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Herbicide safeners: uses, limitations, metabolism, and mechanisms of action

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Abstract

Several methods were examined to minimize crops injury caused by herbicides. Thus increase their selectivity. A selective herbicide is one that controls weeds at rates that do not injure the crop. Herbicides are selective in a particular crop within certain limits imposed by the herbicide, the plant, the application rate, the method and time of application, and environment conditions.

Herbicide safeners are compounds of diverse chemical families. They are applied with herbicides to protect crops against their injury. Using chemical safeners offer practical, efficient and simple method of improving herbicide selectivity. This method has been applied successfully in cereal crops such as maize, rice and sorghum, against pre-emergence thiocarbamate and chloroacetanilide herbicides. Some reports indicate promising results for the development of safeners for post-emergence herbicides in broadleaved crops.

Various hypotheses were proposed explaining mechanisms of action of herbicide safeners: interference with uptake and translocation of the herbicide, alteration in herbicide metabolism, and competition at site of action of the herbicide.

Even though progress was made in the development of herbicide safeners and in understanding their mechanisms of action, more research is needed to elucidate clearly how these chemicals act and why their activity is restricted to particular crops and herbicides.
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Keywords: Safeners; Herbicides; Thiocarbamates; Chloroacetamides; Selectivity

1. Introduction

Adsorbents are substances early used to physically shield the crop seed from contact with the herbicide that otherwise would cause injury. This approach included the use of activated carbon, lignin by products, ion exchange resins, and various clays (Goffrey and Warren, 1969; Gupta and Niranwad, 1976; Blair, 1979; Hoagland, 1989; Burton and Maness, 1992; Yelverton et al., 1992). The requirements of an application technique different from that used for herbicide application, the expense, and inadequate control of weeds have forced the search for a better alternative.

The observation of an antagonistic interaction between the herbicide 2,4-D and the herbicide 2,4,5-T (Hoffman, 1953) led to development of chemicals that may be applied with the herbicide to protect the crop plant against herbicide injury. Research by Hoffman led to the introduction of naphthalic anhydride as the first commercial safener in 1971 against thiocarbamate herbicides in corn (*Zea mays* L.) (Hoffman, 1969, 1978).

The research in this field has proceeded and a large number of chemicals have been screened as potential

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safeners. As related to their terminology, the word safener is used interchangeably with antidotes, antagonists and protectants (Hatzios, 1983).

Among several chloroacetamide chemicals tested, dichlormid (2,2-dichloro-*N*,*N*-diallylacetamide) was shown to be the most active chemical to protect cereal crops against thiocarbamate herbicides (Chang et al., 1973; Pallos et al., 1978). Dichlormid was introduced as a commercial safener in 1972.

The safening activity of oxime ether compounds has been successfully examined and three of them were introduced as commercial safeners (e.g., cyometrinil, oxabetrinil, and CGA-15281) against chloroacetanilide herbicides in sorghum (*Sorghum bicolor*) (Ellis et al., 1980; Chang and Merkle, 1982). Later, the thiazolecarboxylic acid (flurazole) was introduced against alachlor in sorghum (Sacher et al., 1983). Then, the safener fenclorim was introduced against the herbicide pretilachlor in rice (*Oryza sativa* L.) (Hatzios, 1996). Other chemicals such as pyrimidine triazole derivatives (Strelkov et al., 1998), or of undisclosed identity have shown different types of safening activity (Pallos et al., 1978; Dutka and Komives, 1987; Bussler et al., 1991; Komives, 1992; Frazier and Nissen, 1994; Nagy and Balogh, 1995; Repasi et al., 1995; Omokawa et al., 1996; Davies and Caseley, 1999; Sprague et al., 1999).

Some success has been achieved in the protection of broadleaved crops such as soybean (*Glycine max* L.) against metribuzin (Varvina, 1987; Phatak and Varvina, 1989), against chloramben in cucumber (*Cucumis sativus*) (Kneer and Hoppen, 1989), and against sulfonylurea herbicides (Devlin and Zebiec, 1990). Microorganism that degrade EPTC were applied by inoculation and used as safeners in corn (*Zea mays* L.) (Nagy et al., 1991). A list of names of common safeners is listed in Table 1.

This article reviews research on uses, activity, mechanisms of action, and metabolism of herbicide safeners.

Table 1
Chemical nomenclature of herbicide safeners

Compound	Chemical name
1,8-Naphthalic anhydride	Naphthalene-1,8-dicarboxylic anhydride
Dichlormid	*N*,*N*-diallyl-2,2-dichloroacetamide
Cyometrinil	(*Z*)-cyanomethoxyimino(phenyl)acetonitrile
Oxabetrinil	(*Z*)-1,3-dioxolan-2-ylmethoxyimino-(phenyl)acetonitrile
Flurazole	Benzyl-2-chloro-4-trifluoromethyl-1,3-thiazole-5-carboxylate
Fenclorim	4,6-Dichloro-2-phenylpyrimidine
Benoxacor	(*RS*)-4-dichloroacetyl-3,4-dihydro-3-methyl-2*H*-1,4-benzoxazine
Fluxofenim	4-Chloro-2,2,2-trifluoroacetophenone *O*-1,3-dioxolan-2-ylmethyloxime

The review is also focused on the need for further research in this area, particularly using modern techniques to understand safeners mechanisms of action.

2. Uses

Naphthalic anhydride is the most versatile safener. It is less specific botanically and chemically than others. It protects various crops against a wide range of herbicides. Naphthalic anhydride has been tested successfully to protect corn (*Zea mays* L.) against thiocarbamates and chloroacetanilides. It was useful in the protection of rice, grain sorghum (*Sorghum bicolor*), and oats (*Avena sativa* L.) (Hoffman, 1978; Hatzios, 1983), and was capable of providing safening activity against post-emergence application of selected herbicides (Parker, 1983). Naphthalic anhydride enhanced the tolerance of wheat (*Triticum* spp.) (Miller et al., 1978), oats (*Avena sativa* L.) and barley (Chang et al., 1976; Blair, 1978) to Barban. Also its safening activity has been extended to include broadleaved crops such as bean against EPTC (Blair, 1979). Codde (1988) detected its safening activity against the herbicide diclofop-methyl in oats (*Avena sativa* L.). Milhome and Batside (1990) demonstrated that it was active against metsulfuron in corn (*Zea mays* L.).

