 1996; Maqueda et al. 1998; de Santana et al. 2006).

Derivatization of glyphosate: a way ahead

Derivatization of glyphosate may have two kinds of aspects: (1) to detect it in various environmental matrixes and (2) to synthesize new derivatives with high efficiency and least toxicity. Glyphosate is highly soluble in water (1.01 g/100 mL at 20 °C) and easily binds with soils; consequently, it has a minimum runoff in the polar matrix. It has been detected in environmental matrixes in residual levels, and due to lack of chromophoric and fluorophoric groups, it is detectable through derivatization only. Recent review revealed that derivatization is commonly done by acylating agents, alkyl chloro or fluoro formates, benzenesulfonyl and phthalaldehyde (Gill et al. 2017). Derivatized products are analysed by using the advanced techniques including the gas (GC) or liquid chromatographic (LC) techniques. At same time, other techniques like UV–visible, electrophoresis, sensor-based techniques, etc., have been discussed in depth by Gill et al. (2017). GC and LC were the best techniques to detect the

derivatized products, where 10–15 pg (Picogram) of glyphosate and its decomposed products have been detected with excellent recovery.

Various authors have made an attempt to synthesize new derivatives of glyphosate with high efficiency and least toxicity. Recently, derivative of glyphosate has been synthesized having excellent herbicidal activities than glyphosate, more significantly least toxic to the plant growth-promoting strains (Kumar et al. 2017). Also, photopolymerizable and thiocarboxylate-S-esters derivatives of glyphosate have been synthesized with good biological activities (Bogdanova et al. 2007). Chen et al. (2015) have developed a series of novel α-amino phosphonate derivatives containing a pyrimidinyl moiety that was also developed which was biologically active, but having less herbicidal activities than glyphosate. In a nutshell, researchers are looking for the future plant-protecting agent or glyphosate derivative with excellent herbicidal activities as compared to glyphosate.

Conclusion

Glyphosate has covered a long journey from its use to the world's top-selling herbicide. It has huge potential for agriculture due to lower toxicity among other herbicides and excellent water solubility. Due to least toxicity, and excellent water solubility, it has been used excessively all over the world. Consequently, it has entered the water and soil system. The long half-life period of glyphosate under different environmental conditions is the major concern of the future. In the future, there is a need to identify or isolate microorganisms that aid in the decomposition of glyphosate within a short time period under different environmental conditions. Development of analytical methods for the detection of glyphosate is equally important because it has no chromophoric and fluorophoric groups. Also, the synthesis of derivatives of glyphosate with least toxicity and maximum efficiency is also an important gap to fill in the future. Use of nanoparticles for photocatalytic degradation will result in an appreciable reduction in the glyphosate amount in the environmental matrices. The combination of nanoparticles with bioadsorbents to form nanocomposites is expected to show improved performance in terms of the high efficiency of photoinduced charge separation, photostability, better adsorption and improved performance.

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Compliance with ethical standards

Conflict of interest Authors declare that no conflict of interest exists.

Human and animal rights This article does not contain any studies with animals performed by any of the authors.

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