Chapter 10

Herbicide Metabolism in Weeds — Selectivity and Herbicide Resistance

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/61674

Abstract

The metabolic detoxication/bioactivation pathways, the levels and activity of enzymes, and endogenous cofactors mediating these reactions in crops have been well documented; however, much less evidence has been accumulated in weed species. The herbicide metabolism as a selectivity factor is summarized with special attention to acetyl-CoA carboxylases (ACCase)-inhibiting aryloxyphenoxypropionate, protoporphyrinogen IX oxidase (PPO) inhibitor, carotenoid biosynthesis inhibitor clomazone, and acetolactate synthase (ALS) inhibitor imidazolinone and sulfonylurea herbicides in various weed species. The metabolism-based herbicide resistance related to these herbicide classes is also discussed along with the role and level of metabolizing enzymes and cofactors in weed species.

Keywords: Herbicide, metabolism, selectivity, resistance, weed species

1. Introduction

Metabolism, or biotransformation of herbicides, resulting in detoxication or bioactivation of the parent molecules, is a major factor in herbicide resistance and selectivity in plants. Selectivity, the principal basis of herbicide usage, is influenced by many factors such as application methods, differential absorption, translocation, sequestration in plants, and, at subcellular levels, differences in active site sensitivity, as well as rate of metabolism. Among the factors affecting the active internal concentration of the herbicide, the rate of metabolism seems to be of major importance in the selective action, which, in turn, depends on the activity of detoxifying enzymes and concentration of endogenous substrates. Plants metabolize herbicides through various intermediates, mostly to more polar products and insoluble bound residues. The metabolism of herbicides may occur as a three-phase process in plants. Phase I is primary metabolism to convert biologically active molecules into less active compounds

(detoxication) but occasionally into more phytotoxic metabolites (bioactivation). Phase I reactions include oxidation, reduction, and hydrolysis and yield phenolic, *N*-demethylated, carboxylic acid compounds. In phase II reactions, phase I products are converted to even less toxic water-soluble conjugates by glycosyl, glutathione, or amino acid conjugation. In phase III metabolism, conjugates from phase II are transformed to practically nontoxic secondary conjugates or insoluble bound residues.

Much is known about herbicide metabolism in crop plants and the effect of biotransformation products on the biological activity. Metabolism that confers herbicide tolerance in crops also occurs in weeds. Metabolic pathways and rates in both crops and weeds must often be considered together to understand the metabolic basis for crop selectivity. The metabolic detoxication/bioactivation pathways, the levels and activity of enzymes, and the endogenous cofactors mediating these reactions in crops have been well documented [1–3]; however, much less evidence has been accumulated in weed species. On the other hand, repeated use of herbicides with similar chemistry may lead to the selection of herbicide-resistant biotypes with an enhanced capacity to degrade herbicides. Weed species that have evolved resistance to herbicides due to enhanced metabolic capacity have been a major issue [4]. Target-site resistance develops by mutation within a gene coding for an herbicide target-site enzyme or by overproduction of the target enzyme. Non-target-site resistance involves mechanisms that minimize the amount of herbicidally active molecule reaching the target site by reduced uptake and translocation, increased sequestration, and enhanced metabolism.

This chapter provides an overview of herbicide metabolism in weeds as a selectivity factor with special attention to ACCase-inhibiting aryloxyphenoxypropionate, protoporphyrinogen IX oxidase (PPO or protox) inhibitor, carotenoid biosynthesis inhibitory clomazone, and acetolactate synthase (ALS) inhibitor imidazolinone and sulfonylurea herbicides. Moreover, the metabolism-based herbicide resistance is also examined with the abovementioned chemistry of herbicides. Finally, the role and level of metabolizing enzymes and cofactors in weed species are discussed.

2. Metabolism and selectivity of ACCase inhibitor aryloxyphenoxypropionate herbicides in weed species

Aryloxyphenoxypropionates such as diclofop-methyl, fenoxaprop-ethyl, fluazifop-butyl, haloxyfop-methyl, and quizalofop-ethyl are highly selective postemergence herbicides for the control of graminaceous weeds. These herbicides are known inhibitors of the acetyl-CoA carboxylases (ACCase) which are crucial for the biosynthesis of fatty acids catalyzing the production of malonyl-CoA from acetyl-CoA and CO_2 [5].

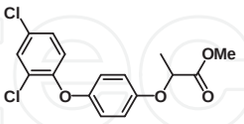
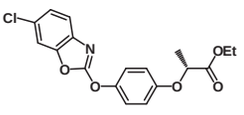
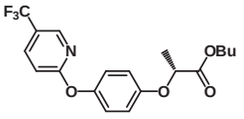
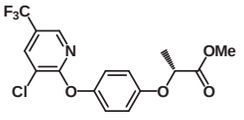
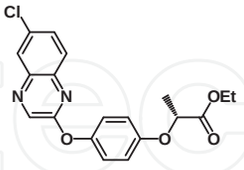
Diclofop-methyl selectivity between tolerant wheat and susceptible wild oat (*Avena fatua*) may be a function of its placement on the plant and the rate of herbicide metabolism, but the ability of wheat to detoxify the herbicide by aryl hydroxylation was found as the primary selective factor [6]. Diclofop-methyl was hydrolyzed rapidly to diclofop acid in both species (Table 1). Neither compound accumulated in the tissues of either species. The major reactions in wheat are the aromatic ring hydroxylation of the 2,4-dichloro-phenyl moiety of the herbicide,

http://dx.doi.org/10.5772/61674

followed by conjugation to form an acidic aryl glycoside. Metabolism of diclofop acid in wheat is catalyzed by cytochrome P450-dependent hydroxylase [7]. In wild oat, a carbohydrate conjugation of the carboxylic group in the diclofop produced a neutral glycosyl ester. The sugar moiety was not characterized positively in either conjugate. The fate of foliarly applied diclofop-methyl was determined in intact plants of barnyardgrass (*Echinochloa crus-galli*), a susceptible grass, proso millet (*Panicum miliaceum*), a moderately susceptible grass, and longspine sandbur (*Cenchrus longispinus*), a tolerant grass [8]. Plant extracts contained diclofop-methyl, diclofop, and unknown water-soluble conjugates. The amounts of water-soluble metabolites were consistent with the tolerance of these species to the herbicide. The ratio of unhydrolyzed diclofop-methyl to diclofop was higher in sensitive species except for tolerant soybeans, indicating that soybeans may possess an additional mechanism or mechanisms for detoxication. The results support the hypothesis that differential metabolism provides a basis for selectivity to foliarly applied diclofop-methyl.

Following widespread applications of ACCase-inhibiting herbicides, resistance to these graminicides developed [4]. In cereal and leguminous grain crop areas of South Australia, a large number of populations of annual ryegrass (*Lolium rigidum*) have developed resistance to diclofop-methyl following selection with this herbicide. However, several diclofop-resistant biotypes also exhibit resistance to various herbicide chemistries such as the aryloxyphenoxy-propionate and cyclohexanedione graminicides, the sulfonylurea herbicides, the dinitroaniline type trifluralin, and, to a lesser extent, the triazinone metribuzin. Mechanism of resistance to the postemergent graminicide diclofop-methyl was corroborated using resistant (SLR 31) and susceptible (SLR2) biotypes of rigid ryegrass (*Lolium rigidum*) [9]. In both biotypes, diclofop-methyl was rapidly demethylated to the herbicidally active metabolite diclofop acid, which, in turn, was metabolized to ester and aryl-*O*-sugar conjugates. Resistant plants had a slightly greater capacity to form inactive sugar conjugates. Despite these differences, resistant plants retained 20% of the herbicidally active diclofop acid 8 days after treatment (DAT) (Table 1), whereas susceptible plants, which were almost lethally injured, retained 10% more diclofop acid. The small differences in the amount of the active and inactive metabolites are unlikely to account for a 30-fold difference in sensitivity to the herbicide at the whole-plant level. The diclofop-related physiological and biochemical differences between susceptible ryegrass biotype SLR 2 and resistant ryegrass biotype SLR 31 seem to be their differential abilities to recover membrane polarization, the higher portion of diclofop acid in shoots of susceptible plants, and a higher capacity of shoots of resistant plants to form conjugated metabolites. Target site-based resistance is the most commonly reported mechanism of resistance to the ACCase-inhibiting herbicides [10]. A resistant VLR 69 biotype of *Lolium rigidum*, resistant to members of at least nine herbicide classes with five mode of action, and a susceptible biotype, VLR 1 with no history of herbicide application, were used to clarify mechanisms responsible for diclofop-methyl resistance. It was found that in addition to enhanced metabolism of PS II-, ALS-, and ACCase-inhibiting herbicides, VLR 69 contains an ACCase that is insensitive to the aryloxyphenoxypropanoate herbicides. This enzyme is between 4- and 29-fold resistant to the aryloxyphenoxypropanoate herbicides, but showed no resistance to sethoxydim and tralkoxydim of ACCase inhibitory cyclohexanedione herbicides. In addition to possessing a resistant ACCase, the resistant biotype shows enhanced metabolism of diclofop-methyl. The susceptible biotype had metabolized 51% of the herbicide to products other than diclofop acid 48 hours

after treatment (HAT), whereas the resistant biotype had metabolized 62% of the herbicide (Table 1).

Herbicide	Structure	% of metabolized herbicide (% of acid form)	Weed species	Ref.
Diclofop-methyl		97 (20) 1 DAT	*Avena fatua*	[6]
		53 (28) 1 DAT	*Ecbinocbloa crus-galli*	[8]
		52 (20) 1 DAT	*Panicum miliaceum*	
		74 (13) 1 DAT	*Cencbrus longispinus*	
		97 (30) 8 DAT	*Lolium rigidum*	[9]
		95 (20) 8 DAT	biotype SLR 2a	
			biotype SLR 31b	
		62 (49)[c] 2 DAT	*Lolium rigidum*	[10]
		51 (38)[c] 2 DAT	biotype VLR 69d	
			biotype VLR 1e	
Fenoxaprop-ethyl		28 (n/a) 3 DAT	*Digitaria ischaenum*	[11]
		92 (85) 1 DAT	*Digitaria ischaenum*	[12]
		96 (35) 3 DAT	*Echinochloa phyllopogon*	[14, 15]
		96 (10) 3 DAT	susceptible biotype	
			resistant biotype	
Fluazifop-butyl		98 (73) 24 DAT	*Agropyron repens*	[16]
		90 (76) 10 HAT	*Digitaria sanguinalis*	[18]
		92 (63) 10 HAT	susceptible biotype	
			resistant biotype	
Haloxyfop-methyl		74 (25) 2 DAT	*Sorghum bicolor*	[19]
		80 (6) 2 DAT	*Setaria glauca*	
Quizalofop-ethyl		92 (38) 5 DAT	*Elytrigia repens*	[20]
		87 (42) 5 DAT	Biotype 2f	
			Biotype 10g	
		62 (29) 4 DAT	*Setaria glauca*	[21]

[a]Susceptible biotype.

[b]resistant to herbicides including diclofop-methyl, haloxyfop-methyl, haloxyfop-ethoxyethyl, fluazifop-butyl, quizalafop-ethyl, fenoxaprop-ethyl, trifluralin, alloxydim, sethoxydim, chlorsulfuron, metsulfuron methyl, and triasulfuron.

[c]% of diclofop-methyl plus diclofop acid in parenthesis.

[d]resistant to members of at least nine herbicide classes with five mode of action.

[e]susceptible biotype with no history of herbicide application.