Dichlormid was effective among other chloroacetamides (when added in small amount) in preventing the onset of EPTC injury to plants (Chang et al., 1973; Pallos et al., 1978). The safening activity of dichlormid was effective against chloroacetanilide herbicides (Leavitt and Penner, 1978), sethoxydim (Hatzios, 1984), and against chlorsulfuron (Ploge, 1989).

Oxime ethers exhibited good chemical and botanical specificity in being highly selective safeners against chloroacetanilide herbicides in grain sorghum (*Sorghum bicolor* L.) (Chang and Merkle, 1982).

Furthermore, the safener flurazole has been introduced commercially against the herbicide alachlor in grain sorghum (*Sorghum bicolor* L.). Flurazole has high degree of chemical specificity failing to protect corn (*Zea mays* L.) against thiocarbamate herbicides (Hatzios, 1986). Later on, the safener fenclorim was introduced to protect rice (*Oryza sativa* L.) against the herbicide pretilachlor (Hatzios, 1993). In summary, safeners activity is determined by selection of the herbicide and the crop. Even though a progress was made in developing effective safeners, more work is needed to formulate an approach of developing safeners reliable in the field and applicable for offering protection when use in low amount against the common used herbicides.

3. Methods of application

Chemical and botanical specificity of the safener determines the most appropriate method of application.

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Napthalic anhydride has limited specificity and offers protection to weeds when applied to soil. Thus it is mainly used as seed coating at a rate of 0.5% (w/w) of seed (Guneyli, 1971; Hoffman, 1978).

Dichlormid has a good availability to plants from soil. Due to simplicity of this method, dichlormid is sold as a pre-packed formulation with the herbicide (Gray and Green, 1982; Hatzios, 1983).

Due to their marginal selectivity and their protection of weeds when applied to soil, oxime ether safeners are used as seed coating of grain sorghum (*Sorghum bicolor* L.) (Ellis et al., 1980). Furthermore, the safener flurazole was effective when applied to soil as seed dressing. It seems that the commonly used safeners are having limitations either in offering protection for certain crops or against specific herbicides. The challenge is to introduce safeners that have wide range of activity in the field.

4. Structure–activity relationship

Among the studies examined structure–activity relationships of safeners, there was disagreement on significance of specific functional group for safenening activity. The presence of a dicarboxylic anhydride group and at least one aromatic ring attached directly to the anhydride was essential for the safening activity of naphthalic anhydride and its analogues (Zama and Hatzios, 1986).

On the other hand, the similarity of structures between chloroacetamide safeners and chloracetanilide herbicides has been studied as a base for their activity (Dutka et al., 1979; Yenne and Hatzios, 1991; Repasi et al., 1995). In a soil-free system, the most effective safener was the one most similar in structure to the herbicide (Stephenson and Chang, 1978). Mono and trichloroacetamides were less effective as safeners compared to dichloro compounds (Dutka et al., 1979). Those chemicals with two substitutes on the nitrogen were more active than those with one group (Dutka et al., 1979). However, dichloroaceto group was essential for activity of chloroacetamide safeners (Dutka and Komives, 1987).

Examination of structure–activity relationship of oxime ethers revealed that presence of oxime and pyridine groups or two oxime groups and an aryl group attached to oxygen in the molecule was essential for the safening activity of oxime ethers (Chang and Merkle, 1982; Chang, 1983).

5. Transformation

Safeners undergo transformation in soil, plant and in mammals. Rate of transformation and transformation products depends upon the safener, the medium where it resides, and environmental factors. In soil, decarboxylation of naphthalic anhydride represented a major pathway of its degradation (Riden and Asbell, 1975). Dichlormid underwent dechlorination, dealkylation, oxidation and hydrolysis following application to soil (Miaullis et al., 1978). Naphthalic acid has been identified as a metabolite of naphthalic anhydride in plants (Codde, 1988).

Dichlormid transformed through oxidation, dealkylation, dechlorination, hydrolysis and conjugation with plant constituents (Miaullis et al., 1978). On the other hand, conjugation of flurazole with glutathione (GSH) has been demonstrated (Breaux et al., 1989).

In mammals, metabolism of dichlormid was similar to that demonstrated in plant and soil. Glycolamide, glyoxamidoxamic acid and dichloroacetic acid were identified as final metabolites of dichlormid (Miaullis et al., 1978).

No published studies examined significance of the degradation products of safeners. Further research is needed examining efficacy and the toxicological impact of these compounds.

6. Limitations and adverse effects

In the field, performance of safeners is influenced by environmental factors such as temperature, soil moisture, soil structure, and the rate of application of the safener. As an example, application of naphthalic anhydride at high rate that that used for the safening activity caused an injury of crops (Blair, 1979). At a commercial rate, injury symptoms such as stunning and chlorosis have been detected following application of naphthalic anhydride in corn (*Zea mays* L.) and sorghum (*Sorghum bicolor* L.) (Thiessen et al., 1980; Hatzios, 1984). Further, performance of naphthalic anhydride against EPTC was marginal in sandy or silt soil compared to clay loam soil (Guneyli, 1971).

Soil incorporation, seed placement, cultivator type and herbicide behavior (e.g. leaching, breakdown) have affected performance of dichlormid (Burt, 1976). The difference in the degree of solubility between EPTC and dichlormid caused leaching of the two compounds at different rate under heavy rainfall or irrigation conditions, causing the loss of the two chemicals from the treated zone, then causing plant injury (Burt and Buzio, 1980). Published reports showed significant reduction in the germination rate of sorghum (*Sorghum bicolor* L.) following the use of oxabetrinil and cyometrinil (Turner et al., 1982; Yenne and Hatzios, 1990). It seems that more research is required to develop safeners that are reliable under vulnerable soil and environmental conditions.

7. Mechanisms of action

Early investigations suggested that safeners might act through a single mechanism that was assumed to be

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common to all crop-herbicide safener combinations (Hatzios, 1983). Ezra et al. (1983) hypothesized that action of safeners may be the result of a series of multiple interactions between safener and herbicide. The fact that the currently available safeners exhibit botanical specificity for graminaceos crops with moderate tolerance to herbicides and chemical selectivity toward soil applied and shoot absorbed thiocarbamates and chloroacetanilides led to a suggestion that the action of safeners relates to physiological, biochemical and molecular function(s). The explanation is that these functions may are unique in these crops or are highly efficient in the graminaceos crops that affected by thiocarbamates and chloroacetanilides and altered by safeners. But it seems that these systems are either not present or not affected to the same extent by herbicides and safeners in other crops (Hatzios, 1997).

