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REVIEW ARTICLE

Mechanisms of herbicide resistance in weeds

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Abstract

In major field crops, synthetic herbicides have been used to control weeds worldwide. Globally, herbicide resistance in weeds should be minimized because it is a major limiting factor for food security. Cross resistance can occur with herbicides within the same or in different herbicide families and with the same or different sites of action. Multiple resistance refers to evolved mechanisms of resistance to more than one herbicide (e.g., resistance to both ALS-inhibitors and ACCase-inhibitors) and this resistance was brought about by separate selection processes. Target site resistance could occur from changes at the biochemical site of action of one herbicide. Non target site resistance occurs through mechanisms which reduce the number of herbicide molecules that reach the herbicide target site. There are currently 480 unique cases (species × site of action) of herbicide resistance globally in 252 plant species (145 dicots and 105 monocots). To date, resistance in weeds has been reported to 161 different herbicides, involving 23 of the 26 known herbicide sites of action. Finally, it can be concluded that we can protect crops associated to herbicide resistant weeds by applications of biochemical, genetic and crop control strategies.

Keywords: non-target site resistance, resistance mechanisms, target site resistance

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Introduction

According to the WSSA (1998), herbicide resistance is “the inherited ability of a plant to survive and reproduce following exposure to a dose of herbicide normally lethal to the wild type”. In a plant, resistance may be naturally occurring or induced by such techniques as genetic engineering or selection of variants produced by tissue culture or mutagenesis”. HRAC (2015) also defined herbicide resistance as “naturally occurring inheritable ability of some weed biotypes within a given weed population to survive a herbicide treatment that should, under normal use conditions, effectively control that weed population”.

Resistance can occur in plants as random and infrequent mutations. Herbicides generally control susceptible plants by binding proteins essential for the development of weeds, which leads to plant death (Nam and Kim, 2015). Several mechanisms in plants can cause herbicide resistance (Bayer CropScience, 2015). On a population level, organisms can have slight mutations in their

genes, whereas, some of these are lethal to the individual, some are beneficial, and some are neutral. Occasionally, the target site of a herbicide can be affected by one of these chance mutations (Bardley et al., 2014).

Through selection, where the applied herbicide is the selection pressure, susceptible plants are killed while herbicide-resistant plants can survive to reproduce without competition with the herbicide-susceptible plants. If the herbicide is continually used, resistant plants successfully reproduce and become dominant in the population. Consequently, evolution of herbicide resistance will increase in a population. Still, depending on the initial frequency of the resistance gene in the population, the reproductive ability of the weed, and the level of competition, it may take several generations for the resistance problem to become apparent.

Herbicide resistant weeds are a global and growing problem (e.g. number of cases, resistant species, etc.) (Table 1 and 2). Although herbicide resistance was reported as early as 1957 against 2,4-D from Hawaii (Bhatti et al., 2013), the first report of herbicide resistance was confirmed in triazine herbicide resistant common groundsel (*Senecio vulgaris*) by Ryan (1970). Since then, in the last four decades, there has been many reports confirming resistance to other herbicides. In recent years, the incidence of herbicide resistance in plants has been rising exponentially compared to that of insecticide or fungicide resistance occurring in insect or fungus populations, respectively (Bhatti

Table 1. The most important herbicide resistant weed species worldwide (Source: Heap, 2017).

Scientific Name	Common name	Number of sites of action
Lolium rigidum	Ryegrass	11
Echinochloa crus-galli var. *crus-galli*	Banyard grass	10
Poa annua	Annual bluegrass	9
Alopecurus myosuroides	Black grass or twitch grass	7
Eleusine indica	Goosegrass	7
Amaranthus palmeri	Pigweed	6
Lolium perenne ssp. *multiflorum*	Italian ryegrass	6
Amaranthus hybridus	Smooth pigweed	6
Ambrosia artemisiifolia	Annual regweed	5
Avena fatua	Common wild oat	5
Conyza canadensis	Fleabane or horseweed	5
Kochia scoparia	Ragweed	5
Raphanus raphanistrum	Wild radish or jointed charlock	5

Table 2. Occurrence of worldwide herbicide resistance (Source: Valverde and Greesel, 2006).

Herbicide	Year of resistance found	Year of reporting
2,4-D	1945	1963
Dalapon	1953	1962
Atrazine	1958	1988
Picloram	1963	1973
Trifluralin	1963	1982
Diclofop	1977	1982
Trialate	1962	1987
Chlorsufuron	1982	1987
Glyphsate	2003	2006

et al., 2013) (Fig. 1). There are currently 480 unique cases (species × site of action) of herbicide resistance globally in 252 species (145 dicots and 105 monocots) (Fig. 2). Weeds have developed resistance to 23 of the 26 known herbicide sites of action and to 161 different herbicides (Heap, 2017) (Fig. 3).