[f]less sensitive on the basis of leaf chlorosis.

[g]sensitive on the basis of leaf chlorosis.

Table 1. Metabolism of aryloxyphenoxypropionate herbicides in weed species

http://dx.doi.org/10.5772/61674

Basis for sensitivity differences among small crabgrass (*Digitaria ischaemum*), oat, and wheat to fenoxaprop-ethyl may be due to differences in the metabolism of fenoxaprop-ethyl among these species [11]. Differential response of crabgrass and oat may be partially explained by differences in absorption and translocation. Metabolism studies indicated that roughly two-thirds of recovered radioactivity in wheat was bound to insoluble constituents or was converted to polar metabolites (Table 1). The amount of these fractions was found only 28% and 40% in crabgrass and oat, respectively. Both unextractable and polar metabolites represent detoxified forms of the parent herbicide. The metabolites proposed were the *O*-glucoside of hydroxy-6-chloro-2,3-dihydro-benzoxazol-2-one, hydroxy-6-chloro,2,3-dihydro-benzoxazol-2-one, and hydroxy-6-chloro-2,3-dihydro-benzoxazol-2-one. The results indicated that the primary selective action of fenoxaprop-ethyl may be due to differences in the metabolism of fenoxaprop-ethyl among crabgrass, oat, and wheat. In another attempt to reveal detoxification pathways of the fenoxaprop-ethyl in wheat, barley, oat, and crabgrass, *in vitro* metabolism studies with excised shoots were carried out [12]. The fenoxaprop-ethyl was rapidly hydrolyzed to fenoxaprop in all four species. However, in oat and crabgrass, the radioactivity remained mainly in the form of fenoxaprop, while in wheat and barley, fenoxaprop underwent rapid displacement of the phenyl group by glutathione (GSH) and/or cysteine resulting in production of *S*-(6-chlorobenzoxazole-2-yl)-glutathione (GSH conjugate), *S*-(6-chlorobenzoxazole-2-yl)-cysteine (cysteine conjugate), and 4-hydroxyphenoxy-propanoic acid. The GSH conjugate also may be catabolized to form *S*-(6-chlorobenzoxazole-2-yl)-cysteine (cysteine conjugate) which was subsequently metabolized to an unidentified metabolite which was speculated to be the *N*-glucoside of the cysteine conjugate (*S*-(6-chlorobenzoxazole-2-yl)-cysteine *N*-glucoside). 4-Hydroxyphenoxy-propionic acid was further metabolized to yield a glucoside conjugate, which upon hydrolysis with acid or β-glucosidase yielded 4-hydroxyphenoxy-propionic acid. The results indicate that GSH, cysteine, and glucose conjugation have a major role in the metabolic detoxification and selectivity mechanism of fenoxaprop-ethyl in grass species. Later, the same authors reported that the amounts of glutathione (GSH) and cysteine are higher in grass species that are moderately tolerant, such as wheat, and moderately susceptible, such as barley and triticale, to fenoxaprop-ethyl than in species that are very susceptible to the herbicide, such as oat, wild oat (*Avena fatua*), yellow foxtail (*Setaria glauca*), large crabgrass (*Digitaria sanguinalis*), and barnyardgrass (*Echinochloa crus-galli*) [13]. *In vitro* experiments at physiological pH demonstrated that fenoxaprop-ethyl may conjugate with GSH nonenzymatically. Therefore, the nonenzymatic conjugation of fenoxaprop-ethyl with glutathione may be an important mechanism for tolerance of some grasses to this herbicide.

The possible mechanism(s) of resistance to fenoxaprop-P-ethyl in late watergrass (*Echinochloa phyllopogon*), a noxious weed of rice, was examined by comparing the absorption, translocation, metabolism of fenoxaprop-ethyl and ACCase susceptibility to fenoxaprop acid (FA) in resistant (R) and susceptible (S) biotypes [14, 15]. Studies of the *in vitro* inhibition of ACCase minimized any differential active site sensitivity as the basis of resistance to fenoxaprop-ethyl. R biotype absorbed more herbicide differences between 3 and 48 h after application than S biotype, but no differences were found in the translocated amounts. Fenoxaprop-ethyl was rapidly de-esterified by hydrolysis in plants to yield FA, which is the active form of the parent compound, and is followed by the formation of water-soluble metabolites. The R biotype

produced 5-fold less FA and approximately 2-fold more nontoxic (polar) metabolites 48 hours after treatment than the S biotype (Table 1). The enhanced GSH and cysteine conjugation was considered as the major mechanism of resistance of the R biotype against fenoxaprop toxicity.

Only few details are available on metabolic fate of fluazifop-butyl in weed species. Fluazifop acid was the major metabolite in quackgrass *(Agropyron repens* = *Elymus repens*) plants treated with fluazifop-butyl, comprising 73% of the extractable radioactivity 24 days after treatment (DAT) [16]. Similarly, in *E. repens,* less than 25% of extractable radioactivity contained metabolites other than fluazifop and fluazifop acid 2 days after treatment [17].

A population of crabgrass (*Digitaria sanguinalis*) has evolved resistance to the herbicide fluazifop-P-butyl following treatment six times of this herbicide. The resistant biotype was found resistant to other aryloxyphenoxypropanoate herbicides such as haloxyfop-methyl and quizalofop-P-ethyl, and to a lesser extent to the cyclohexanedione herbicide sethoxydim, but was not resistant to clethodim [18]. ACCase enzymes extracted from plants of both resistant and susceptible biotypes were equally sensitive to both chemistries of herbicides. Absorption of fluazifop-butyl and translocation of the radiolabel from ^{14}C fluazifop-butyl were similar in plants of both biotypes. Leaves of both resistant and susceptible species rapidly hydrolyzed fluazifop-butyl to fluazifop acid. However, a more rapid rate of metabolism of fluazifop acid was shown in the resistant plants to unknown metabolites. Enhanced metabolism of fluazifop acid which is more phytotoxic than its ester analog was postulated as a mechanism of resistance.

Metabolism of haloxyfop-methyl in intact plants of shattercane (*Sorghum bicolor*) and yellow foxtail (*Setaria glauca*) resulted in a rapid hydrolysis of the parent herbicide to haloxyfop acid in all three species [19]. Haloxyfop-methyl levels 48 and 96 h after application were below 25%, and significant quantities of polar products were detected. Nevertheless, in shattercane, which is more susceptible than yellow foxtail, a higher level (30% 2 DAT) of haloxifop acid was observed than in the yellow foxtail (~10%) at the same time (Table 1). This may explain the observed selectivity between the tolerant and the susceptible weed species.

Selective action of quizalofop-ethyl in a sensitive (Biotype 10) and a less sensitive (Biotype 2) quackgrass (*Elytrigia repens*) biotypes was partially attributed to differential rates of metabolism [20]. Conversion of the relatively inactive applied form (quizalofop-ethyl) to the biologically active form (quizalofop) occurred rapidly and further conversion of quizalofop to polar metabolites occurred more slowly. However, in both biotypes, the level of quizalofop was similar regardless of time, indicating that differential sensitivity of acetyl-CoA carboxylase, which is the molecular target of quizalofop, could be involved in determining the overall response of the biotypes to quizalofop. De-esterification of quizalofop-P-ethyl into quizalofop-P acid was rapid in the treated leaf of yellow foxtail (*Setaria glauca*) [21]. Further metabolism resulted in a glucose conjugate and a phenolic metabolite. Four days after treatment, the parent herbicide accounted for 38% of all metabolites, while the acid, the glucose conjugate, and the phenolic derivative accounted for 29%, 28%, and 4% of all metabolites, respectively (Table 1).

http://dx.doi.org/10.5772/61674

3. Metabolism and selectivity of protoporphyrinogen IX oxidase inhibitory herbicides in weed species

Protoporphyrinogen oxidase (PPO), the last common enzyme in heme and chlorophyll biosynthesis, is the target of several classes of herbicides acting as inhibitors in both plants and mammals [22]. PPO inhibitor herbicides inhibit the enzyme, protoporphyrinogen oxidase (called also as protox), which is essential for the synthesis of chlorophyll. Susceptible plants accumulate toxic levels of protoporphyrinogen IX (proto IX) which reacts with oxygen and light to form singlet oxygen. Singlet oxygen causes rapid lipid peroxidation, membrane destruction, desiccation, and death. PPO inhibitors belonging to different chemical families have been developed as wide-spectrum agricultural herbicides. PPO inhibitory diphenyl ethers, *N*-phenylphthalimides, oxadiazoles, oxazolidinediones, phenylpyrazoles, pyrimidindiones, thiadiazoles, and phenyltriazolinones are all herbicidally active molecules. These compounds have been shown as environmentally safe molecules exhibiting low mammalian toxicities, low application rates with broad herbicidal activity controlling both monocot and dicot weeds, rapid onset of action, and long-lasting effect [23].

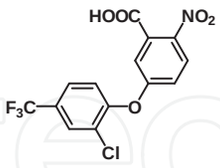
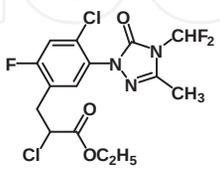
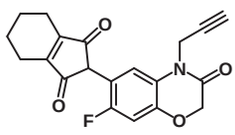
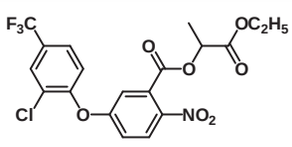
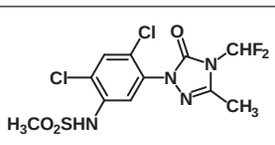
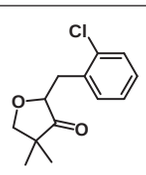
Diphenyl ether herbicide types, acifluorfen and lactofen, are used postemergence in soybean for selective control of annual morning glory and other broadleaf weed species. The rate of metabolism of acifluorfen was inversely related to susceptibility of plants such as common ragweed (*Ambrosia artemisiifolia*) > common cocklebur (*Xanthium pensylvanicum*) > soybean to the herbicide [24]. The more rapid penetration and translocation, coupled with slower metabolism of acifluorfen by the weed species in comparison to soybean, may account for the difference in susceptibility of the weeds and soybean to acifluorfen. However, metabolites were not identified in this study. Another research with [chlorophenyl-^{14}C]- and [nitrophenyl-^{14}C]acifluorfen showed that the diphenyl ether bond was rapidly cleaved by the attack of homoglutathione (hGSH) in soybean leaves and resulted in two major types of metabolites [25]. Catabolism of the initially formed hGSH conjugate (*S*-(3-carboxynitrophenyl)-γ-glutamyl-cysteinyl-β-alanine) of carboxynitrophenyl moiety of the herbicide yielded a cysteine conjugate (*S*-(3-carboxy-4-nitrophenyl)cysteine), while the 2-chloro-4-trifluoromethylphenol formed after diphenyl ether cleavage by hGSH conjugated to D-glucose which was further metabolized by malonyl conjugation, resulting in the malonyl-glucose metabolite. Experiments to clarify selectivity of acifluorfen and lactofen in pitted morning glory (*Ipomoea lacunosa*) and ivyleaf morning glory (*Ipomoea hederacea*) showed that translocation and metabolism of acifluorfen were minimal in both morning glory species [26]. However, decreased absorption of acifluorfen may account for greater tolerance of ivyleaf morning glory to acifluorfen. The translocation and metabolism of lactofen were also minimal in both morning glory species. Apparently, pitted morning glory and ivyleaf morning glory convert lactofen to acifluorfen inside treated leaves. The degree of this conversion was similar for both species. Quantities of other lactofen metabolites were less than 3% in both morning glory species. The results indicated that pitted morning glory would be more effectively controlled by acifluorfen than lactofen on the basis of differential penetration of these two herbicides into treated leaves.