Similarity between the site(s) of uptake and action of both safeners and herbicides in the coleoptiles region of the plant shoot led to a suggestion that safeners might counteract herbicides at the site of uptake or action (Gray and Joo, 1976). The fact that the available safener should be applied simultaneously or before application of the herbicide indicates they prevent but not reverse the injury caused by the herbicide (Hatzios, 1983; Stephenson and Ezra, 1985). Details of proposed mechanisms of actions of the available safeners are outlined below.

7.1. Absorption and/or translocation

Safeners effect on absorption/translocation of the herbicide could be through chemical interaction, biochemical disruption of some processes that may cause an alteration in pattern of uptake and distribution of the herbicide, or by competition at the site(s) of entry with the herbicide (Hatzios, 1983). Previous studies showed that safeners reduced uptake and/or translocation of herbicides (Ezra and Gressel, 1982; Ketchersid et al., 1982; Fuerst, 1987; Varvina, 1987; Fuerst et al., 1991), simulated the uptake (Zama and Hatzios, 1986; Milhome and Batside, 1990), or resulted of no effect (Marton et al., 1978; Rubin et al., 1985; Lamoureux and Rusness, 1992).

7.2. Metabolism

Tolerance of plant to the herbicide correlates with rate of detoxification (Hatzios and Penner, 1985; Breaux et al., 1987; Dodge, 1990). Safeners might alter herbicide metabolism directly by acting as chemicals activators of particular functional group(s) in the herbicide, or by affecting biological system(s) (e.g. enzymes) involved in herbicide metabolism (Hatzios, 1983; Fuerst et al., 1995). Alteration of herbicide metabolism has been proposed as the most likely mechanism of action of safeners (Sagral, 1978; Zama and Hatzios, 1986; Gronwald, 1989; Fuerst et al., 1991; Tal et al., 1993; Burton et al., 1994).

Metabolism of thiocarbamates and chloroacetanilides is believed to be catalyzes by mixed function oxidase enzymes (Casida et al., 1975; Komives and Dutka, 1989; Morteland et al., 1993). Published studies suggested that saferens could induce activity of the mixed function oxidase enzymes. This induction may enhance oxidation and hydroxylation of the herbicides (Hubbell and Casida, 1977; Dutka and Komives, 1983; Brooks et al., 1987; Komives and Dutka, 1989; Barta and Dutka, 1991; Burton and Maness, 1992; Morteland et al., 1993; Jablonkai and Hatzios, 1994; Frear and Swanson, 1996). However, there is no conclusive evidence correlate induction of these enzymes by the action of the available safeners.

Conjugation of herbicides with GSH is a common pathway of metabolism. Rate of conjugation is related to tolerance of plant to a herbicide (Jablonkai and Hatzios, 1991; Tal et al., 1993; Cummins et al., 1999). Published studies showed that safeners increased GSH content in plants (Casida et al., 1975; Yenne and Hatzios, 1990; Fuerst et al., 1991; Ekler et al., 1993; Farago et al., 1994), and/or induced activity of glutathione-*S*-transferase (GST) enzyme (Hubbell and Casida, 1977; Holt et al., 1985; Lay and Niland, 1985; Komives and Dutka, 1986; Fuerst et al., 1993; Jepson et al., 1994; Miller et al., 1994; Schroder and Pflugmacher, 1996; Richers et al., 1997). The suggestion is that an increase of GSH content of in the activity of the enzyme that catalyze conjugation if the herbicide may increase rate of metabolism of the herbicide into non-toxic metabolites. In this aspect, elucidation a conclusive mechanisms of action of safeners will remain a challenge that requires further research.

7.3. Competition at site(s) of action

One of the proposed hypotheses of safeners mechanisms of action is that safeners may counteract action of the herbicide at the target site(s) buy affecting physiological and biochemical process involved in the action of the herbicide (Chang and Merkle, 1982; Hatzios, 1983; Wilkinson, 1985; Walton and Casida, 1995). Some of these effects are listed in Table 2. Mechanism of action of thiocarbamate and chloroacetanilide herbicides has not been fully elucidated. Their effects on plants show that more than one site of action is involved in their mechanism of action. Symptoms of injury caused by thiocarbamates included stunting and dark-green leathery leaves (Harvey et al., 1975), inhibition of shoot growth (Deal and Hess, 1980), failure of young leaves to unroll (Donald, 1981); twisting of shoots (Barta et al., 1983), and distorted, brittle and hard leaves (Sagral, 1978). Safeners could compete with herbicides at the target site either by preventing the herbicide from

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Table 2
Effects of safeners on physiological or biochemical systems

Safener	Effect	Crop	Reference
Dichlormid	Lipid biosynthesis	Corn (*Zea mays* L.)	Sagral (1978); Ezra et al. (1983)
1,8-Naphthalic anhydride and dichlormid	Fatty acid synthesis	Corn (*Zea mays* L.)	Wilkinson (1978)
Fenclorim	Acetate incorporation into lipid	Rice (*Oryza sativa* L.)	Han and Hatzios (1991)
Dichlormid	Cuticle formation	Corn (*Zea mays* L.)	Barta and Dutka (1989)
Dichlormid	Protein synthesis	Corn (*Zea mays* L.)	Sagral (1978)
1,8-Naphthalic anhydride and dichlormid	Membrane permeability	Onion roots	Mellis et al. (1982)
Fenclorim	Long chain fatty acids	Rice (*Oryza sativa* L.)	Wu et al. (2000)

reaching or acting on the target site, or through acting at a different site producing an effect that alter physiological or biochemical process which ultimately lead to counter action of the herbicide (Hatzios, 1996). Previous studies examined several site of actions of herbicides and the effect of safeners of these sites.

