

Herbicide resistance is complex: a global review of cross-resistance in weeds within herbicide groups

Review

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Abstract

Herbicides have been placed in global Herbicide Resistance Action Committee (HRAC) herbicide groups based on their sites of action (e.g., acetolactate synthase-inhibiting herbicides are grouped in HRAC Group 2). A major driving force for this classification system is that growers have been encouraged to rotate or mix herbicides from different HRAC groups to delay the evolution of herbicide-resistant weeds, because in theory, all active ingredients within a herbicide group physiologically affect weeds similarly. Although herbicide resistance in weeds has been studied for decades, recent research on the biochemical and molecular basis for resistance has demonstrated that patterns of cross-resistance are usually quite complicated and much more complex than merely stating, for example, a certain weed population is Group 2-resistant. The objective of this review article is to highlight and describe the intricacies associated with the magnitude of herbicide resistance and cross-resistance patterns that have resulted from myriad target-site and non-target site resistance mechanisms in weeds, as well as environmental and application timing influences. Our hope is this review will provide opportunities for students, growers, agronomists, ag retailers, regulatory personnel, and research scientists to better understand and realize that herbicide resistance in weeds is far more complicated than previously considered when based solely on HRAC groups. Furthermore, a comprehensive understanding of cross-resistance patterns among weed species and populations may assist in managing herbicide-resistant biotypes in the short term by providing growers with previously unconsidered effective control options. This knowledge may also inform agrochemical company efforts aimed at developing new resistance-breaking chemistries and herbicide mixtures. However, in the long term, nonchemical management strategies, including cultural, mechanical, and biological weed management tactics, must also be implemented to prevent or delay increasingly problematic issues with weed resistance to current and future herbicides.

Introduction

Globally, there are 530 unique cases (species by site of action) of herbicide-resistant weeds, encompassing 272 weed species (155 dicots and 117 monocots) that have evolved resistance to 168 different herbicides from 21 of the 31 known herbicide sites of action (Heap 2024). Weed scientists often classify herbicide-resistant weeds based on their resistance to various Weed Science Society of America (WSSA)/Herbicide Resistance Action Committee (HRAC) Herbicide Groups (G) to simplify their messages about proper and effective weed management strategies to ensure grower success; however, it is not a completely accurate classification system and sometimes leads to oversimplification. Herbicide resistance is far more nuanced. In many cases, herbicide-resistance patterns are specific to: (1) chemical family, (2) active ingredient, (3) site of action amino acid substitution, (4) mechanism of resistance, (5) application timing, (6) temperature at herbicide application, (7) homozygous versus heterozygous loci containing resistance gene(s), and/or (8) genome (as in polyploid weeds).

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Herbicide-resistance mechanisms are generally divided into target-site resistance (TSR) and non-target site resistance (NTSR) mechanisms (Jugulam and Shyam 2019; Murphy and Tranel 2019; Powles and Yu 2010). TSR is conferred by an altered target site or amplification of the target gene, resulting in overexpression of the target enzyme that limits herbicide phytotoxicity (Powles and Yu 2010). NTSR includes mechanisms that reduce the amount of active herbicide reaching the target site and may involve reduced retention, decreased absorption, impaired translocation, enhanced metabolism, and/or subcellular sequestration of the herbicide (Devine and Eberlein 1997; Gaines *et al.* 2020; Nandula *et al.* 2019; Yu and Powles 2014). As several reviews of resistance mechanisms in weeds have recently been published (Baek *et al.* 2021; Barker *et al.* 2023; Chen *et al.* 2021; Jhala *et al.* 2023, 2024; Takano *et al.* 2021), the aim of this review is not to provide comprehensive details about these mechanisms. Additionally, we do not intend to review each HRAC grouping, particularly when only a single active ingredient is typically used in the field (e.g., G10 [glufosinate] and G22 [paraquat]), thus limiting a relevant discussion of cross-resistance patterns. Instead, the goals of this review are to (1) highlight and describe examples of herbicide resistance in weeds that are not straightforward based on HRAC groups alone, (2) understand the reasons why these variations in patterns and magnitude of resistance occur (when mechanisms are known), and (3) identify possible opportunities for exploiting these nuances to improve current weed management strategies. Ultimately, by highlighting examples of how herbicide cross-resistance patterns can be complex, we aim to promote further discussion on how best to communicate these intricacies in a meaningful way to diverse audiences via outreach and extension activities. Hopefully, this information will ensure grower success in the short and long term by offering opportunities to be more adept and efficient when utilizing herbicides for managing herbicide-resistant biotypes.