The phenyl-triazolinone, carfentrazone-ethyl, is a selective postemergence herbicide against troublesome weeds such as morning glories (*Ipomoea spp*) and velvetleaf (*Abutilon theophrasti*) in soybean fields. The herbicide was more rapidly metabolized in the crop than in the weed species, with 27%, 54%, and 60% of the parent compound remaining in soybean, ivyleaf morning glory (*Ipomoea hederacea*), and velvetleaf, the most sensitive species, respectively (Table 2) [27]. The free acid metabolite, carfentrazone, was produced by all species and accounted for 21–27% of the absorbed herbicide. At least two unidentified metabolites were observed in each species. Unknown metabolites were four to five times more abundant in soybean than in the weed species. Both carfentrazone-ethyl and carfentrazone were potent inhibitors of PPO with high binding constants (258 nM and 285 nM, respectively). Based on metabolism studies, the selectivity of carfentrazone ethyl was partially attributed to the lower accumulation of proto IX in soybean than in the weeds which was associated with the enhanced ability of soybean to metabolize more carfentrazone than the weeds.

Sulfentrazone, also a phenyl-triazolinone herbicide, exhibits activity toward weeds commonly associated with soybeans. Consistent with field observation, sicklepod (*Senna obtusifolia*) exhibited considerable tolerance to sulfentrazone, and coffee senna (*Cassia occidental*) showed relatively high sensitivity to this herbicide in greenhouse tests [28]. There is little sulfentrazone metabolized in the roots of sicklepod and coffee senna, indicating that most of the radioactivity reaching the foliage is the parent molecule. There were differences in the ability of sicklepod and coffee senna to metabolize sulfentrazone in the foliage. After 9 h, only 8% of the parent compound remained in sicklepod, whereas coffee senna contained almost 83% (Table 2). The tolerance of sicklepod to sulfentrazone is primarily due to a relatively high rate of metabolism of the herbicide compared to coffee senna. The primary detoxification reaction appeared to be oxidation of the methyl group on the triazolinone ring, resulting in the formation of the more polar hydroxymethyl derivative. Although the biological activity of the hydroxymethyl and carboxylic acid derivatives of sulfentrazone is not known, it has been reported that the methyl group on position 3 of the triazolinone ring is necessary for maximum biological activity and that its replacement by other substituents resulted in 3- to 6-fold decrease in biological activity. Further studies on the metabolism of root-absorbed sulfentrazone in peanut, prickly sida (*Sida spinosa*), and pitted morning glory (*Ipomoea lacunosa*) indicated that all plant species are able to metabolize sulfentrazone [29]. One day after treatment, 5%, 27%, and 32% of the radiolabeled sulfentrazone in the shoots of peanut, prickly sida, and pitted morning glory, respectively, was present as unmetabolized sulfentrazone. The initial concentrations of sulfentrazone in the shoots at 3 and 6 HAT correspond to reported tolerance levels; peanut was the most tolerant among these species, whereas prickly sida and pitted morning glory were moderately tolerant and susceptible to the herbicide, respectively. On this basis, tolerance in peanut is largely due to its ability to rapidly metabolize sulfentrazone.

The *N*-phenylphthalimide, flumioxazin, a preemergence herbicide, is used for weed control in peanut. Flumioxazin also acts by inhibiting protoporphyrinogen oxidase. Experiments to investigate the basis of differential tolerance of peanut, ivyleaf morning glory (*Ipomoea hederacea*), and sicklepod (*Senna obtusifolia*) to root-absorbed flumioxazin were conducted [30]. No translocation of absorbed radiolabel from the herbicide was observed at all harvest times.

http://dx.doi.org/10.5772/61674

Herbicide	Structure	Metabolized herbicide, % (time after treatment)	Weed species	Ref.
Acifluorfen		44 (7 DAT) 55 (7 DAT)	*Ambrosia artemisiifolia* *Xantbium pensylvanicum*	[24]
		4 (4 DAT) 11 (4 DAT)	*Ipomoea lacunose* *Ipomoea hederacea*	[26]
Carfentrazone-ethyl		46 (1 DAT) 39 (1 DAT)	*Ipomoea hederacea* *Abutilon theophrasti*	[27]
Flumioxazin		59 (3 DAT) 76 (3 DAT)	*Ipomoea hederacea* *Senna obtusifolia*	[30]
Lactofen		19 (4 DAT) 19 (4 DAT)	*Ipomoea lacunose* *Ipomoea hederacea*	[26]
Sulfentrazone		73 (1 DAT) 68 (1 DAT)	*Sida spinosa* *Ipomoea lacunosa*	[29]
		92 (9 HAT) 17 (9 HAT)	*Senna obtusifolia* *Cassia occidentalis*	[28]
Clomazone		50 (4 DAT) 60 (4 DAT) 55 (4 DAT)	*Amaranthus hybridus* *Amaranthus retroflexus* *Amaranthus lividus*	[35]
		35 (3 DAT) 54 (3 DAT)	*Amaranthus retroflexus* *Abutilon theophrasti*	[36]
		84 (7 DAT)	*Echinocloa oryzoides*	[37]
		N/Aa N/Ab	*Echinocloa phyllopogon* resistant biotype sensitive biotype	[38]

[a]Resistant plants accumulated 6- to 12-fold more of the monohydroxylated metabolite than susceptible plants.

[b]susceptible plants accumulated 2.5-fold more of the phytotoxic metabolite 5-ketoclomazone.

Table 2. Metabolism of protoporphyrinogen oxidase (PPO) inhibitor herbicides and metabolism of the carotenoid biosynthesis inhibitor clomazone in weed species

Ivyleaf morning glory contained the highest portion (41%) of unmetabolized herbicide 3 DAT, whereas sicklepod and peanut contained only 24% and 11% parent herbicide, respectively (Table 2). Results indicated a slower metabolism of flumioxazin by susceptible ivyleaf morning glory as compared with tolerant sicklepod and peanut. Nevertheless, no metabolites were reported in this study. Under aerobic conditions in an aquatic environment, hydrolytic cleavage of flumioxazin and separation of the phthalimido and benzoxazin moieties at the amine bridge are the major degradation reactions [31]. Metabolism studies in rats revealed that cytochrome P450-related monooxygenases are involved in the metabolism, yielding 3-OH- and 4-OH-flumioxazin derivatives [32, 33].

4. Metabolism of carotenoid biosynthesis inhibitor clomazone in weeds

Clomazone belongs to the group of isoxazolidinones, and acts by inhibiting the biosynthesis of photosynthetic pigments of both chlorophyll and carotenoids. Clomazone is not a protox inhibitor herbicide. Clomazone inhibits the 1-deoxy-D-xylulose 5-phosphate (DXP) synthase, the first enzyme of the non-mevalonate isoprenoid pathway in plastids which generates isopentenyl pyrophosphate for the biosynthesis of terpenes and terpenoids [34]. As a consequence of clomazone action impaired chloroplast development and pigment loss occur in susceptible plants. At higher light intensities, reactive singlet oxygen initiates membrane lipid peroxidation in the absence of carotenoids or at extremely reduced carotenoid levels.

Differential metabolism or differential rate of metabolism of clomazone did not appear to explain the tolerance of soybean (48% clomazone metabolized in 4 days) and smooth pigweed (*Amaranthus hybridus*, 50%) or the susceptibility of redroot pigweed (*Amaranthus retroflexus,* 60%) and livid pigweed (*Amaranthus lividus,* 55%) to this herbicide (Table 2) [35]. Tolerant soybeans and *Amaranthus hybridus* absorbed less root-applied clomazone than sensitive species after 4 days. It was postulated that clomazone may be a proherbicide that is metabolized to an active form by both tolerant and susceptible plants and differences at the site of action (carotenoid biosynthesis) may account for the selectivity. Differences in clomazone uptake, distribution, and metabolism among corn, soybean, smooth pigweed (*Amaranthus hybridus*), and velvetleaf (*Abutilon theophrasti*) were either insignificant or poorly correlated to selectivity and, therefore, cannot account for the tremendous differences in clomazone sensitivity among these species [36]. These observations indicate, indirectly, that differences at the site of action may account for selectivity.

Rice, a relatively tolerant species, and early watergrass (*Echinochloa oryzoides*), a relatively susceptible species, were exposed to clomazone to determine biotransformation of the herbicide [37]. More metabolized residue was measured in watergrass compared to rice (84% vs. 68%). Metabolism yielded hydroxylated derivatives, β-D-glucoside conjugates, and several other unidentified polar metabolites in both plants, but higher metabolite concentrations were detected in watergrass. The level of 5-ketoclomazone, the active metabolite of the parent compound, was significantly higher in early watergrass than in rice (21 and 5.7 pmol/g, respectively). Selectivity of clomazone between rice and the weed species is likely due to

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differential metabolism, when the susceptible watergrass metabolized higher amount of clomazone than the tolerant rice. This result suggested that metabolism activated clomazone to herbicidally more active derivative. *Echinochloa phyllopogon* (late watergrass) is a major weed of California rice that has evolved cytochrome P450-mediated metabolic resistance to different herbicides with multiple modes of action. Evaluation of the differential clomazone metabolism with resistant and susceptible biotypes of late watergrass was carried out to explore whether enhanced oxidative metabolism also confers clomazone resistance in *E. phyllopogon* [38]. Late watergrass plants hydroxylated mostly the isoxazolidinone ring of clomazone, and clomazone hydroxylation activity of resistant biotypes was higher than that of susceptible plants. The major metabolites were the mono- and dihydroxylated derivatives of the isoxazolidinone ring. In resistant plants, 6- to 12-fold more monohydroxy metabolite was detected than in susceptible plants. On the other hand, susceptible plants accumulated 2.5-fold more of the herbicidally active 5-ketoclomazone (Table 2). Oxidative metabolism appears to confer multiple herbicide resistance to *E. phyllopogon* with cross-resistance to clomazone by enhanced herbicide metabolism and less concentration of the phytotoxic active metabolite in resistant plants.

5. Metabolism and selectivity of acetolactate synthase (ALS) inhibitor herbicides in weed species

The endogenous ALS (also known as acetohydroxy acid synthase, AHAS) gene is involved in the biosynthesis of branched-chain amino acids (valine, leucine, and isoleucine), catalyzing the formation of 2-acetolactate or 2-aceto-2-hydroxybutyrate [39]. ALS is the site of action of several structurally diverse classes of herbicides such as sulfonylureas, imidazolinones, and triazolopyrimidine sulfonamides [40]. ALS inhibitors are quite unique inhibitors since they do not show structural similarity to the natural substrates, such as pyruvate and α-ketobutyrate, cofactors, such as thiamine diphosphate and flavin adenine dinucleotide, and allosteric effectors, such as valine, leucine, and isoleucine, of the enzyme. Inhibition of ALS results in deficiency of the amino acid pool and triggers a decrease in protein biosynthesis, which eventually leads to reduced rate of cell division. This process eventually kills the plants after showing symptoms in meristematic tissues where biosynthesis of amino acids primarily takes place [41].