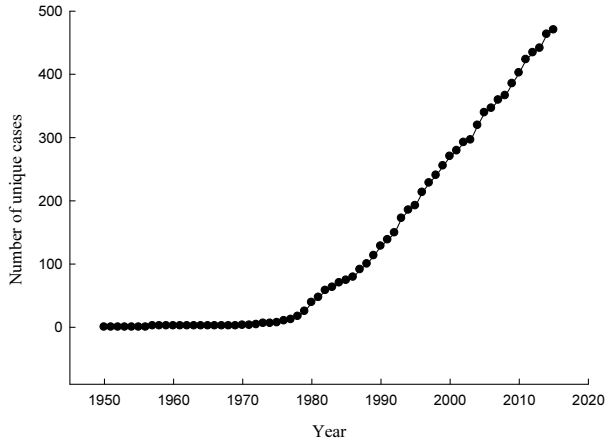

Fig. 1. Increase in herbicide resistant weed species by year (Source: Heap, 2016).

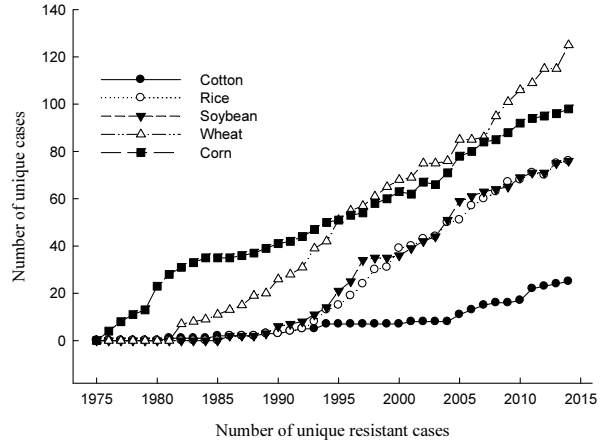

Fig. 2. Increase in herbicide resistant weed species by selected crops (Source: Heap, 2016).

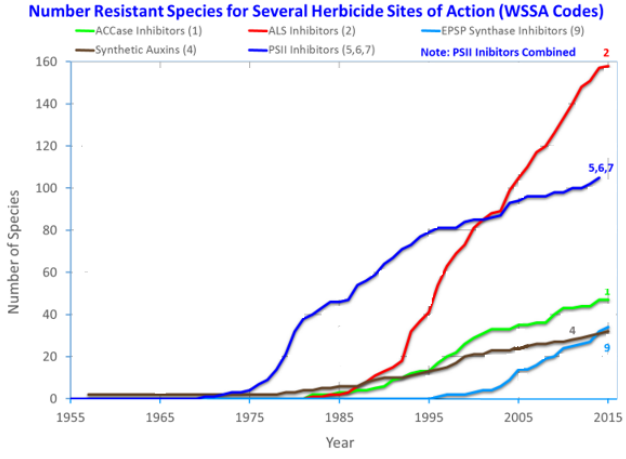

Fig. 3. Increase in resistant weed species according to sites of herbicidal action (Source: Heap, 2016).

The article aims to summarize the current state of understanding on herbicide resistance, identify significant gaps in the research, and possibly presume where future research on herbicide resistance may be headed.

Types of herbicide resistance

Herbicides attack one or more locations in a weed species. These locations can be enzyme proteins, non-enzyme proteins, cell division mechanism, etc., which are defined as 'sites of action'. Powles and Yu (2010) mentioned that herbicide resistance is an evolutionary process that strongly depends on genetic factors (frequency and number of resistant genes, mechanisms of inheritance, fitness costs associated with resistant alleles), weed species (self- or cross-pollination, pollen movement, seed production, dispersion, longevity), herbicide (chemistry, mode of action, residual activity), and operation factors (herbicide dose, environmental variables). In general, weed populations have the ability to develop resistance to one or more herbicide active ingredients. One way of classifying herbicide resistance is based on the mode of action represented by the biochemical mechanism by which an active ingredient affects the target plant (Kim et al., 2015).

Herbicide cross resistance

Cross-resistance occurs when a plant is resistant to one class of herbicide within one group or several herbicide classes within one group. The resistant biotype has evolved by selection pressure from herbicides attacking acetolactate synthase (ALS) that will be resistant to all herbicides and act on a particular site (Vargas and Wright, 2004). For example, after the extensive use of herbicide A in a field, a weed biotype could evolve to become resistant to herbicide A but is found also to be resistant to herbicide B, although herbicide B was never used in that field (Won et al., 2015a).