7.3.1. Lipid synthesis

Lipid biosynthesis has been detected as a site of action of thiocarbamates and chloroacetanilides (Wilkinson and Smith, 1975; Hatzios, 1991). Dichlormid reversed inhibition of lipid biosynthesis that caused by EPTC in corn (*Zea mays* L.) (Sagral, 1978; Ezra et al., 1983). Naphthalic anhydride and dichlormid countered thiocarbamates effects on fatty acid synthesis in corn (*Zea mays* L.). Application of fenclorim with pretilachlor reversed inhibition of acetate incorporation into total lipid that caused by pretilachlor (Han and Hatzios, 1991). Wu et al. (2000) suggested that the herbicides pretilachlor and metolachlor may inhibit the synthesis of very long chain fatty acids or of the incorporation of unsaturated fatty acids into non-lipids of rice (*Oryza sativa* L.). Such inhibition might be counteracted by the safeners fenclorim, benoxacor and fluxofenim.

7.3.2. Epicuticular wax

Degradation of epicuticular wax layer increases plant susceptibility to environmental stresses and increase rate of transpiration resulting in an increase of uptake of herbicides from soil (Barta and Dutka, 1989). Herbicides and safeners interfered with cuticle formation in an opposite ways in corn (*Zea mays* L.) (Leavitt and Penner, 1978; Barta et al., 1983; Barta and Dutka, 1989).

7.3.3. Protein synthesis

Inhibition of protein synthesis by thiocarbamates and chloroacetanilides has been reported (Deal et al., 1980; Ndahi, 1988). Sagral (1978) reported dichlormid reversed inhibition of protein synthesis caused by EPTC in corn (*Zea mays* L.). Han and Hatzios (1991) showed that safeners reduced inhibition of valine incorporation into protein in rice (*Oryza sativa* L.) that caused by pretilachlor.

7.4. Other sites of action

Inhibition of the biosynthesis of gibberellins by thiocarbamates and chloroacetanilides was reversed by dichlormid in corn (*Zea mays* L.) (Wilkinson, 1985). Alteration of membrane permeability by EPTC and metolachlor was prevented by dichlormid and naphthalic anhydride in onion roots (Mellis et al., 1982). Sagral (1978) reported that dichlormid countered inhibition of photosynthesis as a result of CO_2 fixation caused by EPTC in corn (*Zea mays* L.).

8. Pro-safeners

Rubin and Casida (1985), and Rubin and Kirino (1989) examined several chemicals that exert safening activity after transformation(s) steps. An example of pro-safener is the compound L-oxothiazolidine-4-carboxylate (OTC) that transform into cysteine that is incorporated into GSH, and GSH in turn conjugates with herbicides (Hilton and Pillai, 1986; Ploge, 1989; Hilton et al., 1990).

9. Microbial safeners

Genes encoding for enzymes that degrade herbicides may be incorporated into appropriate plastids. Then introduced into bacteria colonizing roots or seeds of susceptible plants. This method has shown to be successfully to provide protection to corn (*Zea mays* L.) against thiocarbamates injury (Nagy et al., 1991, 1995; Veylder et al., 1997).

10. Conclusion

In summary there is no conclusive mechanism explaining action of the available safeners. The suggestion

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that safeners act through a single mechanism unrealistic and the interaction of a series of steps leading to safening is likely.

It seems that interference of safeners with GSH and related systems is the most common hypothesis trying to explain the mechanisms of action of safeners. Since this is related directly to an enhancement of their detoxification in the plants. However, the work unraveling the mechanisms of action of herbicide safeners will continue to challenge the ingenuity of investigators in the future. Selected areas that need to be investigated further include:

(1) The mechanisms of safener action should be extended to the molecular level. Recent report examining structure–activity relationship between safeners and herbicides using comparative molecular field analysis is promising (Bordas et al., 2000).
(2) Effect of safeners on gene expression in plants and weather theses regulatory effects of safeners are related to the biochemical and physiological effects exerted by the antagonized herbicides is an area of research (Veylder et al., 1997).
(3) The physiological, biochemical and molecular interactions between herbicides and safeners on plants should establish which effects of safeners and herbicides are of primary or secondary importance and if the secondary effects are totally unrelated to safening activity.
(4) Do safeners conjugate with GSH. Is this conjugation catalyzed by specific GST enzymes or by the same GST enzymes that catalyze the conjugation of the herbicides? Dixon et al. (1998) reported that the safener dichlormid and the herbicide metolachlor enhanced expression of GST II subunit in corn (*Zea mays* L.).
(5) What is the role of mixed-function oxidases in the metabolism of herbicides whose effects are counteracted by safeners? Are they induced by safeners? Ohkawa et al. (1999) reported the involvement of cytochrome P450 monooxygenases in the mode of action of safeners. Are other oxidative enzymes such as peroxygenases, peroxidases, lipooxygenases, etc., involved in the metabolism or action of selected safeners.
(6) What is the impact of safeners on herbicide environmental fate. Their effect on herbicides metabolism by soil microorganisms, especially in soils where high herbicide residue may exist? What is the effect of that on the amount of the herbicide available to the plant, as well as the influence on the carry over problems, and their effects on herbicide enhanced degradation and to environmental consideration? Recent report ruled out effect of the safener dichlormid on photodegradation of the herbicide EPTC (Abu-Qare and Duncan, 2002).

References

Abu-Qare, A.W., Duncan, H.J., 2002. Photodegradation of the herbicide EPTC and the safener dichlormid, alone and in combination. Chemosphere 46, 1183–1189.

Barta, I.C., Dutka, F., 1989. Effects of thiocarbamate herbicides and dichlormid antidote on cuticular transpiration of corn. Cereal Res. Commun. 17, 135–140.

Barta, I.C., Dutka, F., 1991. Interaction of maize cytochrome P450 with safeners and 1-aminobenztriazole. Brit. Crop Prot. Conf-Weeds 3, 1127–1132.

Barta, I.C., Komives, T., Dutka, F., 1983. Effects of EPTC and its antidotes on epicultucular wax of corn. Develop. Food Sci. 11, 277–283.

Blair, A.M., 1978. Interaction between barabn and protectants on maize, oats, barley. Weed Res. 18, 65–74.

Blair, A.M., 1979. The interaction of protectants with EPTC on field bean and triallate on wheat. Anal. Appl. Biol. 92, 105–109.

Bordas, B., Komives, T., Szanto, Z., Lopatal, A., 2000. Comparative three-dimensional quantitative structure: activity relationships study of safeners and herbicides. J. Agric. Food Chem. 48, 926–931.