5.1. Metabolism of imidazolinone herbicides in weeds

The imidazolinones are important ALS-inhibiting herbicides. The most significant members of this chemistry are imazamethabenz-methyl, imazaquin, imazethapyr, imazapyr, and imazamox. The basic structural requirements for this class include an aromatic/pyridine ring with 5′-carboxylic acid or carboxylic ester function as well as an adjacent *ortho*-imidazolinone ring. The crop selectivity of imidazolinones is primarily related to the differential metabolism of the herbicide between the crops and targeted weeds [40]. The wide range of selectivity of this herbicide series is probably a function of the balance of oxidative and hydrolytic metabolism at substituents other than the imidazolinone ring. Imidazolidinone-resistant crops

contain a selective mutation in the ALS gene which encodes an ALS enzyme that no longer binds these herbicides, although metabolism may play a role in determining the level of tolerance of the resistant crop.

Imazamethabenz-methyl, actually a racemic mixture of *meta* and *para* 2-imidazolinone toluates in the ratio of 3:2, is an imidazolinone-type herbicide controlling wild oat (*Avena fatua*) in maize and wheat. The unesterified carboxylic acids are also herbicidally active, exhibiting no selectivity. The initial metabolism by hydrolytic activation of the esters of the separate isomers resulted in hydrolysis of ester only in wild oat among these species 2 weeks after foliar treatment. The hydrolysis of herbicidally more active *meta*-isomer produced a 2- to 3-fold greater concentration of the free acid than the *para*-isomer [42]. In maize and wheat, detoxication takes place *via* rapid oxidation of the aryl methyl group to the corresponding alcohol followed by glucose conjugation. Apparently, the primary mechanism of resistance to imazamethabenz-methyl in wild oat is due to reduced metabolism of imazamethabenz-methyl to the biologically active imazamethabenz. *Meta*-isomer was metabolized to the acid form to a greater extent in the susceptible biotype than in the resistant biotype [43].

Imazaquin is a broad-spectrum herbicide developed for the use in soybean. Imazaquin can be used both preemergence and postemergence on both broadleaf and grass weeds. In order to understand the selectivity between crop plant and weed absorption, translocation and metabolism of imazaquin in soybean (*Glycine max*), common cocklebur (*Xanthium strumarium*), and velvetleaf (*Abutilon theophrasti*) were investigated [44]. Imazaquin was metabolized rapidly by soybean and velvetleaf but appeared to be metabolized slowly by cocklebur. The order of tolerance of these three species to imazaquin was soybeans > velvetleaf > cocklebur. This order of tolerance was directly correlated in young plants with the half-life of imazaquin within the tissue. Soybean metabolized imazaquin more rapidly (half-life 3 days) than velvetleaf (half-life 12 days), which was more rapid than cocklebur (half-life 30 days) (Table 3). Velvetleaf exhibited increased tolerance to imazaquin with age, which was attributed partially to greatly reduced absorption of the herbicide by older leaves and more rapid metabolism of the herbicide. The rate of metabolism was greatest in older plants, the half-life of imazaquin decreasing from 12 days at the cotyledonary stage to 4.5 days at the four-leaf stage. However, no identified metabolite was reported. Basis for greater imazaquin tolerance of entireleaf morning glory (*Ipomoea hederacea*) than pitted morning glory (*Ipomoea lanucosa*) to postemergence applications of imazaquin initiated uptake, translocation, and metabolism studies [45]. Entireleaf morning glory metabolized slightly more imazaquin than pitted morning glory in treated leaves. The difference of tolerance of these species is attributed to reduced absorption and translocation and increased metabolism of the herbicide in the entireleaf morning glory (Table 3). Metabolism data indicate that imazaquin susceptibility of pitted and entireleaf morning glory represent a moderate susceptibility similar to velvetleaf. Results indicated that imazaquin was translocated by both xylem and phloem in pitted and entireleaf morning glory. However, less absorption and translocation of imazaquin and/or its metabolites in entireleaf morning glory than in pitted morning glory probably contribute to its greater tolerance to foliar applications.

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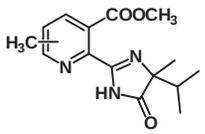
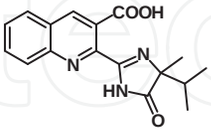
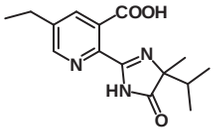
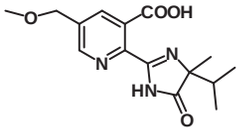
Herbicide	Structure	Half-life	Metabolized herbicide (%)	Weed species	Ref.
Imazamethabenz-methyl			72%[a] 14 DAT	*Avena fatua*	[42]
			49%[b] 7 DAT	*Avena fatua*	[43]
			54%[c] 7 DAT	susceptible biotype	
				resistant biotype	
Imazaquin		30 days		*Xanthium strumarium*	[44]
		12 days		*Abutilon theophrasti*	
			30% 8 DAT	*Ipomoea lacunose*	[45]
			42% 8 DAT	*Ipomoea hederacea*	
Imazethapyr		14 h		*Desmodium tortuosum*	[46]
		24 h		*Cassia obtusifolia*	
		32 h		*Amaranthus retroflexus*	
			14%[d] 8 DAT	*Euphorbia esula*	[47]
			47%[e] 8 DAT		
			81%[f] 14 DAT	*Ambrosia artemisiifolia*	[48]
			68%[f] 14 DAT	*Ambrosia trifida*	
Imazamox		42 h		*Secale cereal*	[49]
		84 h		*Aegilops cylindrica*	
		7.7 h		*Myriophyllum spicatum*	[50]

[a]28% Parent herbicide and 8% acid.

[b]51% parent herbicide and 13% acid.

[c]28% parent herbicide and 8% acid.

[d]% of metabolized herbicide in the leaves.

[e]% of metabolized herbicide in the roots.

[f]% of metabolized herbicide in the treated leaf.

Table 3. Metabolism of imidazolinone herbicides in weed species

Sicklepod (*Cassia obtusifolia*) and Florida beggarweed (*Desmodium tortuosum*) are troublesome weeds in peanut and soybean production. Evaluation of the differential response of these species as well as redroot pigweed (*Amaranthus retroflexus*) following foliar and/or root applications of imazethapyr showed that redroot pigweed was the most sensitive, with sicklepod and Florida beggarweed being intermediate [46]. The half-life of foliar-applied imazethapyr was 6.6 days in soybean, 6.5 days in peanut, 14.4 days in Florida beggarweed, 24.0 days in sicklepod, and 32.1 days in redroot pigweed (Table 3). The tolerance of these species to foliar-applied imazethapyr was related to the half-life of foliar-applied imazethapyr within the plants. Nevertheless, no identified metabolites were reported. Leafy spurge (*Euphorbia esula*) is an introduced, herbaceous, perennial weed that infests large areas of

rangeland in Canada. Metabolism studies revealed that greater than 90% of the imazethapyr was unmetabolized 2 DAT in leafy spurge [47]. Crown, roots, and adventitious shoot buds had metabolized an average of 61, 36, and 47% of the imazethapyr, respectively, while only 14% was metabolized in the treated leaf 8 DAT. The primary metabolite was postulated as 5-hydroxyethyl-imazethapyr. Two metabolites of imazethapyr were observed in both common (*Ambrosia artemisiifolia*) and giant ragweed (*Ambrosia trifida*) [48]. These metabolites were identified as the α-hydroxyethyl analog of imazethapyr and its glucose conjugate. Common ragweed showed a consistently higher rate of imazethapyr metabolism to the glucose conjugate than giant ragweed.

Jointed goatgrass (*Aegilops cylindrica*) and feral rye (*Secale cereal*) respond differently to imazamox. Jointed goatgrass appeared to be susceptible, and feral rye was tolerant to foliar application [49]. Biological half-lives for imazamox in jointed goatgrass and feral rye were determined on a whole-plant basis. The half-life of imazamox was 42 h in feral rye and 84 h in jointed goatgrass (Table 3). Differential response can be attributed to differences in both translocation and metabolism. Feral rye translocated more imazamox to root tissue and exuded a large proportion of radiolabel into the sand media. Eurasian water milfoil (*Myriophyllum spicatum)* is a submersed invasive species. Approximately 70% of the absorbed imazamox was found in the bound fraction 24 HAT, while 10% detected as soluble metabolites [50]. Only 19% remained as intact imazamox. The metabolism study indicated 69% of absorbed ^{14}C-imazamox was found in the bound fraction 144 HAT, while 12% appeared as soluble metabolites, and only 21% as intact imazamox. Based on predicted values, the half-life of imazamox in Eurasian water milfoil was short (7.65 h) (Table 3).

5.2. Metabolism of sulfonylurea herbicides in weeds

Sulfonylureas represent a great advance in crop protection and have revolutionized herbicide research and weed control in the 1980s by introducing an unprecedented mode of herbicide action. The high potency of sulfonylureas decreased the previously applied high herbicide rates from kg/ha to as low as 1 g/ha. These molecules possess remarkably low mammalian toxicity, and advantageous environmental properties. The target site for sulfonylurea herbicides is also the ALS, the first common enzyme responsible for the biosynthesis of the branched-chain amino acids. Sulfonylureas are generally extremely potent inhibitors of ALS, regardless of plant species, and differential sensitivities at the target site play little, if any, role in their selective action [2]. Rather, differential metabolism has been implicated in their crop selectivity.

A major factor responsible for the selectivity of chlorsulfuron as a postemergence herbicide for small grains is the ability of the monocot plants to metabolize the herbicide [51]. Tolerant monocotyledonous plants such as wheat, oats, barley, wild oats (*Avena fatua*), annual bluegrass (*Poa annua*), johnsongrass (*Sorghum halapense*), and giant foxtail (*Setaria faberii*) rapidly metabolize chlorsulfuron to a polar, inactive product. This metabolite was characterized as the O-glycoside of chlorsulfuron in which the phenyl ring underwent hydroxylation followed by sugar conjugation. Sensitive broadleaf cleavers (*Galium aparine*) showed no metabolism of chlorsulfuron. Metabolism of chlorsulfuron took place in both roots and shoots in the root-

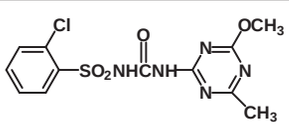
http://dx.doi.org/10.5772/61674

treated moderately susceptible chamomile (*Matricaria chamomilla*) and in susceptible Johnny–jump-up (*Viola tricolor*) at different rates [52]. The more sensitive Johnny–jump-up metabolized less herbicide to a polar water-soluble sugar conjugate in shoots than chamomile. The basis for differences in response of eastern black nightshade (*Solanum ptycanthum*), a tolerant species, and velvetleaf (*Abutilon theophrasti*), a susceptible species, to foliar-applied chlorsulfuron is also the differential rate of degradation [53]. Little metabolism of chlorsulfuron occurred in the sensitive, broadleaf species of velvetleaf. The rapid metabolism of chlorsulfuron in eastern black nightshade would appear to be responsible for the tolerance. The ability of flax (*Linum usitatissimum*) and black nightshade (*Solanum nigrum*) to metabolize chlorsulfuron was studied to determine if metabolism contributes to their tolerance to chlorsulfuron [54]. Shoot-treated plants metabolized more than 90% of parent herbicides. The major metabolite contained hydroxylated 4-methyl group of the triazine ring of chlorsulfuron. A second major metabolite was determined to be a carbohydrate conjugate of the hydroxymethyl derivative. Plants were more tolerant to 4-hydroxymethyl chlorsulfuron applications than to chlorsulfuron. These results suggest that metabolism may be the basis of selectivity to chlorsulfuron for tolerant broadleaf plants as well as for grasses. In the case of grasses, metabolism occurs on the phenyl ring [51], whereas in broadleaves, it occurs on the heterocyclic ring.