The phenomenon of cross resistance is important for both practical and scientific reasons. If cross resistance to a range of herbicides limits weed control options, agricultural producers and agrochemical manufacturers can experience substantial economic loss and other problems. Unravelling the biochemical and genetic basis of cross resistance and implementing sustainable weed control programs are important scientific challenges (Powles and Preston, 2016).

Herbicide multiple resistance

The mechanism of multiple resistance is due to changes at the site of herbicide action. It refers to a weed biotype that has developed mechanisms of resistance to multiple modes or sites of action of herbicide [e.g. ALS-inhibitors and acetyl-CoA carboxylase (ACCase)-inhibitors] and for which this resistance was brought-on by separate selection processes (Won et al., 2015b). For example, if a weed biotype develops resistance to herbicide A, after herbicide B is used in the same field and the biotype develops resistance to herbicide B. The plant is now resistant to herbicides A and B through two separate selection processes.

An individual plant (or a population) possesses two or more different resistance mechanisms which provide resistance to a single herbicide or different classes of herbicides. The most complicated situations in which weeds are difficult to control may be those where multiple resistance mechanisms involving both target site and non-target site resistance mechanisms are occurring within the same individual or population (Powles and Preston, 2016).

Mechanisms of herbicide resistance

Mechanisms of herbicide resistance can be broadly grouped into two categories: target site resistance and non-target site resistance (Dekker and Duke, 1995). Herbicide resistance generally includes diverse mechanisms that utilize changes in biochemical processes within weed plants, for example, changes to exterior structures, and changes to germination period. Target site mutation and enhanced metabolism in non-target site resistance are the most commonly encountered mechanisms (Kwon et al., 2015). It is currently believed that non-target site resistance mechanisms involve multiple genes (Table 3).

Table 3. Diversity of selected herbicide resistance mechanisms (Source: Bayer CropScience, 2015).

Resistant class	Mechanism
Target-site	Target-site mutation
	Increased gene copy number
	Enzyme overexpression
Non target-site	Enhanced metabolism
	Differential uptake
	Differential redistribution
	Sequestration
	Delayed germination
	Rapid necrosis/defoliation

Target site resistance

Target-site resistance occurs when the target enzyme of a herbicide becomes less sensitive or insensitive to the herbicide. The loss of sensitivity is usually associated with a gene-coding mutation for a protein, which can lead to conformational changes in the structure of the protein. The physiological changes can impair the ability of herbicides to attach to the specific binding site of the enzyme, reducing or eliminating the herbicidal activity (Hanson et al., 2013). In short, target site resistance refers to a structural change to the binding site of herbicide molecule to confer resistance or when the target site is overexpressed through gene amplification (Delye et al., 2013).

a) Resistance to acetolactate synthase inhibiting herbicides

Over the past decades, the most important field of study in herbicide chemistry has been that of ALS inhibiting herbicides. There are 15 chemical classes of herbicides which have been described as inhibitors of ALS. Of these, sulfonylurea, imidazolinone, and triazolopyrimidine herbicides have been commercially used worldwide (Saari et al., 1994).

ALS is a key enzyme in the biosynthesis of branched chain amino acids leucine, valine, and isoleucine in plants (Fig. 4). The Inhibition of ALS causes rapid growth cessation in susceptible species. ALS inhibitors have been widely used since the early 1980s. Their extensive use has led to the evolution of resistance in many weed species because ALS herbicides have the ability to control a broad spectrum of weed species at very low application rates.

Target site-based ALS resistance is due to point mutations that occur within discrete conserved domains of the ALS gene. Most resistance mutations occur with two additional substitutions, Phe116Leu and Phe149Ser, in the resistant biotype of greater beggarticks which were not reported in herbicide resistant ALS gene (Boutsalis et al., 1999).

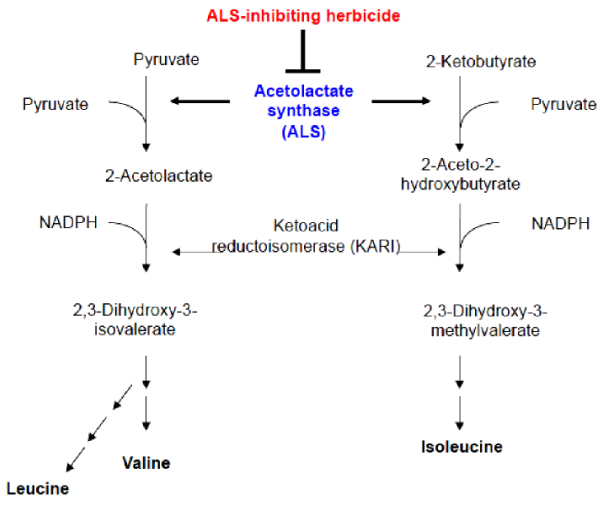

Fig. 4. ALS is a primary target site of action for at least four structurally distinct classes of herbicides. ALS is under feedback regulation by valine, leucine, and isoleucine (Source: Endo et al., 2013).