Breaux, E.J., Hoobler, M.A., Patanella, J.E., Leyes, G.A., 1989. Mechanisms of action of thiazole safeners. In: Hatzios, K.K., Hoagland, R.E. (Eds.), Crop Safeners for Herbicides: Development, Uses and Mechanisms of Action. Academic Press, New York, pp. 163–175.

Breaux, E.J., Patanella, J.E., Sanders, E.F., 1987. Chloroacetanilide herbicides selectivity: analysis of glutathione and homoglutathione in tolerant, susceptible and safened seedlings. J. Agric. Food Chem. 35, 474–478.

Brooks, R.L., Ketchersid, M.L., Merkle, M.G., 1987. Effects of sorghum seed safeners on sorghum mixed function oxidases. Proc. South Weed Sci. Soc. 40, 328–330.

Burt, G.W., 1976. Factors affecting thiocarbamate injury to corn II. Soil incorporation, seed placement, leaching and breakdown. Weed Sci. 24, 327–330.

Burt, G.W., Buzio, C.A., 1980. Leaching of EPTC and R-25788 in soil. Weed Sci. 28, 241–246.

Burton, J.D., Maness, E.P., 1992. Constitutive and inducible bentazone hydroxylation in shattercane (*Sorghum bicolor*) and Johnson grass (*S.halapense*). Pestic. Biochem. Physiol. 1, 40–49.

Burton, J.D., Maness, E.P., Monks, D.W., Robinson, D.K., 1994. Sulfonylurea selectivity and safener activity in a landmark and a merit sweet corn. Pestic. Biochem. Physiol. 48, 163–172.

Bussler, B.H., White, R.H., Williams, E.L., 1991. MON 13900: a new safener for gramineous crops. Brit. Crop Prot. Conf-Weeds 1, 39–44.

Casida, J.E., Kimmel, E.C., Ohkawa, H., Ohkawa, R., 1975. Sulfoxidation of thiocarbamate herbicides and metabolism of thiocarbamate sulfoxides in living mice and liver enzyme systems. Pestic. Biochem. Physiol. 5, 1–11.

Chang, F.Y., Stephenson, G.R., Anderson, G.W., Bandeen, J.D., 1976. Control of wild oats in oat with barabn plus antidote. Weed Sci. 22, 546–549.

Chang, F.Y., Stephenson, G.R., Bandeen, J.D., 1973. Comparative effects of three EPTC antidotes. Weed Sci. 21, 292–295.

Chang, T.S., 1983. Structure–activity relationships of oximes and related compounds as seed safeners. Ph.D. Dissertation. Texas A&M University.

Chang, T.S., Merkle, M.G., 1982. Oximes as seed safeners for grain sorghum (*Sorghum bicolor* L.) to herbicides. Weed Sci. 30, 70–73.

Codde, T.M., 1988. Studies on the mechanisms of herbicide safening with particular reference to the interaction of 1,8-naphthalic anhydride and diclofop-methyl in cultivated oats (*Avena sativa* L.). Ph.D. Thesis. Wye College, University of London.

Cummins, I., Cole, D.J., Edwards, R., 1999. A role of glutathione transferases functioning as glutathione peroxidases in resistance to multiple herbicides in black-grass. Plant J. 18, 285–292.

Davies, J., Caseley, J.C., 1999. Herbicide safeners: a review. Pestic. Sci. 55, 1043–1058.

Deal, L.M., Hess, F.D., 1980. An analysis of growth inhibitory characteristics of alachlor and metolachlor. Weed Sci. 28, 168–175.

Deal, L.M., Reeves, J.T., Larkins, B.A., Hess, F.D., 1980. Use of in vitro protein synthesizing system to test the mode of action of chloroacetamides. Weed Sci. 28, 334–340.

Devlin, R.M., Zebiec, I.I., 1990. Effect of BAS-145-138 as an antidote for sulfonylurea herbicides. Weed Technol. 4, 337–340.

Dixon, D.P., Cole, D.J., Edwards, R., 1998. Purification, regulation and cloning of a glutathione transferase (GST) from maize resembling the auxin-inducible type-III GSTs. Plant Mol. Biol. 36, 75–87.

Dodge, A.D., 1990. The mode of action and metabolism of herbicides. In: Hance, R.J., Holly, K. (Eds.), Weed Control Handbook: Principles. Blackwell Scientific Publications, Oxford, pp. 201–206.

Donald, W.M., 1981. EPTC effects in the lettuce (*Lactuca sativa* L.) hypocotyl bioassay for gibberellins. Weed Sci. 29, 490–499.

Dutka, F., Komives, T., 1983. On the mode of action of EPTC and its antidotes. In: Miyamoto, J., Kearney, P.C. (Eds.), Pesticide Chemistry: Human Welfare and the Environment. Pergamon, Oxford, pp. 213–218.

Dutka, F., Komives, T., 1987. MG-191: a new selective herbicide antidote. In: Greenhalgh, R., Roberts, T.R. (Eds.), Pesticide Science and Biotechnology. Blackwell Scientific Publications, Oxford, pp. 201–204.

Dutka, F., Komives, T., Marton, A.F., Hulesch, A., Kodor-Crosba, K., Karpati, M., 1979. Structure–activity relationship of herbicide antidotes. Proc. 19 Hung. Meet. Biochem. 19, 108–112.

Ekler, Z., Dutka, F., Stephenson, G.R., 1993. Safener effects on acetochlor toxicity, uptake, metabolism and glutathione-*S*-transferase activity in maize. Weed Res. 33, 311–318.

Ellis, F.J., Peek, J.W., Boehle, J.J., Muller, G., 1980. Effectiveness of a new safener for protecting sorghum (*Sorghum bicolor* L.) from metolachlor injury. Weed Sci. 30, 70–73.

Ezra, G., Flowers, H.M., Gressel, J., 1983. Rapid multilevel interactions of a thiocarbamate herbicide and its protectants in maize cell culture. In: Miyamoto, J., Kearney, P.C. (Eds.), Pesticide Chemistry: Human Welfare and the Environment, vol. 3. Pergamon, Oxford, pp. 225–231.

Ezra, G., Gressel, J., 1982. Rapid effects of thiocarbamate herbicide and its chloroacetamide protectants on macromolecular synthesis and glutathione levels in maize cell culture. Pestic. Biochem. Physiol. 17, 48–58.