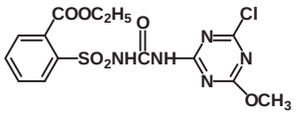
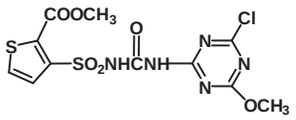
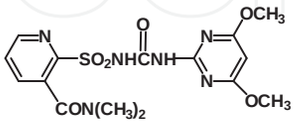
Resistance to ALS inhibitor herbicides in weeds was first discovered in 1987 [55, 56]. Since then numerous weed species have become resistant to sulfonylureas and imidazolidines. Several mutations in the ALS gene are capable of conferring resistance to ALS inhibitor herbicides [57]. Metabolism studies with cross-resistant (SLR31) and two susceptible (VLR1 and VLR6) biotypes of rigid ryegrass (*Lolium rigidum*) proved that there was no difference in the metabolite profiles from susceptible and resistant ryegrass [58]. Metabolism rate of chlorsulfuron in cross-resistant ryegrass SLR31 was approximately double than in the susceptible biotype (VLR1). Half-life of chlorsulfuron was 6 h in the cross-resistant biotype as compared to 12 h in the susceptible species (Table 4). The increased rate of detoxification of chlorsulfuron in the cross-resistant SLR31 biotype was found to be solely related to chlorsulfuron resistance since the diclofop-methyl-resistant biotype VLR6, which in turn, is susceptible to chlorsulfuron, metabolized chlorsulfuron at the same rate as the chlorsulfuron and diclofop-methyl-susceptible biotype VLR1. Metabolism of chlorsulfuron in wheat took place at a higher rate than any ryegrass biotype having half-life of 2 h. Major metabolite of chlorsulfuron metabolism was identical in wheat and ryegrass biotypes, the glycosylated derivative of chlorsulfuron hydroxylated in the phenyl ring [51]. The metabolic detoxication of chlorsulfuron was faster in both roots and shoots of the resistant rigid rygrass biotype SR4/84 than in susceptible biotype SRS2, and the chlorsulfuron sensitivity between these biotypes could be explained by differential rate of metabolism [59]. Despite the correlation between enhanced metabolism and reduced plant sensitivity, no quantitative agreement can be described. The 4-fold increase in rate of metabolism (R/S, 4) resulted in 23-fold increase of chlorsulfuron tolerance of the resistant biotype (R/S, 23). Environmental factors can also affect plant injuries and metabolism rates caused by ALS-inhibiting herbicides. The major pathway of the chlorsulfuron metabolism proposed was a phenyl ring hydroxylation followed by glycosylation, while the sulfonylurea bridge cleavage results in 2-chloro-benzenesulfonamide and 2-amino-4-methyl-6-methoxy-triazine metabolite as minor products.

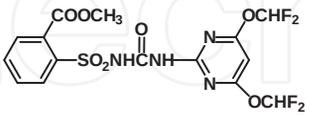
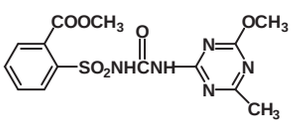
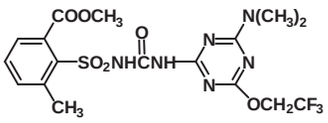
A biotype VLR69 of rigid ryegrass (*Lolium rigidum*) resistant to some ALS exhibited greater capacity to detoxify chlorsulfuron than the susceptible VLRl population [60]. The half-life of chlorsulfuron in the resistant culms was 3 versus 6 h in the susceptible culms. The difference in rate of metabolism between the two biotypes was similar to that observed between the resistant biotype SLR31 and susceptible biotype VLR1 [58]. Uptake of chlorsulfuron into the cut shoots was similar for both biotypes. The metabolites observed in VLR69 have the same high-performance liquid chromatography (HPLC) elution profile as those of SLR 1 and VLRI, indicating that the enhanced detoxification was not due to the production of novel metabolites. A biotype of *Lolium rigidum* Gaudin (VLR69) showed multiple resistances to at least nine dissimilar herbicide chemistries. ALS, the target site for chlorsulfuron, was found sensitive to chlorsulfuron in VLR69 biotype, and only about 5% of the population contained a chlorsulfuron-resistant ALS. Studies supported the enhanced chlorsulfuron metabolism in the resistant biotype. While 22% of the herbicide was metabolized 6 HAT by the resistant biotype, only 8% was metabolized by the susceptible biotype VLR1 (Table 4) [61].

Chlorimuron-ethyl is a highly active sulfonylurea herbicide for preemergence and postemergence use in soybeans. Studies on soybean selectivity to chlorimuron-ethyl showed that the selectivity was not based on differential active site sensitivity [62]. ALS from tolerant soybeans is just as sensitive to chlorimuron-ethyl as ALS preparations from diverse sensitive weeds. While the metabolic half-life of chlorimuron ethyl in soybean was 1–3 h following foliar application, in redroot pigweed (*Amaranthus retroflexus*), common cocklebur (*Xanthium pensylvancium*), and common morning glory (*Ipomoea purpurea*), half-life values ranged between 24 and >48 h. It is interesting to note that the methyl ester analog of chlorimuron-ethyl is metabolized much more slowly by soybeans (half-life > 12 h) (Table 4). The metabolism of chlorimuron-ethyl in soybean seedlings yielded homoglutathione conjugate as the primary metabolite by displacement of the pyrimidinyl chlorine with the cysteine sulfhydryl group of homoglutathione [63]. Minor metabolite of chlorimuron-ethyl was its de-esterified free acid. These metabolites were found inactive against plant ALS, and the tolerance of soybean to chlorimuron-ethyl was demonstrated as a result of rapid metabolism to herbicidally inactive products.

Herbicide	Structure	Half-life, h or metabolized herbicide, %	Weed species	Ref.
Chlorsulfuron		92% 1 DAT	*Poa annua*	[51]
		92% 1 DAT	*Avena fatua*	
		>80% 1 DATa	*Sorghum halapense*	
		>80% 1 DATa	*Setaria faberii*	
		0%	*Galium aparine*	
		69% 6 DAT	*Viola tricolor*	[52]
		18% 6 DAT	*Matricaria chamomilla*	
		81% 3 DAT	*Solanum ptycanthum*	[53]

http://dx.doi.org/10.5772/61674

Herbicide	Structure	Half-life, h or metabolized herbicide, %	Weed species	Ref.
		7% 3 DAT	*Abutilon tbeophrasti*	
		92% 1 DAT	*Linum usitatissimum*	[54]
		92% 1 DAT	*Solanum nigrum*	
		31% 8 HAT	*Lolium rigidum*	[58]
		54% 8 HAT	biotype VLR1[b]	
		33% 8 HAT	biotye SLR31[c]	
			biotype VLR6[d]	
		1[f] and 3[g]	*Lolium rigidum*	[59]
		4[f] and 13[g]	biotype SR4/84	
			biotype SRS2	
		3	*Lolium rigidum*	[60]
		6	biotype VLR69[b]	
			biotype VLR1[e]	
		22% 6 HAT	*Lolium rigidum*	[61]
		8% 6 HAT	biotype VLR69[b]	
			biotype VLR1[e]	
Chlorimuron-ethyl		>30	*Xanthium pensylvanicum*	[62]
		>30	*Amaranthus retroflexus*	
		>48	*Xanthium pensylvanicum*	[63]
		24–48	*Amaranthus retroflexus*	
		20–24	*Ipamoea purpurea*	
Thifensulfuron-methyl		50% 3 DAT	*Abutilon theophrasti*	[65]
		50% 3 DAT	*Anoda cristata*	
		>48	*Amaranthus retroflexus*	[63, 64]
		>48	*Chenopodium album*	
		>48	*Abutilon theophrasti*	
		30	*Ipomoea purpurea*	
Nicosulfuron		31% 3 DAT	*Sorghum halapense*	[66]
		>72	*Sorghum bicolor*	[67]
		36	*Eriochloa villosa*	
		39% 3 DAT	*Sorghum halapense*	[70]
		60% 3 DAT	*Echinochloa crus-galli*	
		59% 3 DAT	*Setaria faberii*	
		70% 3 DAT	*Solanum ptychanthum*	
		7% 3 DAT	*Brachiaria platyphylla*	[68]
		47% 3 DAT	*Cynodon dactylon*	[69]

Herbicide	Structure	Half-life, h or metabolized herbicide, %	Weed species	Ref.
		58% 3 DAT	*Zoysia japonica*	
		51% 3 DAT	*Lolium arundinaceum*	
		37% 3 DAT	*Agrostis stolonifera*	
		36% 3 DAT	*Poa annua*	
Primisulfuron		1.5	*Echinochloa crus-galli*	[71]
		12	*Cynodon dactylon*	
		3.5	*Digitaria sanguinalis*	
		>24	*Pueraria lobata*	
		6.0	*Panicum texanum*	
		>72	*Sorghum bicolor*	[67]
		<4	*Eriochloa villosa*	
		48% 3 DAT	*Sorghum halapense*	[70]
		24% 3 DAT	*Echinochloa crus-galli*	
		29% 3 DAT	*Setaria faberii*	
		54% 3 DAT	*Solanum ptychanthum*	
		90% 3 DAT	*Brachiaria platyphylla*	[68]
Metsulfuron-methyl		0% 4 DAT	*Oxytropis sericea*	[74]
		0% 4 DAT	*Astragalus mollissimus*	
Triflusulfuron		36	*Brassica napus*	[75]
		80	*Matricaria inodora*	
		61	*Veronica persica*	
		7	*Chenopodium album*	

[a]Estimated value.

[b]susceptible to diclofop-methyl and chlorsulfuron at normal field rates.

[c]resistant to both diclofop-methyl and chlorsulfuron.

[d]resistant to diclofop-methyl but susceptible to chlorsulfuron.

[e]this biotype is resistant to herbicides in 10 chemical classes, including the sulfonylureas and imidazolinones.

[f]half-life in shoots; [g]half-life in roots.

Table 4. Metabolism of sulfonylurea herbicides in weed species

Thifensulfuron-methyl differs from most other sulfonylurea herbicides in several respects. It is a short-residual herbicide, by virtue of its high susceptibility to microbial degradation in the soil. Soybeans metabolize thifensulfuron-methyl relatively rapidly, with half-life of 4–6 h (Table 4) [64]. The very sensitive species, including velvetleaf (*Abutilon theophrasti*), pigweed (*Amaranthus retroflexus*), and lambsquarters (*Chenopodium album*), metabolize the herbicide

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much more slowly, with half-lives greater than 48 h. Morning glory (*Ipomoea purpurea*), which is moderately sensitive, metabolizes thifensulfuron-methyl somewhat more rapidly but still more slowly (half-life of 30 h) than soybeans. The primary metabolite of thifensulfuron-methyl in soybean seedlings is its de-esterified free acid (thifensulfuron acid), which is herbicidally inactive and inactive against ALS. Soybean tolerance to thifensulfuron-methyl results from rapid de-esterification to inactive free acid. Further metabolism studies with tolerant soybean, moderately tolerant soybean, and spurred anoda (*Anoda cristata*) as well as susceptible velvetleaf (*Abutilon theophrasti*) showed that differential rate of metabolism seems to be a contributing factor in the selectivity of thifensulfuron-methyl between the two soybean cultivars and velvetleaf [65]. The metabolic basis for the moderate tolerance of spurred anoda to thifensulfuron-methyl was not clear. The two soybean cultivars metabolized 62–70% of absorbed thifensulfuron methyl at 3 days after treatment, while velvetleaf and spurred anoda metabolized about 50% of the absorbed herbicide (Table 4). The major metabolite formed in all species appeared to be de-esterified thifensulfuron acid.