Recently, Powles and Preston (2016) examined ALS gene sequences from resistant biotypes of higher plants that showed a substitution at a proline residue (173) in a highly-conserved region of the enzyme known as 'domain A'. No alteration was observed in domain A of ALS for a resistant biotype of *Salsola iberica*. However, the proline substitutions vary in the substitutions of threonine, alanine, serine, histidine, and glutamine. Guttieri et al. (1992) stated that ALS from three resistant weed species and observed Thr substitution in *Kochia scoparia* and a His substitution in *Lactuca serriola* at Pro 173. Moreover, a biotype of *Xanthium strumarium* was highly resistant to imidazolinone herbicides but was not cross resistant to sulfonylurea or triazolopyrimidine herbicides. Therefore, there must be several possible mutations of the ALS gene, which confer resistance to sulfonylurea and imidazolinone herbicides and yet retain enzyme function. The variations in target site resistance among herbicide-resistant mutants indicate that the binding domains for the various classes of ALS-inhibiting herbicides do not fully overlap (Powles and Preston, 2016).

b) Resistance to acetyl-CoA carboxylase inhibiting herbicides

During the 1970s and 1980s, two chemically dissimilar herbicide groups, the aryloxyphenoxypropionic acid (APP) and cyclohexanedione (CHD) herbicides, which target the plastid enzyme acetyl-CoA carboxylase (ACCase), were commercially developed and widely applied (Devine and Shimabukuro, 1994).

ACCase catalyzes a two-step condensation of acetyl-CoA with bicarbonate to form malonyl-CoA. In the first step, biotinylated enzyme is carboxylated in the presence of bicarbonate and ATP. In the second step, the carboxyl group is transferred to acetyl-CoA to form malonyl-CoA by the carboxylated enzyme (Devine and Shukla, 2000). ACCase is a biotinylated, multifunctional protein located in the stroma of plastids. It catalyzes the ATP carboxylation of ACCase to form malonyl CoA that is the precursor of fatty acids (Fig. 5).

These herbicides are lethal to many Graminaceae but harmless to dicot species. Dicot plastids contain the prokaryotic form of ACCase which is resistant to APP and CHD herbicides. Monocots lack the prokaryotic form due to the loss of *accD* gene in chloroplast genome. The absence of prokaryote form of ACCase and loss of *accD* gene induce herbicide sensitivity (Konishi and Sasaki, 1994).

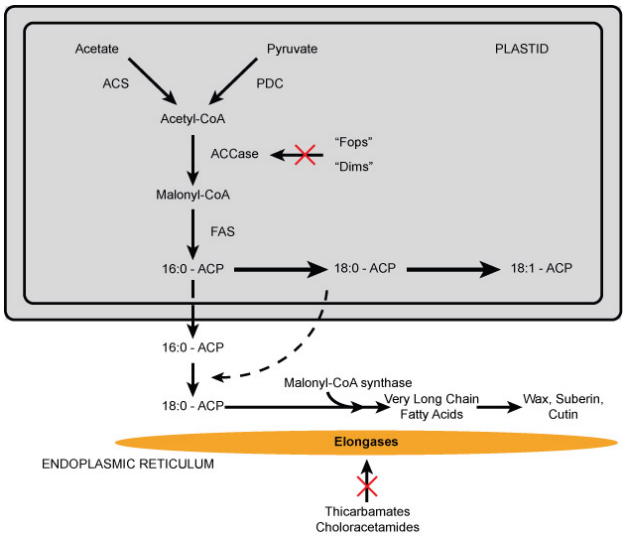

Fig. 5. Diagram of fatty acid synthesis and elongation in higher plants (ACCase-acetyl-CoA carboxylase, ACP-acyl carrier protein, ACS-acetyl-CoA synthase, CoA-coenzyme A, dims-cyclohexanedione inhibitors, FAS-fatty acid synthase, fops-aryloxyphenoxy propionate inhibitors, PDC-pyruvate dehydrogenase complex (Source: Gronwald, 1992).

Following extensive use of ACCase-inhibiting herbicides, resistance to these graminicides has become widespread and been reported worldwide, e.g., *Lolium rigidum* in Australia, *L. multiflorum* in Oregon, and wild oats (*Avena* spp.) in Australia and N. America (Devine and Shimabukuro, 1994).