Farago, S., Brunold, C., Kreuz, K., 1994. Herbicide safeners and glutathione metabolism. Physiol. Plantarum 91, 537–542.

Frazier, T.L., Nissen, S.J., 1994. Influence of crop safeners on the interaction of primisulfuron and terbufson in corn (*Zea mays* L.). Weed Sci. 42, 168–171.

Frear, D.S., Swanson, H.R., 1996. Cytochrome-P450-independent hydroxylation of prosulfuron (CGA 152005) by wheat seedling microsomes. J. Agric. Food Chem. 44, 3658–3664.

Fuerst, E.P., 1987. Understanding the mode of action of chloroacetanilide and thiocarbamate herbicides. Weed Technol. 1, 270–277.

Fuerst, E.P., Irzyk, G.P., Miller, K.D., 1993. Partial characterization of glutathione *S*-transferase isozymes induced by the herbicide safener benoxacor in maize. Plant Physiol. 102, 795–802.

Fuerst, E.P., Irzyk, G.P., Miller, K.D., McFarland, J.E., Eberlein, C.V., 1995. Mechanism of action of the herbicide safener benoxacor in maize. Pestic. Sci. 43, 242–244.

Fuerst, E.P., Lamoureux, G.L., Ahrens, W.H., 1991. Mode of action of the dichloroacetamide antidote BAS 145-138 in corn. Pestic. Biochem. Physiol. 39, 138–148.

Goffrey, D.L., Warren, G.F., 1969. Inactivation of herbicides by activated carbon and other adsorbents. Weed Sci. 17, 16–19.

Gray, R.A., Green, L.L., 1982. The evolution of practical crop safeners. Proc. Brit. Crop Prot. Conf-Weeds 2, 431–437.

Gray, R.A., Joo, G.F., 1976. Site of uptake and action of thiocarbamate herbicide antidotes in corn seedlings. In: Pallos, F.M., Casida, J.E. (Eds.), Chemistry and Action of Herbicide Antidotes. Academic Press, New York, pp. 67–84.

Gronwald, J.W., 1989. Influence of herbicide safeners on herbicide metabolism. In: Hatzios, K.K., Hoagland, E.R. (Eds.), Crop Safeners for Herbicides: Development, Uses and Mechanisms of Action. Academic Press, New York, pp. 103–128.

Guneyli, E., 1971. Factors affecting the action of 1,8-naphthalic anhydride in corn treated with ethyl dipropylthiocarbamate (EPTC). Ph.D. Dissertation. Oregon State University.

Gupta, O.P., Niranwad, N.K., 1976. Increasing herbicide selectivity in maize and cow peas by seed treatment with activated carbon and NA. PANS 29, 86–89.

Han, S., Hatzios, K.K., 1991. Physiological interactions between the herbicide pretilachlor and the safener fenclorim on rice. Pestic. Biochem. Physiol. 29, 270–280.

Harvey, B.M., Chang, F.Y., Fletcher, R.H., 1975. Relationship between *S*-ethyldipropylthiocarbamate injury and peroxidase activity in corn seedlings. Can. J. Botany 53, 225–230.

Hatzios, K.K., 1983. Herbicide antidotes: development, chemistry and, mode of action. Adv. Agro. 36, 265–316.

Hatzios, K.K., 1984. Biochemical and physiological mechanisms of herbicide antidotes. In: Duke, S.O. (Ed.), Biochemical and Physiological Mechanism of Herbicide Action. Tallahassee, Florida, pp. 7–30.

Hatzios, K.K., 1986. Interaction of the safener flurazole with chloroacetanilide and thiocarbamate herbicides in maize. Can. J. Plant Sci. 66, 353–359.

Hatzios, K.K., 1991. Effects of the herbicide sethoxydim and the safener dichlormid on lipid synthesis and acetyl-CoA carboxylase activity of grain sorghum. Z. Naturforsch. 46C, 934–938.

Hatzios, K.K., 1993. An overview of the uses and action of herbicide safeners. Pesticides/Environment: Molecular Biological approaches. In: Mitsui, T. (Ed.), Proceedings of the first International Symposium on Pesticide Science. Tokyo, Japan, pp. 155–165.

Hatzios, K.K., 1997. Manipulation of crop tolerance to herbicides with safeners. In: De Prado, R., Garcia Torres, L., Jorrin, J. (Eds.), Weed and Crop Resistance to Herbicides. Kluwer Academic Publishers, Dordrecht, pp. 229–237.

Hatzios, K.K., Penner, D., 1985. Interaction of herbicide with other chemicals in higher plants. Rev. Weed Sci. 1, 1–63.

Hilton, J.L., Pillai, P., 1986. L-2-oxathiazolidine-4-carboxylic acid protection against tridiphane toxicity. Weed Sci. 34, 669–675.

Hilton, J.L., Pillai, P., Norman, H.A., 1990. Fate of safening agent L-2-oxothiazolidine-4-carboxylic acid in sorghum (*Sorghum bicolor*). Weed Sci. 38, 201–205.

Hoagland, R.E., 1989. The use of activated carbon and other adsorbents as herbicide safeners. In: Hatzios, K.K., Hoagland, R.E. (Eds.), Crop Safeners for Herbicides: Development, Uses and Mechanisms of Action. Academic Press, New York, pp. 243–281.

Hoffman, O.L., 1953. Inhibition of auxin by 2,4,6-trichlorophenoxy acetic acid. Plant Physiol. 28, 622–628.

Hoffman, O.L., 1969. Chemical antidotes for EPTC in corn. Abst. Weed Sci. Soc. Am. 9, 12.

Hoffman, O.L., 1978. Herbicide antidotes: from concept to practice. In: Pallos, F.M., Casida, J.E. (Eds.), Chemistry and Action of Herbicide Antidotes. Academic Press, New York, pp. 1–13.

Holt, D.C., Lay, V.J., Clark, E.D., Dinsmore, A., Jepson, I., Bright, S.W., Greenland, A.J., 1985. Characterization of the safener-induced glutathione *S*-transferase isoform II from maize. Planta 196, 295–303.

Hubbell, J.P., Casida, J.E., 1977. Metabolic fate of *N*,*N*-dialkylcarbomyl moiety of thiocarbamate herbicides in rats and corn. J. Agric. Food Chem. 25, 404–413.