Johnsongrass (*Sorghum halapense*) is a major perennial weed infesting many crop production areas. Nicosulfuron can be used to selectively control both seedling and rhizome johnsongrass in corn. Selectivity studies showed that 40% of nicosulfuron applied to the leaf surface of corn was absorbed into the leaf and the herbicide was rapidly metabolized with a half-life of 2 h (Table 4) [66]. Within 20 h, the parent herbicide was almost completely metabolized. Johnsongrass absorbed similar amount as corn; however, there was no perceptible metabolism of nicosulfuron in the treated leaves up to 24 h and 3 DAT; only 31% was metabolized. Research carried out to elucidate mechanism(s) of nicosulfuron and primisulfuron selectivity in corn, woolly cupgrass (*Eriochloa villosa*), and shattercane (*Sorghum bicolor*) revealed that corn absorbed less than one half the nicosulfuron and primisulfuron that woolly cupgrass and shattercane absorbed [67]. Corn rapidly metabolized nicosulfuron and primisulfuron, with a half-life of less than 4 h (Table 4). Shattercane metabolized the herbicides more slowly, with a half-life greater than 72 h for nicosulfuron and 36 h for primisulfuron. Nicosulfuron and primisulfuron half-lives were greater than 72 h and less than 4 h, respectively, in woolly cupgrass. Selectivity with nicosulfuron and primisulfuron is likely based on metabolism to non-phytotoxic compounds. Corn tolerance to nicosulfuron and primisulfuron was also attributed to reduced herbicide penetration and translocation below the treated leaf.

Broadleaf signalgrass (*Brachiaria platyphylla*) is sensitive to nicosulfuron and resistant to primisulfuron, but corn is resistant to both. By 72 HAT, broadleaf signalgrass under conditions of high light and temperature had metabolized nearly 90% of the primisulfuron absorbed, but less than 7% of the nicosulfuron absorbed was metabolized during the same time (Table 4) [68]. Corn rapidly metabolized both herbicides. These results suggest that differential activity of nicosulfuron and primisulfuron on broadleaf signalgrass may be based on differential rates of metabolism to non-phytotoxic compounds; uptake and translocation differences agree with the differential broadleaf signalgrass activity. In addition, environment has the potential to affect rates of sulfonylurea absorption, translocation, and metabolism. In nicosulfuron selectivity studies, relative tolerance of grasses from high to low was Bermuda grass (*Cynodon dactylon*) = zoysiagrass (*Zoysia japonica*)> tall fescue (*Lolium arundinaceum*) > creeping bentgrass

(*Lolium arundinaceum*) > annual bluegrass (*Poa annua*) [69]. At 72 HAT, annual bluegrass metabolized 36% of absorbed nicosulfuron, which was less than Bermuda grass, tall fescue, and zoysiagrass that metabolized 47–58% (Table 4). Creeping bentgrass metabolism of nicosulfuron was similar to annual bluegrass. Tall fescue had similar levels of metabolism to Bermuda grass and zoysiagrass, averaging 67%, at 168 HAT but produced fewer metabolites. Turfgrass tolerance to nicosulfuron is associated with relative herbicide concentrations in shoots and differential species metabolism.

The physiological basis for nicosulfuron and primisulfuron selectivity in corn, johnsongrass (*Sorghum halapense*), barnyardgrass (*Echinochloa crus-galli*), giant foxtail (*Setaria faberii*), and eastern black nightshade (*Solanum ptychanthum*) was established [70]. The levels of sensitivity were as follows, corn tolerant to both herbicides, seedling johnsongrass sensitive to both herbicides; barnyardgrass sensitive to nicosulfuron and tolerant to primisulfuron, giant foxtail sensitive to nicosulfuron and tolerant to primisulfuron, and eastern black nightshade tolerant to nicosulfuron and sensitive to primisulfuron. Selectivity of nicosulfuron and primisulfuron in corn, johnsongrass, barnyardgrass, and giant foxtail can primarily be attributed to differential rate of herbicide metabolism. Both herbicides were more rapidly metabolized by tolerant species. However, selectivity of these herbicides in eastern black nightshade could not be explained by differential herbicide absorption, translocation, or metabolism. The tolerance of eastern black nightshade to nicosulfuron and its sensitivity to primisulfuron were directly related to the sensitivity of ALS toward these molecules. ALS from eastern black nightshade was more sensitive to primisulfuron. Studies on the tolerance to primisulfuron of weeds such as Bermuda grass (*Cynodon dactylon*), crabgrass (*Digitaria sanguinalis*), kudzu (*Pueraria lobata*), Texas panicum (*Panicum texanum*), and particularly the tolerant barnyardgrass (*Echinochloa crus-galli*) showed that barnyardgrass was the fastest at metabolizing primisulfuron with an *in vivo* half-life about 1.5 h followed by crabgrass (3.5 h), Texas panicum (6 h), Bermuda grass (12 h), and kudzu (>24 h) (Table 4) [71]. The mechanism of tolerance of barnyardgrass was determined to be the metabolism and not an insensitive target enzyme, ALS. Two major classes of metabolites were produced and were found to be non-inhibitory to ALS. The metabolism proceeds through ring hydroxylation of the pyrimidine moiety followed by glycosylation.

Metsulfuron-methyl is an effective herbicide for use against broadleaf weeds and some grasses but is safe for use on wheat. Metabolism of metsulfuron-methyl in wheat and barley yielded a phenolic derivative formed after phenyl ring hydroxylation, a glucosyl conjugate of the phenolic metabolite as well as a hydroxymethyl derivative from hydroxylation of the methyl substituent of the triazine ring [72]. Hydrolysis of the sulfonylurea bridge resulted in several other unconjugated metabolites. Nevertheless, no de-esterified metabolites were detected. On the other hand, soybean seedlings do not metabolize metsulfuron-methyl and are correspondingly quite intolerant of this herbicide (GR50 < 0.5 g/ha). Soybeans exhibit an interesting specificity for de-esterification. The ethyl ester of chlorimuronethyl is de-esterified, while the methyl ester of metsulfuron-methyl is not, even though both compounds possess a phenyl ring. It was speculated that soybeans are incompetent to de-esterify ortho phenyl methyl ester sulfonylureas but are capable of this reaction with certain higher phenyl esters and even the methyl ester of thiophene sulfonylureas [73]. The locoweeds, woolly loco (*Astragalus mollissi-*

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mus) and silky crazyweed (*Oxytropis sericea*), contribute to livestock poisoning in the western United States. Silky crazyweed compared to woolly loco was more than 10 times as sensitive to increasing rates of herbicide. Nevertheless, no metabolism of metsulfuron was observed in these broadleaf weed species [74]. Selectivity differences between these locoweed genera to metsulfuron most likely are due to sensitivity differences at sites of action.

Triflusulfuron-methyl is a postemergence sulfonylurea herbicide for the control of annual and perennial broadleaf weeds and grasses in sugar beets. The mechanism of selectivity was studied by comparing the response of sugar beets with that of sensitive weeds such as rapeseed (*Brassica napus*), scentless false mayweed (*Matricaria inodora*), and common field-speedwell (*Veronica persica*) and a moderately tolerant lambsquarters (*Chenopodium album*) [75]. A good correlation between metabolism and plant tolerance does exist. Sugar beets metabolize triflusulfuron methyl very rapidly (half-life of < 1 h), while lamb's-quarters have an intermediate rate (half-life of 7 h) and sensitive weeds have slow rates of metabolism (half-lives of > 35 h) (Table 4). The initial metabolism of triflusulfuron methyl in sugar beets involves nucleophilic attack by glutathione at the urea carbonyl group, producing the *S*-(*N*-triazolylcarbamoyl)glutathione conjugate plus 7-methyl saccharin and its free acid which are all herbicidally inactive. Although the data strongly suggest enzymatic involvement, attempts to determine if glutathione-*S*-transferase was involved failed.

6. Metabolizing enzymes in weed species

Metabolism of herbicides in weed species generally produces identical metabolites that were formed in crop plants. Metabolizing enzymes such as glutathione-*S*-transferases (GSTs), cytochrome P450 oxygenases (P450s), glycosyl, and malonyl transferases more or less are well characterized in crop plants [76]. However, only few details have been published on these metabolizing enzymes and cofactors in weeds. The only exception is the glutathione-*S*-transferase superfamily which is widely studied in weeds. GSTs are a ubiquitous group of enzymes catalyzing the conjugation of electrophilic substrates with the tripeptide glutathione (GSH). GSH conjugation has been established as a major detoxication reaction in the metabolism of several classes of herbicides. An atrazine-resistant biotype of *Abutilon theophrasti* was reported to have 4-fold higher GST activities toward the herbicide than those found in the susceptible biotype [77]. The role of GSTs in the selectivity of chloroacetanilide herbicides has been well described in numerous monocot and dicot weed species [78-83].

Both monocot and dicot weeds contain the level of non-protein thiols (mostly GSH) comparable to that of maize (Table 5) [80]. Since the activity of GST enzymes toward herbicidal substrates in weed species is inferior to that of maize, we can conclude that the contribution of nonenzymatic GSH conjugation can be substantial in the metabolism of herbicide in weed species.

The involvement of cytochrome P450 monooxygenases in herbicide detoxication and selectivity has been well demonstrated in plants [84]. However, only few cytochrome P450-mediated herbicide metabolisms were carried out with microsomes from weed species.

Weed species[a]	GSH nmol g^{-1} fresh wt	GST(CDNB) nmol mg^{-1} prot h^{-1}	GST(acetochlor) pmol mg^{-1} prot h^{-1}	Cyt P450 pmol mg^{-1} prot
Avena fatua	267 ± 17	2869 ± 160	922 ± 85	41 ± 11
Bromus secalinus	492 ± 28	676 ± 43	684 ± 79	N/A
Bromus inermis	N/A	N/A	N/A	ND[b]
Echinocloa crus-galli	391 ± 24	170 ± 23	517 ± 49	17 ± 8
Amaranthus retroflexus	140 ± 11	56 ± 8	356 ± 39	10 ± 4
Abutilon theophrasti	309 ± 27	59 ± 7	ND	51 ± 24
Xanthium strumarium	273 ± 12	70 ± 9	874 ± 76	ND
Maize[c]	488 ± 16	986 ± 92	4567 ± 347	67 ± 14

[a]7-day-old etiolated weed seedlings.

[b]ND, not detectable.

[c]4-day-old etiolated maize seedlings.

Table 5. Glutathione contents, GST activities, and cytochrome P450 levels of monocot and dicot weeds and maize

Microsomes from naphthalic anhydride-treated and untreated shattercane and johnsongrass catalyzed the hydroxylation of bentazon [85]. The results indicated that bentazon hydroxylation in shattercane and johnsongrass is mediated by a constitutive and an inducible cytochrome P450 monooxygenase enzyme. Primisulfuron, but not nicosulfuron, was hydroxylated in woolly cupgrass (*Eriochloa villosa*) microsomes [86]. Neither nicosulfuron nor primisulfuron was hydroxylated in shattercane (*Sorghum bicolor*) microsomes. Bentazon and primisulfuron inhibited nicosulfuron hydroxylation in corn microsomes. Bentazon, but not nicosulfuron, also inhibited primisulfuron hydroxylation in the corn microsomes. This indicates that the three herbicides can interact at the same cytochrome P450(s) in corn. Primisulfuron hydroxylation was not inhibited by either bentazon or nicosulfuron in woolly cupgrass microsomes. This suggests that the cytochrome P450(s) for primisulfuron hydroxylation are different between corn and woolly cupgrass.