Resistance to APP and CHD herbicides is due to an alteration in the target enzyme, making it less sensitive to inhibition by these herbicides. In *L. rigidum*, repeated use of either an APP herbicide or a CHD herbicide has led to target site resistance to both the APP and CHD herbicides; however, in both cases, the level of resistance to APP was greater than to CHD. A biotype of *L. multiflorum*, resistant to APP herbicides, showed no target site resistance to the CHD herbicides (Gronwald et al., 1992). Resistance to APP herbicides in the wild oat species *A. fatua* and *A. sterilis* is endowed by resistant forms of the ACCase enzyme (Maneechote et al., 1994).

Grasses have two ACCase genes to code for cytosolic and plastidic forms of enzyme (Park et al., 2016a). The plastidic form is the target of APP and CHD herbicides. APP and CHD herbicides induce a rapid depolarisation of plant cell membrane potentials by allowing the influx of protons. Cells from root tips and coleoptiles of some biotypes of *L. rigidum* resistant to APP and CHD herbicides are able to reestablish the membrane potential following removal of the herbicides from the bathing solution (Shimabukuro and Hoffer, 1992). This ability to repolarise the membrane potential following removal of the herbicide is not observed in susceptible biotypes. Repolarisation is pH-dependent in susceptible biotypes (Holtum et al., 1994).

A point mutation has been identified in the ACCase-resistant grasses, *Setaria viridis*, in which the substitution of leucine for isoleucine in the chloroplastic ACCase at position 1781 provided resistance to sethoxydim (CHD herbicide) (Yu et al., 2007). In addition, six other positions Trp 1999 Cys, Trp 2027 Cys, Ile 2041 Asn, Asp 2078 Gly, Cys 2088 Arg, and Gly 2096 Ala have been reported to ACCase target point mutations in different grass weed species (Delye, 2005). However, point mutation of Ile to Leu is most common and causes resistance to mainly all ACCase inhibiting herbicides (Powles and Yu, 2010). The Trp 2027 Cys, Ile 2041 Asn and Gly 2096 Ala mutations confer resistance only to AOPP herbicides. The Asp 2078 Gly mutation confers resistance to many AOPP and CHD

herbicides including clethodim. The Trp 1999 Cys mutation confers resistance only to AOPP herbicide fenoxaprop (Liu et al., 2007).

c) Resistance to photosystem II inhibiting herbicides

Numerous chemically dissimilar herbicide classes act by inhibiting photosynthetic electron transfer at photosystem II (PS II) (Lim et al., 2016). The triazine and substituted urea herbicide groups are toxic to plants because they are potent and specific inhibitors of photosynthesis at PS II. Triazine and phenylurea herbicides can block the transfer of electrons from the electron donor (QA) to the mobile electron carrier (QB) (Sundby et al., 1993). They bind to the plastoquinone (PQ)-binding site of the D1 protein in PS II reaction of the photosynthetic electron transport chain.

PS II inhibiting herbicides binding to D1 protein inhibit electron transport with two major consequences: (1) a shortage of reduced $NADP^+$ which is necessary for CO_2 fixation and (2) formation of free radicals (H_2O_2, OH^-, Chl^3) which induce photooxidation of chlorophylls and unsaturated lipid in chloroplast (Devine and Shukla, 2000).

In maize production in many parts of the world, triazine herbicides were persistently used for weed control which led to widespread resistance of target weeds (Ryan, 1970). Triazine resistance is due to target site resistance endowed by a modification at the herbicide target site, D1 protein of PSII (Park et al., 2016b). Biotypes that are highly resistant to triazine herbicides as a result of a modified D1 protein cannot be resistant to chemically distinct substituted urea herbicides, despite the fact that the substituted urea herbicides are also potent PSII inhibitors (Gronwald, 1994).

In most cases, a Ser 264 mutation to Gly in the D1 protein is responsible for conferring resistance in weed biotypes (Trebst, 1991; Devine and Shukla, 2000) (Fig. 6). A Ser 264 Thr mutation has been reported recently in a resistant biotype of *Portulaca oleracea* at high level of resistance to atrazine and to linuron, a substituted urea herbicide (Devine and Shukla, 2000). Both mutations reduce disruption of the photosynthetic electron transport caused by PS II inhibiting herbicides.