Jablonkai, I., Hatzios, K.K., 1991. Role of glutathione and glutathione-*S*-transferase in the selectivity of acetolachlor in maize and wheat. Pestic. Biochem. Physiol. 41, 221–232.

Jablonkai, I., Hatzios, K.K., 1994. Microsomal oxidation of the herbicide EPTC and acetolachlor and of the safener MG-191 in maize. Pestic. Biochem. Physiol. 48, 98–109.

Jepson, I., Bracknell, M., Lay, U.J., Holt, D.C., Bright, S.W., Greenland, A.J., 1994. Cloning and characterization of maize herbicide safener induced cDNAs encoding subunits of glutathione *S*-transferase isomers I, II and 1V. Plant Mol. Biol. 26, 1855–1866.

Ketchersid, M.L., Vieter, D.M., Merkle, M.G., 1982. CGA-43089 effects on metolachlor uptake and membrane permeability in grain sorghum (*Sorghum bicolor*). J. Plant Growth Regul. 1, 285–294.

Kneer, L.D., Hoppen, H.J., 1989. Naphtalam as a safener against chlormben in cucumber (*Cucumis sativus*). Weed Technol. 3, 445–449.

Komives, T., 1992. Herbicide safeners: chemistry, mode of action, applications. Weed Abstract 41, 553–560.

Komives, T., Dutka, F., 1986. Biochemical mode of action of the safener MG-191. Proc. EWRS Symp., 381–385.

Komives, T., Dutka, F., 1989. Effect of herbicide safeners on levels and activity of cytochrome P450 and other enzymes in corn. In: Hatzios, K.K., Hoagland, R.E. (Eds.), Crop Safeners for Herbicides: Development, Uses, and Mechanisms of Action. Academic Press, New York, pp. 129–145.

Lamoureux, G.L., Rusness, D.G., 1992. The mechanisms of action of BAS 145 138 as a safener for chloimuron ethyl, glucoside conjugation and acetolacetate synthase. Pestic. Biochem. Physiol. 42, 128–139.

Lay, M., Niland, A.M., 1985. Biochemical response of inberd and hybrid corn (*Zea mays* L.) to R-25788 and its distribution with EPTC in corn seedlings. Pestic. Biochem. Physiol. 23, 131–140.

Leavitt, J.R., Penner, D., 1978. Prevention of EPTC induced epicuticular wax aggregation on corn (*Zea mays* L.) with R-25788. Weed Sci. 26, 47–50.

Marton, A.F., Appokovacs, A.V., Komives, T., Fodor-Corsba, K., Dutka, F., 1978. Comparison of the uptake and translocation of EPTC in a susceptible and a resistance plants. Proc. Hung. Annu. Meet-Biochem. 18, 111–112.

Mellis, J.M., Pillai, P., Davis, D.E., Truelone, B., 1982. Metolachlor and alachlor effects on membrane permeability and lipid synthesis. Weed Sci. 30, 399–404.

Miaullis, J.B., Thomas, V.M., Gray, R.A., Murphy, J.J., Hollingrowth, R.M., 1978. Metabolism of R-27588 (*N,N*-diallyl-2,2-dichloroacetamide) in corn plants, rats and soil. In: Pallos, F.M., Casida, J.E. (Eds.), Chemistry and Action of Herbicide Antidotes. Academic Press, New York, pp. 109–131.

Milhome, H., Batside, J., 1990. Uptake and phytotoxicity of the herbicide metsulfuron methyl in corn root tissues in the presence of the safener 1,8-naphthalic anhydride. Plant Physiol. 93, 730–738.

Miller, K.D., Irzyk, G.P., Fuerst, E.P., 1994. Benoxacor treatment increases glutathione *S*-transferase activity in suspension cultures of *Zea mays* L. Pestic. Biochem. Physiol. 48, 123–134.

Miller, S.D., Nalewaja, J.D., Pudelko, J., 1978. Effect of herbicide antidotes on barban. Weed Sci. 26, 116–118.

Morteland, D.E., Corbin, F.T., McFarland, J.E., 1993. Oxidation of multiple substrates by corn shoot microsomes. Pestic. Biochem. Physiol. 47, 206–214.

Nagy, J., Balogh, K., 1995. A new safener for EPTC in corn. Proc. Brit. Crop Prot. Conf-Weeds 1, 107–111.

Nagy, J., Kecskes, M., Nagy, I., 1991. Microbial herbicide safeners. Pestic. Sci. 31, 116–118.

Nagy, I., Schoots, G., Compernolle, F., Proost, P., Vanderleyden, J., Mot, R., 1995. Degradation of the thiocarbamate herbicide EPTC (*S*-ethyl-dipropylthiocarbamate) and biosafening by *Rhodococus* sp. Strain NI86/Z1 involve in inducible cytochrome P450 and aldehyde dehydrogenase. J. Bacteriol. 177, 676–687.

Ndahi, W.B., 1988. Effect of chloroacetamide herbicides and antidotes on protein synthesis, nucleotide content, ethylene generation and toxicity on pearl millet (*Pennisetan americanum*) and grain sorghum (*Sorghum bicolor*). Ph.D. Dissertation. Ohio State University.

Ohkawa, H., Tsujii, H., Shimoji, M., Imajuku, Y., Imaishi, H., 1999. Cytochrome P450 biodiversity and plant protection. J. Pestic. Sci. 24, 197–203.

Omokawa, H., Wu, J., Hatzios, K.K., 1996. Mechanism of safening action of dymuron and its two monomethyl analogues against bensulfuron-methyl injury to rice (*Oryza sativa*). Pestic. Biochem. Physiol. 55, 54–63.

Pallos, F.M., Gray, A., Arneklev, D.R., Broke, M.E., 1978. Antidotes protect corn from thiocarbamate herbicides injury. In: Pallos, F.M., Casida, J.E. (Eds.), Chemistry and Action of Herbicide Antidotes. Academic Press, New York, pp. 15–20.

Parker, C., 1983. Herbicide antidotes. A review. Pestic. Sci. 14, 40–48.

Phatak, S.C., Varvina, C.D., 1989. Growth regulators, fungicides, and agrochemicals safeners. In: Hatzios, K.K., Hoagland, R.E. (Eds.), Crop Safeners for Herbicides: Development, Uses and Mechanisms of Action. Academic Press, New York, pp. 299–315.