The role of cytochrome P450 monooxygenases in enhanced metabolism of resistant weed species has also been documented [87, 88]. Cytochrome P450 levels in *Avena fatua* and *Abutilon theophrasti* were found comparable to P450 content of maize (Table 5) [89]. Cytochrome P450 content in the microsomal membrane fraction of *Avena fatua* was 2.4-fold greater than in *Echinochloa crus-galli*. Among dicotyledonous plants, *Abutilon theophrasti* contained 5.1-fold higher level of P450 as compared to that of *Amaranthus retroflexus*.

Since the primisulfuron metabolism in barnyardgrass proceeds through hydroxylation of the pyrimidine moiety followed by formation of glycosyl conjugate we can assume that glycosyl transferases are also present in weed species [71].

http://dx.doi.org/10.5772/61674

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References

[1] Katagi T, Mikami N. Primary metabolism of agrochemicals in plants. In: Roberts T, editor. Metabolism of agrochemicals in plants.Chichester: Wiley; 2000. pp. 43-106.

[2] Owen WJ. Herbicide metabolism as basis for selectivity. In: Roberts T, editor. Metabolism of agrochemicals in plants.Chichester: Wiley; 2000. pp. 211-258.

[3] Rao VS. Principles of weed science. 2nd ed. Enfield: Science Publishers; 2000. 555p.

[4] Yu Q, Powles S. Metabolism-based resistance and cross resistance in crop weeds: A threat to herbicide sustainability and global crop production. Plant Physiology.2014, 166:1106-1118.

[5] Shaner DL. Herbicide safety relative to common targets in plants and mammals.Pesticide Management Science.2003, 60:17-24.

[6] Shimabukuro RH, Walsh WC, Hoerauf RA. Metabolism and selectivity of diclofop-methyl in wild oat and wheat.Journal of Agricultural and Food Chemistry.1979, 27:615-623.

[7] McFadden JJ, Frear DS, Mansager ER. Aryl hydroxylation of diclofop by a cytochrome P450-dependent monooxygenase from wheat, Pesticide Biochemistry and Physiology.1989, 34:92-100.

[8] Boldt PF, Putnam AR. Selectivity mechanisms for foliar applications of diclofop-methyl. II. Metabolism. Weed Science. 1981, 29:237-241.

[9] Holtum JAM, Matthews JM, Hausler RE, Liljegren DR, Powles SB. Cross-resistance to herbicides in annual ryegrass (*Loliumrigidum*). III. On the mechanism of resistance to diclofop-methyl. Plant Physiology.1991, 97:1026-1034.

[10] Preston C, Tardif FJ, Christopher JT, Powles SB. Multiple resistance to dissimilar herbicide chemistries in a biotype of *Loliumrigidum* due to enhanced activity of several herbicide degrading enzymes. Pesticide Biochemistry and Physiology.1996, 54:123–134.

[11] Lefsrud C, Hall JC. Basis for sensitivity differences among crabgrass, oat, and wheat to fenoxaprop-ethyl. Pesticide Biochemistry and Physiology. 1989, 34:218–227.

[12] Tal JA, Romano ML, Stephenson GR, Schwan AL, Hall JC. Glutathione conjugation: A detoxification pathway for fenoxaprop-ethyl in barley, crabgrass, oat, and wheat. Pesticide Biochemistry and Physiology. 1993, 46:190-199.

[13] Tal JA, Hall JC, Stephenson GR. Non-enzymatic conjugation of fenoxaprop-ethyl with glutathione and cysteine in several grass species.Weed Research. 1995, 35:133–139.

[14] Bakkali Y, Ruiz-Santaella JP, Osuna MD, Wagner J, Fischer AJ, De Prado R. Late watergrass (*Echinochloaphyllopogon*): Mechanisms involved in the resistance to fenoxaprop-p-ethyl. Journal of Agricultural and Food Chemistry.2007, 55:4052-8.

[15] Bakkali Y, Ruiz-Santaella JP, De Prado R, Rodriguez JM, Fischer AJ. Resistance mechanisms to fenoxaprop-p-ethyl in a late watergrass (*Echinochloaphyllopogon*) biotype from California. In: Proceedings of the BCPC International Congress; 31 Oct–2 Nov 2005. Glasgow,Alton: The British Crop Protection Council; 2005. Vol. 1, pp. 181-186.

[16] Hendley P, Dicks JW, Monaco TJ, Slyfield SM, Tummon OJ, Barrett JC. Translocation andmetabolism of pyridinyloxy-phenoxypropionate herbicides in rhizomatous quackgrass (*Agropyronrepens*). Weed Science. 1985, 33:11-24.

[17] Coupland D. Pre-treatment environmental effects on the uptake, translocation, metabolism, and performance of fluazifop-butyl in *Elymusrepens*. Weed Research. 1989, 29:289-297.

[18] Hidayat I, Preston C. Enhanced metabolism of fluazifop acid in a biotype of *Digitaria-Sanguinalis* resistant to the herbicide fluazifop-p-butyl. Pesticide Biochemistry and Physiology.1997, 57:137–146.

[19] Buhler DD, Swisher BA, Burnside OC. Behavior of ^{14}C-haloxyfop-methyl in intact plants and cell cultures. Weed Science. 1985, 33:291-299.

[20] Tardif FJ, Leroux GD, Translocation of glyphosate and quizalofop and metabolism of quizalofop in quackgrass biotypes (*Elytrigiarepens*). Weed Technology. 1991, 5:525-531.

[21] Culpepper S, York AC, Jordan DL, Corbin FT, Sheldon YS. Basis for antagonism in mixtures of bromoxynil plus quizalofop-p applied to yellow foxtail (*Setariaglauca*). Weed Technology. 1999, 13:515-519.

[22] Yu H-B, Cheng X-M, Li B. 1(Heterocyclyl),2,4,5-tetrasubstituted benzenes as protoporphyrinogen-IX oxidase inhibiting herbicides. In: Hasaneen MN, editor. Herbicides – Properties, synthesis and control of weeds. InTech: Rijeka; 2012. pp. 103-118.

[23] Theodoridis G, Liebl R, Zagar C. Protoporphyrinogen IX oxidase inhibitors. In: Krämer W, Schirmer U, Jeschke P, Witschel M, editors. Modern crop protection com-

pounds, Vol. 1-3, 2nd ed. Weinheim: Wiley; 2012. pp. 165-195. DOI: 10.1002/9783527644179.

[24] Ritter RL, Coble HD. Penetration, translocation, and metabolism of acifluorfen in soybean (*Glycine max*), common ragweed (*Ambrosia artemisiifolia*), and common cocklebur (*Xanthium pensylvanicum*). Weed Science. 1981, 29:474-480.

[25] Frear DS, Swanson HR, Mansager ER. Acifluorfen metabolism in soybean: Diphenylether bond cleavage and the formation of homoglutathione, cysteine, and glucose conjugates. Pesticide Biochemistry and Physiology.1983, 20:299-310.

[26] Higgins JM, Whitwell T, Corbin FT, Carter GE Jr, Hill HS Jr. Absorption, translocation, and metabolism of acifluorfen and lactofen in pitted morningglory (*Ipomoea lacunosa)* and ivyleafmorningglory (*Ipomoea hederacea*). Weed Science. 1988, 36:141-145.

[27] Dayan FE, Duke SO, Weete JD, Hancock HG. Selectivity and mode of action of carfentrazone-ethyl, a novel phenyl triazolinone herbicide.Pesticide Science.1997, 51:65-73.

[28] Dayan, FE, Weete JD, Hancock HG. Physiological basis for differential sensitivity to sulfentrazone by sicklepod (*Sennaobtusifolia*) and coffee senna (*Cassia occidentalis*). Weed Science. 1996, 44:12–17.

[29] Thomas WE, Troxler SC, Smith WD, Fisher LR, Wilcut JW. Uptake, translocation, and metabolism of sulfentrazone in peanut, prickly sida (*Sidaspinosa*), and pitted morningglory (*Ipomoea lacunosa*). Weed Science. 2005, 53:446-450.

[30] Price AJ, Wilcut JW, Cranmer JR.Physiological behavior of root-absorbed flumioxazin in peanut, ivyleafmorningglory (*Ipomoea hederacea*), and sicklepod (*Sennaobtusifolia*). Weed Science. 2004, 52:718-724.

[31] Flumioxazin. 2013. Available from: http://www.mass.gov/eea/docs/agr/pesticides/aquatic/flumioxazin.pdf [Accessed: 2015-01-14].

[32] Tomigahara Y, Matsui M, Matsunaga H, Isobe N, Kaneko H, Nakatsuka I, Yoshitake A, Yamane S. Metabolism of 7-fluoro-6-(3,4,5,6-tetrahydrophthalimido)-4-(2-propynyl)-2H-1,4-benzoxazin-3(4H)-one (S-53482) in rat. 1. Identification of a sulfonic acid type conjugate. Journal of Agricultural and Food Chemistry.1999, 47:305–312.

[33] Tomigahara Y, Onogi M, Kaneko H, Nakatsuka I, Yamane S. Metabolism of 7-fluoro-6-(3,4,5,6-tetrahydrophthalimido)-4-(2-propynyl)-2H-1,4-benzoxazin-3(4H)-one (S-53482, flumioxazin) in the rat: II. Identification of reduced metabolites.Journal of Agricultural and Food Chemistry.1999, 47:2429–2438.

[34] Ferhatoglu Y, Barrett M. Studies of clomazone mode of action. Pesticide Biochemistry and Physiology.2006, 85:7–14.

[35] Vencill WK, Hatzios KK, Wilson HP. Absorption, translocation, and metabolism of 14C-clomazone in soybean (*Glycine max*) and three *Amaranthus* weed species. Journal of Plant Growth Regulation.1990, 9:127-132.

[36] Liebl RA, Norman MA. Mechanism of clomazone selectivity in corn (*Zea mays*), soybean (*Glycine max*), smooth pigweed (*Amaranthushybridus*), and velvetleaf (*Abutilon theophrasti*). Weed Science. 1991, 39:329-332.

[37] TenBrook PL, Tjeerdema RS.Biotransformation of clomazone in rice (*Oryza sativa*) and early watergrass (*Echinochloaoryzoides*).Pesticide Biochemistry and Physiology. 2006, 85:38–45.

[38] Yasuor H, Zou W, TolstikovVV, Tjeerdema RS, Fischer AJ. Differential oxidative metabolism and 5-ketoclomazone accumulation are involved in *Echinochloaphyllopogon* resistance to clomazone. Plant Physiology.2010, 153:319–326.

[39] Duggleby RG, Pang SS. Acetohydroxyacid synthase. Journal of Biochemistry and Molecular Biology. 2000, 33:1–36.

[40] Krämer W, Schirmer U, Jeschke P, Witschel M, editors. Modern crop protection compounds, volume 1-3. 2nd ed. Weinheim: Wiley; 2012. 1608 p. DOI: 10.1002/9783527644179.

[41] Zhou Q, Liu W, Zhang Y, Liu KK. Action mechanisms of acetolactate synthase-inhibiting herbicides. Pesticide Biochemistry and Physiology. 2007, 89:89–96.