Trebst (1991) demonstrated that amino acid changes between positions 211 and 275, from Phe 211 to Ser, Gly 256 to Asp, and Leu 275 to Phe, could confer herbicide resistance in many organisms. A range of mutations within the QB

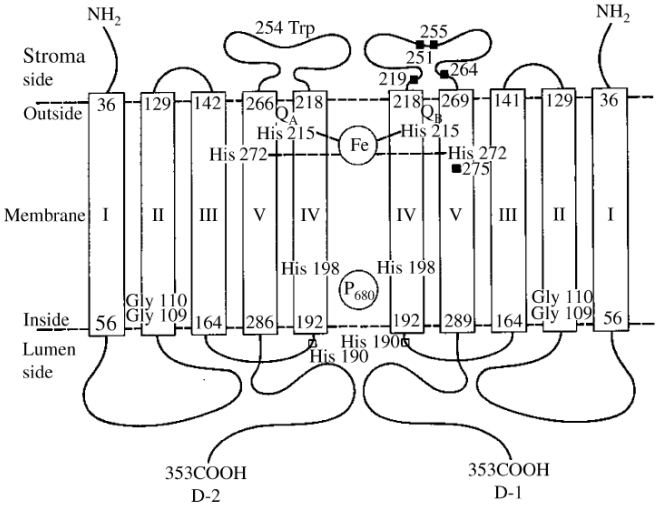

Fig. 6. Diagrammatic explanation of the D1/D2 protein complex in photosystem II. D1 mutation sites concerning resistance are represented by solid squares (Source: Devine and Shukla, 2000).

binding site of the D1 protein providing resistance to triazine herbicides have been identified in unicellular algae such as *Chlamydomonas*, *Euglena*, *Synechocystis*, and *Synechococcus*. Although various mutations have been identified in lower plants, mutation in higher plants has only been identified on position 264 Ser in triazine-resistant weed species. And, susceptibility to the PS II inhibitors may be due to an alternation in the D1 polypeptide subunit of PS II.

d) Resistance to 5-enolpyruvylshikimate-3-phosphate synthase inhibiting herbicides

The herbicidal effects of glyphosate are due to the inhibition of the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), an enzyme from the shikimate pathway, which leads to prevention of the biosynthesis of the amino acids phenylalanine, tyrosine, and tryptophan (Fig. 7).

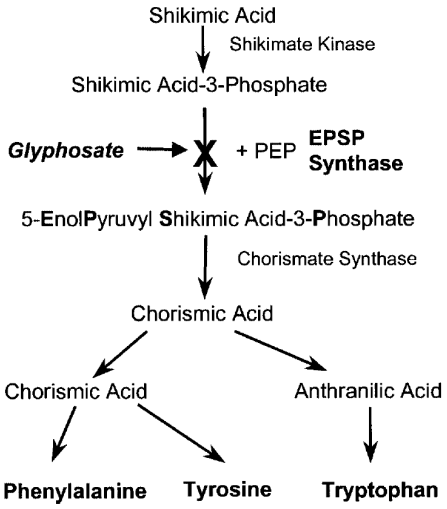

Fig. 7. Glyphosate mode of action (Source: Dill, 2005).

The EPSPS gene in plants contains coding sequence for a transit peptide used to direct the protein to the chloroplast. The transit peptide, variable in sequence and length among different species, is cleaved upon chloroplast delivery, producing the mature EPSPS protein.

Reported mutations conferring glyphosate resistance in weeds change the hydrophobic Pro106 amino acid of EPSPS to the hydrophobic amino acids Ala or Leu, or the hydrophilic amino acids Ser or Thr. The Pro106 codon (CCx) can mutate to the commonly reported Ser, Ala, and Thr through substitutions at the first base of the codon (TCx, GCx, and ACx, respectively). Substitutions at the second base of the codon can produce Leu (CTx), Arg (CGx), Gln (CAA/G), or His (CAC/TT). Pro106Arg, Gln, and His mutations have not been reported to date. While Gln is hydrophilic, both Arg and His are positively charged and may be disruptive to the active site. EPSPS target-site mutations have been reported in six species, most frequently in the genus *Lolium*, including *L. rigidum* and *L. multiflorum* (Sammons and Gaines, 2014).

Glyphosate resistance resulting from amplification of EPSPS gene, leads to increased levels of transcript production and EPSPS activity. Consequently, sufficient EPSPS is produced to titrate out the glyphosate. In some cases, overexpression is lost when the selection pressure is changed or when plants are regenerated (Devine and Shukla, 2000).

Non target site resistance

Non target site resistance is associated with physiological mechanisms aimed at reducing the amount of herbicide reaching the target site (Im et al., 2016). These mechanisms mainly consist of decreased rates of herbicide penetration and herbicide translocation, and also an increased rate of herbicide sequestration or metabolism. Enhanced metabolization of herbicidal compounds enables the majority of non-target site resistance cases (Powles and Yu, 2010).