Ploge, N.D., 1989. Studies into the modification of herbicide activity by chemical safeners and synergists. Ph.D. Thesis. University of Bath, UK.

Repasi, J., Hulesch, A., Suvegh, G., Dutka, F., 1995. Reduction of chloroacetanilide herbicide injury (*Zea mays*) with some structurally new dichloroacetamide derivatives used as safeners. Pestic. Sci. 45, 283–284.

Richers, D.E., Irzyk, G.P., Jones, S.S., Furest, E.P., 1997. Partial characterization of glutathione *S*-transferases from wheat (*Triticum* spp.) and purification of a safener-induced glutathione *S*-transferase from *Triticum Tavschii*. Plant Physiol. 1114, 1461–1470.

Riden, J., Asbell, W.J., 1975. The fate of the protectant 1,8-naphthalic anhydride in corn plants. Environ. Qual. Safety Suppl. 3, 175–179.

Rubin, B., Casida, J.E., 1985. R-25788 effects on chlorosulfuron injury and acetohydroxy acid synthesase activity. Weed Sci. 33, 462–468.

Rubin, B., Kirino, O., 1989. Herbicide pro-safeners: chemistry, safening activity and mode of action. In: Hatzios, K.K., Hoagland, R.E. (Eds.), Crop Safeners for Herbicides: Development, Uses and Mechanisms of Action. Academic Press, New York, pp. 317–336.

Rubin, B., Kirino, O., Casida, J.E., 1985. Chemistry and action of *N*-phenylmaeamic acids and their progenitors as selective antidotes. J. Agric. Food Chem. 33, 489–494.

Sacher, R.M., Lee, L.F., Sacher, D.E., Howe, R.K., 1983. Synthesis and application of novel thiazoles as herbicide antidotes. In: Miyamoto, J., Kearney, P.C. (Eds.), Pesticide Chemistry: Human Welfare and the Environment, vol. 1. Pergamon, Oxford, pp. 165–168.

Sagral, E.G., 1978. Toxicity, selectivity, uptake, distribution and site of action of EPTC in corn (*Zea mays* L.) as affected by herbicide antidotes. Ph.D. Dissertation. Virginia Polytechnic Institute and State University.

Schroder, P., Pflugmacher, S., 1996. Induction of glutathione *S*-transferase activity in Norway spruce by xenobiotics and herbicide safeners. J. Appl. Bot. 70, 97–100.

Sprague, C.L., Penner, D., Kells, J., 1999. Enhancing the margin of selectivity of RPA 201772 in *Zea mays* with antidotes. Weed Sci. 47, 492–497.

Stephenson, G.R., Chang, F.Y., 1978. Comparative activity and selectivity of herbicide antidotes. In: Pallos, F.M., Casida, J.E. (Eds.), Chemistry and Action of Herbicide Antidotes. Academic Press, New York, pp. 35–61.

Stephenson, G.R., Ezra, G., 1985. Use of subtoxic pretreatment to improve crop tolerance to herbicides. Am. Chem. Soc. Ser. 276, 96–104.

Strelkov, V.D., Dyadyuchenko, L.V., Isakova, L.I., Ugryumov, E.P., Sokolov, M.S., 1998. Antidote activity of pyrimidine triazole derivatives. Agrokhimiya 12, 49–51.

Tal, A., Romano, M.L., Stephenson, G.R., Schwan, A.L., Hall, J.C., 1993. Glutathione conjugation: a detoxification pathway for fenoxaprop-ethyl in barley, carbgrass, oat and wheat. Pestic. Biochem. Physiol. 46, 190–199.

Thiessen, E.P., Stephenson, G.R., Anderson, G.W., 1980. Factors influencing 1,8-naphthalic anhydride activity as an antidote to barban in oats. Can. J. Plant Sci. 60, 1005–1013.

Turner, C., Clark, D.R., Helseth, W., Dill, T.R., King, J., Seifried, E.B., 1982. CGA-92194 a new safener to protect sorghum from metolachlor injury. Proc. South. Weed Sci. 35, 388–390.

Varvina, C., 1987. Plant growth regulators as herbicide safeners for metribuzin induced injury to soybean (*Glycine Max*). Ph.D. Dissertation. University of Georgia.

Veylder, V.L., Montagu, V.M., Inze, D., 1997. Herbicide safener-inducible gene expression in Arabidopsis thaliana. Plant Cell Physiol. 38, 568–577.

Walton, J.D., Casida, J.E., 1995. Specific binding of a chloroacetamide herbicide safener in maize at a site that also binds thiocarbamate and chloroacetanilide herbicides. Plant Physiol. 109, 213–219.

Wilkinson, R.E., 1978. 2-Chloro-*N,N*-di-2-propylenacetamide reversal of cartoenogenic inhibition by low concentration of norflurazon. Pestic. Biochem. Physiol. 29, 146–151.

Wilkinson, R.E., 1985. Gibberellins influence and membrane disruption by thiocarbamate herbicides. Pestic. Biochem. Physiol. 24, 103–111.

Wilkinson, R.E., Smith, A.E., 1975. Reversal of EPTC induced fatty acids synthesis inhibition. Weed Sci. 23, 90–92.

Wu, J., Hwang, I.T., Hatzios, K.K., 2000. Effects of chloroacetanilide herbicides on membrane fatty acid desaturation and lipid decomposition in rice, maize, and sorghum. Pestic. Biochem. Physiol. 66, 161–169.

Yelverton, F.H., Worsham, A.D., Peedin, G.E., 1992. Activated carbon reduces tobacco (*Nicotiana tabacum*) injury from soil-applied herbicides. Weed Technol. 6, 3210–3316.

Yenne, S.P., Hatzios, K.K., 1990. Influence of oxime ether safeners on glutathione content and glutathione related enzyme activity in seeds and seedlings of grain sorghum. Z. Naturforsch. 45C, 96–106.

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Yenne, S.P., Hatzios, K.K., 1991. Molecular comparison of selected herbicides and their safeners by computer-aided molecular modelling. J. Agric. Food Chem. 38, 1950–1956.

Zama, P., Hatzios, K.K., 1986. Effects of CGA-92194 on the chemical reactivity of metolachlor with glutathione and metabolism of metolachlor in sorghum (*Sorghum bicolor*). Weed Sci. 34, 834–841.