[42] Brown MA, Chiu TY, Miller P. Hydrolytic activation versus oxidative degradation of Assert herbicide, an imidazolinone aryl-carboxylate, in susceptible wild oat versus tolerant corn and wheat.Pesticide Biochemistry and Physiology.1987, 27:24–29.

[43] Nandula VK, Messersmith CG. Imazamethabenz-resistant wild oat (*Avenafatua L.*) is resistant to diclofop-methyl. Pesticide Biochemistry and Physiology.2002, 74:53–61.

[44] Shaner DL, Robson PA. Absorption, translocation, and metabolism of AC 252 214 in soybean (*Glycine max*), common cocklebur (*Xanthium strumarium*), and velvetleaf (*Abutilon tbeophrasti*). Weed Science. 1985, 33:469–471.

[45] Risley MA, Oliver LR. Absorption, translocation, and metabolism of imazaquin in pitted (*Ipomoea lacunosa*) and entireleaf (*Ipomoea hederacea var. integriuscula*) morningglory. Weed Science. 1992, 40:503–506.

[46] Cole TA, Wehtje GR. Wilcut JW, Hicks TV. Behavior of imazethapyr in soybeans (*Glycine max)*, peanuts (*Arachishypogaea*), and selected weeds. Weed Science. 1989, 37:639–644.

[47] Nissen SJ, Masters RA, Stougaard RN. Imazethapyr absorption and fate in leafy spurge (*Euphorbia esula*). Weed Science. 1994, 42:158–162.

[48] Ballard TO, Foley ME, Bauman TT. Absorption, translocation, and metabolism of imazethapyr in common ragweed (*Ambrosia artemisiifolia*) and giant ragweed (*Ambrosia trifida*). Weed Science. 1995, 43:572–577.

[49] Pester TA, Nissen SJ, Westra P. Absorption, translocation, and metabolism of imazamox in jointed goatgrass and feral rye. Weed Science. 2001, 49:607–612.

[50] Vassios JD, Nissen SJ, Brunk GR. Imazamox absorption, desorption, and metabolism by Eurasian watermilfoil. Journal of Aquatic Plant Management.2011, 49:44–49.

[51] Sweetser PB, Schow GS, Hutchison JM. Metabolism of chlorsulfuron by plants: Biological basis for selectivity of a new herbicide for cereals. Pesticide Biochemistry and Physiology.1982, 17:18–23.

[52] Müller F, Kang BH, Maruska FT. Fate of chlorsulfuron in cultivated plants and weeds and reasons for selectivity. Mededelingen Faculteit Landbouwwetenschappen Rijksuniversiteit Gent. 1984, 49/3b:1091–1108.

[53] Hageman LH, Behrens R. Basis for response differences of two broadleaf weeds to chlorsulfuron. Weed Science. 1984, 32:162–167.

[54] Hutchison JM, Shapiro R, Sweetser PB. Metabolism of chlorsulfuron by tolerant broadleaves. Pesticide Biochemistry and Physiology. 1984, 22:243–247.

[55] Mallory-Smith CA, Thill DC, Dial MJ. Identification of sulfonylurea herbicide-resistant prickly lettuce (*Lactuca serriola*). Weed Technology. 1990, 4:163–168.

[56] Primiani MM, Conerman JC, Saari LL. Resistance of kochia (*Kochia scoparia*) to sulfonylurea and imidazolinone herbicides. Weed Technology. 1990, 4:169–172.

[57] Saari LL, Maxwell CA. Target-site resistance for acetolactate sythase inhibitor herbicides. In: De Prado R, Jorrin J, Garcia-Torres L, editors. Weed and crop resistance to herbicides. Dordrecht: Kluwer; 1997. pp. 81–88.

[58] Christopher JT, Powles SB, Holtum JAM, Liljegren DR. Cross-resistance to herbicides in annual ryegrass (*Loliumrigidum*). II. Chlorsulfuron resistance involves a wheat-like detoxification system. Plant Physiology.1991, 95:1036–1043.

[59] Cotterman JC, Saari LL. Rapid metabolic inactivation is the basis for cross-resistance to chlorsulfuron in diclofop-methyl-resistant rigid ryegrass (*Lolium rigidurn*) biotype SR4/84. Pesticide Biochemistry and Physiology. 1992, 43:182–192.

[60] Burnet MWM, Christopher JT, Holtum JAM, Powles SB. Identification of two mechanisms of sulfonylurea resistance within one population of rigid ryegrass (*Lolium rigidum*) using a selective germination medium. Weed Science. 1994, 42:468–473.

[61] Preston C, Tardif FJ, Christopher JT, Powles SB. Multiple resistance to dissimilar herbicide chemistries in a biotype of *Loliumrigidum* due to enhanced activity of several herbicide degrading enzymes. Pesticide Biochemistry and Physiology.1996, 54:123–134.

[62] Brown HM, Neighbors SM. Soybean metabolism of chlorimuron ethyl: Physiological basis for soybean selectivity. Pesticide Biochemistry and Physiology.1987, 29:112–120.

[63] Brown HM, Fuesler TP, Ray TB, Strachan SD. Role of plant metabolism in crop selectivity of herbicides. In: Frehse H, editor. Pesticide chemistry: Advances in international research, development and legislation. Weinheim: VCH; 1991. pp. 257–266.

[64] Brown HM, Wittenbach EA, Forney DR, Strachan SD. Basis for soybean tolerance to thifensulfuron methyl. Pesticide Biochemistry and Physiology. 1990, 37:303–313.

[65] Walker LM, Hatzios KK, Wilson HP. Absorption, translocation, and metabolism of 14C-thifensulfuron in soybean (*Glycine max*), spurred anoda (*Anoda cristata*), and velvetleaf (*Abutilon theophrasti*). Journal of Plant Growth Regulation. 1994, 13:27–32.

[66] Obrigawitch TT, Kenyon WH, Kuratle H. Effect of application timing on rhizome johnsongrass (*Sorghum halepense*) control with DPX-V9360. Weed Science. 1990, 38:45–49.

[67] Hinz JRR, Owen MDK. Nicosulfuron and primisulfuron selectivity in corn (*Zea mays*) and two annual grass weeds. Weed Science. 1996, 44:219–223.

[68] Gallaher K, Mueller TC, Hayes RM, Schwartz O, Barrett M. Absorption, translocation, and metabolism of primisulfuron and nicosulfuron in broadleaf signalgrass (*Brachiaria-platyphylla*) and corn. Weed Science. 1999, 47:8–12.

[69] Sidhu SS, Yu J, McCullough P. Nicosulfuron absorption, translocation, and metabolism in annual bluegrass and four turfgrass species. Weed Science. 2014, 62:433–440. DOI: http://dx.doi.org/10.1614/WS-D-13-00182.1.

[70] Carey JB, Penner D, Kells JJ. Physiological basis for nicosulfuron and primisulfuron selectivity in five plant species. Weed Science. 1997, 45:22–30.

[71] Neighbors S, Privalle LS. Metabolism of primisulfuron by barnyard grass.Pesticide Biochemistry and Physiology.1990, 37:145–153.

[72] Anderson JJ, Priester TM, Shalaby LM. Metabolism of metsulfuron methyl in wheat and barley.Journal of Agricultural and Food Chemistry.1989, 37:1429–1434.

[73] Brown HM, Wittenbach EA, Forney DR, Strachan SD. Basis for soybean tolerance to thifensulfuron methyl. Pesticide Biochemistry and Physiology. 1990, 37:303–313.

[74] Sterling TM, Jochem HS. Uptake, translocation, and metabolism of picloram and metsulfuron methyl by two locoweed species. Weed Science. 1995, 43:13–17.

[75] Wittenbach VA, Koeppe MK, Lichtner FT, Zimmerman WT, Reiser RW. Basis of selectivity of triflusulfuron methyl in sugar beets (*Beta vulgaris*). Pesticide Biochemistry and Physiology, 1994, 49:72–81.

[76] Cole DJ, Edwards R. Secondary metabolism of agrochemicals in plants. In: Roberts T, editor. Metabolism of agrochemicals in plants.Chichester: Wiley; 2000. pp. 107–154.

[77] Anderson MP, Gronwald JW. Atrazine resistance in a velvetleaf (*Abutilon theophrasti*) biotype due to enhanced glutathione S-transferase activity.Plant Physiology. 1991. 96:104–109.

[78] Hatton PJ, Dixon D, Cole DJ, Edwards R. Glutathione transferase activities and herbicide selectivity in maize and associated weed species. Pesticide Science.1996, 46:267–275.

[79] Andrews CJ, Skipsey M, Townson JK, Morris C, Jepson I, Edwards R. Glutathione transferase activities toward herbicides used selectively in soybean. Pesticide Science. 1997, 51:213–222.

[80] Hatton PJ, Cummins I, Price LJ, Cole DJ, Edwards R. Glutathione transferases and herbicide detoxification in suspension-cultured cells of giant foxtail (*Setariafaberii*). Pesticide Science.1998, 53:209–216.

[81] Cummins I, Bryant DN, Edwards R. Safener responsiveness and multiple herbicide resistance in the weed black-grass (*Alopecurusmyosuroides*). Plant Biotechnology Journal.2009, 7:807–820.

[82] Del Buono D, Scarponi L, Espen L. Glutathione S-transferases in *Festucaarundinacea*: Identification, characterization and inducibility by safenerbenoxacor. Phytochemistry.2007, 68:2614–2624.

[83] Jablonkai I, Hulesch A, Dutka F. Influence of herbicides and safeners on glutathione content and glutathione S-transferase activities of monocot and dicot weeds. In: De-Prado R, Jorrin, Garcia-Torres L, Marshall G, editors. Proceedings of the International Symposium on Weed and Crop Resistance to Herbicides.Cordoba (Spain); 1995. pp. 89–91.

[84] Siminszky B. Plant cytochrome P450-mediated herbicide metabolism. Phytochemistry Reviews. 2006, 5:445–458.

[85] Burton JD, Maness EP. Constitutive and inducible bentazon hydroxylation in shuttercane (*Sorghum bicolor*) and Johnsongrass (*Sorghum halapense*).Pesticide Biochemistry and Physiology.1992, 44:40–49.

[86] Hinz JRR, Owen MDK, Barrett M. Nicosulfuron, primisulfuron, and bentazon hydroxylation by corn (*Zea mays*), woolly cupgrass (*Eriochloavillosa*), and shattercane (*Sorghum bicolor*) cytochrome P-450. Weed Science. 1997, 45:474–480.Burnett MWM, Loveys BR, Holtum JAM, Powles SB. A mechanism of chlortoluron resistance in *Loliumrigidum*.Planta.1993, 190:182–189.

[87] Burnett MWM, Loveys BR, Holtum JAM, Powles SB. A mechanism of chlortoluron resistance in *Loliumrigidum*.Planta.1993, 190:182–189.

[88] Burnett MWM, Loveys BR, Holtum JAM, Powles SB. Identification of two mechanisms of sulfonylurea resistance within one population of rigid ryegrass (*Loliumrigidum*) using a selective germination medium. Weed Science. 1994, 42:153–157.

[89] Jablonkai I, Hulesch A. Cytochrome P450 levels of monocot and dicot weeds and influence of herbicides, safeners and P450 inhibitors on enzyme contents. In: Brown H, Cussans GW, Devine MD, Duke SO, Fernandez-Quintanilla, Helweg A, Labrada RE, Landes M, Kudsk P, Streibig JC, editors. Proceedings of the 2nd International Weed Control Congress.Copenhagen (Denmark); 1996. Vol. 3, p. 789–794.

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