Non target herbicide resistance can be induced by a plant detoxification process that follows four phases (Yuan et al., 2006) (Fig. 8). Phase 1 is detoxification in which certain functional groups can be exposed by activating herbicide molecules for phase 2 enzymes. Oxidation is a typical phase 1 detoxification reaction which can be carried out by P450 monooxygenases or mixed function oxidases. Phase 2 detoxification includes conjugation of a bulky hydrophilic molecule to the activated xenobiotic. Phase 3 detoxification consists of transporting the conjugated molecule into the vacuole or extracellular space. ABC transporter genes are the most common transporters in phase 3. Phase 4 detoxification is the degradation of the conjugated molecule in the vacuole or extracellular spaces (Oh et al., 2016).

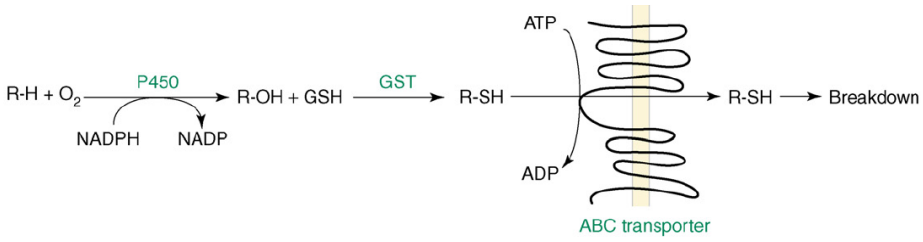

Fig. 8. P450, GST, glycosyltransferase and ABC transporter gene-encoded resistance activities. There is a four-step detoxification process: the monooxygenase activity for P450 genes, the GST conjugation reaction for GST genes, the ATP-dependent transport of small molecules via ABC transporters, and subsequent detoxification in vaculoes (Source: Yuan et al., 2006).

a) Cytochrome P450 monooxygenases

Recent studies on enzymes revealed that herbicide resistance in non-target sites is associated with cytochrome P450 monooxygenases (Cyt P450) which increases the rate of metabolisms and also have the capacity to either de-alkylate or ring-hydroxylate these herbicides. Control of such non-target site resistant weed populations can be difficult with herbicides because Cyt P450 enzymes are able to detoxify a wide range of herbicidal compounds *in vitro* (Moreland et al., 1993).

An increase in metabolism due to the involvement of Cyt P450 was first found in non-target site based P450 mediated herbicide resistance in *L. rigidum* biotypes in Australia and phenyl urea resistant *Phalaris minor* in Asia (Werck-Reichhart et al., 2000).

Cyt P450 is a monooxygenase that inserts one atom of oxygen into inert hydrophobic molecules to transform them into more reactive P450 and helps plants to combat harmful chemicals by converting them into less phytotoxic compounds. P450 substrates and P450 reductases bond to endoplasmic reticulum via N-terminal region. P450 reductases channel electrons from NADH to P450 protein by transferring them from FAD to FMN (Werck-Peichhart et al., 2000) (Fig. 9).

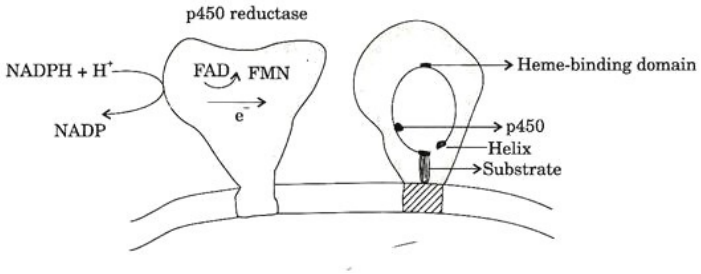

Fig. 9. Structure and nomenclature of plant cytochromes P450 (Source: Werck-Peichhart et al., 2000).

b) Glutathione S-transferases

Glutathione S-transferases (GSTs) are multifunctional enzymes which catalyze the conjugation of glutathione to various substrates to form a polar S-glutothionylated product (R-SG) (Fig. 8). GSTs are important detoxification components in phase 2 detoxification because substrates are often hydrophobic and electrophilic toxic chemicals. GST genes allow to detoxify a wide range of chemicals (Yuan et al., 2006). Kissoudis et al (2015) indicated that in metabolismics analysis of WT tobacco plants, alachlor toxicity translated an abiotic stress response accompanied by down regualtion of primary metabolism precursors. GmGSTU4 overexpression leads to greater induction of protective compounds and detoxification of the secondary metabolism (Fig. 10). Functional characteristics of GST genes in crops described that GSTs related with herbicide metabolism. Recently, comparative analysis of rice genomic sequences with maize and wheat GSTs led to product of rice GST gene had activity toward chloroacetanilide herbicides. A transgenic approach has been useful to study the overexpression of GST genes to confer herbicide resistance (Yuan et al., 2006).

GST activity was studied by using a model substrate (1-chloro-2,4-dinitrobenzene) where conjugation of GST with substrates can be detected by light absorbance. Correlations between herbicide resistance in weed and GST activity were revealed in velvetleaf (*Abutilon theophrasti*), in which increased glutathione was found in association with

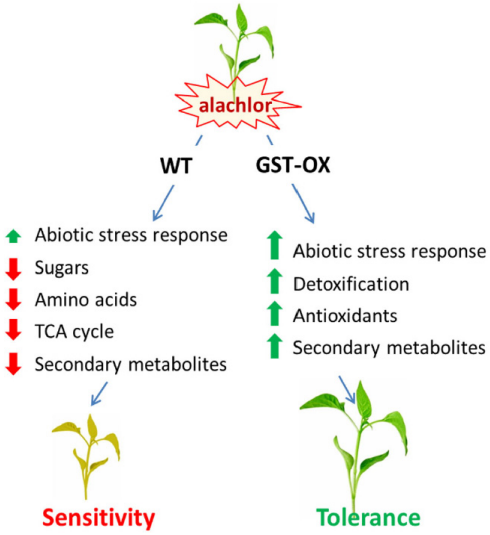

Fig. 10. The differential metabolic regulation of WT and GST-OX tobacco plants underlying the increased tolerance to alachor after GmGSTU4 overexpression in GST-OX plants (Source: Kissoudis et al., 2015).

herbicide resistance (Anderson and Gronwald, 1991). In some cases, increasing GST activity is accompanied by increasing GST gene expression. Functional characterizations of GST genes in crops point out GSTs have a role in herbicide metabolism. Currently, comparative analysis of rice genomic sequences with maize and wheat GSTs led to the molecular cloning of rice GST gene. The transgenic approach has been useful to study the overexpression of GST genes to confer herbicide resistance (Cho and Kong, 2005).

c) ABC transporter genes

In the biochemical modification of herbicide through metabolism, ABC transporter is involved in herbicide resistance in compartmenting the herbicide and its metabolites. Also, ABC transporter can be involved in phase 3 detoxification. The ABC transporter can be associated to membrane and targeted by one or two transports of molecules may be dependent on ATP hydrolysis (Fig. 8). It serves in a wide range of functions including sequestration of secondary metabolites, translocation of fatty acids, and phospholipids, excretion of toxic compounds, transport of chlorophyll catabolites, as well as cell homeostasis (Schulz and Kolukisaglu, 2006).

Plant ABC proteins play an important role not only in the transport of hormones, lipids, metals, and secondary metabolites, but also contribute to plant-pathogen interactions, modulation of ion channels, and removal of certain molecules such as xenobiotics and other toxic compounds out of cells (Tani et al., 2015).

Since 1993, it has been shown that ABC transporters could transport glutathionate-conjugated chemicals. AtMRP1 gene of *Arabidopsis* which was characterized as a ABC transporter gene, was found to be functionally involved in the removal of the GS-conjugated herbicide metolachlor (Yuan et al., 2006).

Experiments indicated that glyphosate upregulates ABC transporters in the several *Conyza canadensis* resistant biotypes (Yuan et al., 2006). It was also documented recently that ABC transporters could sequestrate glyphosate into vacuoles, rendering it harmless (Shaner, 2009). More direct evidence of ABC transporter-mediated herbicide resistance comes from genetic engineering experiments. Overexpression of AtPgp1, a multi-drug-resistant resistance gene, or the garden pea homolog psNTP9 were shown conferring multi herbicide resistance in *Arabidopsis* (Windsor et al., 2003). Beside herbicide resistance, kanamycin resistance has also been found in transgenic plants overexpressing an ABC transporter gene (Mentewab and Stewart, 2005).

Conclusion

Synthetic herbicides have been used to control weeds globally. Herbicide resistance in weeds is a product of evolution in cultivated fields, responding to the selection pressure laid by the use of such herbicides. The diversity of herbicide resistance mechanisms observed vary rapidly currently. The study of herbicide resistance can help demonstrate how plants release biological defenses. Also, fundamental research on the mechanistic and genetic basis of resistance must contribute to search for processes concerning the evolutionary path of herbicide resistant weeds while stewarding the available herbicides and herbicide resistant crop technologies. An improved technology and more integrated understanding of resistance will be the key to manage in facing the herbicide resistance challenge.

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