Group 1-Resistant Weeds

The G1 herbicides consist of at least 21 active ingredients divided into aryloxyphenoxy propionates (FOPs), cyclohexanediones (DIMs), and phenylpyrazoline (DEN) (HRAC 2024; Wenger *et al.* 2019). Acetyl-coenzyme A carboxylase (ACCase)-inhibiting (G1) herbicides exert their action by binding to the carboxyl-transferase domain of plastid ACCase of most grass weeds with limited inhibition of cytoplasmic isoforms (Focke and Lichtenthaler 1987). Crystallography studies have shown FOPs and DIMs share two anchoring points, but overall probe different regions at the active site of the carboxyltransferase domain (Zhang *et al.* 2004). Pinoxaden, a DEN herbicide, binds at a similar location despite its distinct chemical structure (Xiang *et al.* 2009; Yu *et al.* 2010). To date, 51 grass weed species have evolved resistance to G1 herbicides (Heap 2024). Target-site resistance to G1 herbicides is frequently due to an amino acid substitution in the ACCase binding site (Powles and Yu 2010). Resistance mutations at ACCase codon positions 1781, 1999, 2027, 2041, 2078, 2088, and 2096, are documented in a wide range of grass weed species and populations (Takano *et al.* 2021). At least 17 allelic variants (Iso-1781-Leu/The/Ala, Trp-1999-Cys/Ser/Leu, Trp-2027-Cys/Leu, Ile-2041-Asn/Val/Thr, Asp-2078-Gly/Glu, Cys-2088-Arg/Phe, and Gly-2096-Ala/Ser) have been recorded so far, with all but the Cys-2088-Phe change associated with resistance to at least one G1 herbicide (Gaines *et al.* 2020; Kaundun 2014; Takano *et al.* 2021). Some mutations, such as Asp-2078-Gly endow broad

resistance to all G1 herbicides (Xiang *et al.* 2009; Yu *et al.* 2010; Zhang *et al.* 2004).

Blackgrass (*Alopecurus myosuroides* Huds.)

In *A. myosuroides*, the Trp-2027-Cys amino acid substitution conferred resistance to FOPs and DEN but not DIMs (Li *et al.* 2014; Petit *et al.* 2010). In contrast, the Ile-2041-Asn mutation confers resistance to fenoxaprop, clodinafop, and haloxyfop, but plants were only moderately resistant to pinoxaden and sensitive to cycloxydim (Délye *et al.* 2008; Petit *et al.* 2010). The Ile-1781-Leu mutation in *A. myosuroides* conferred resistance to all G1 herbicides, except clethodim at the labeled rate (120 g ha⁻¹) in Europe (Délye *et al.* 2008; Scarabel *et al.* 2011). The Gly-2096-Ala mutation endowed resistance to fenoxaprop, clodinafop, haloxyfop, and cycloxydim, while some individuals survived a full rate of clethodim (120 g ha⁻¹), leading the authors to speculate that possible control failures may occur in the field with clethodim if the rate is reduced or grasses are taller than the recommended weed height at application (Délye *et al.* 2008). Analysis of a large number of *A. myosuroides* populations from France has shown NTSR was prevalent and that fenoxaprop was more affected than clodinafop and pinoxaden (Petit *et al.* 2010).

Lolium spp.

Italian Ryegrass [*Lolium perenne* L. ssp. *multiflorum* (Lam.) Husnot], *Rigid Ryegrass* (*Lolium rigidum* Gaudin), and *Perennial Ryegrass* (*Lolium perenne* L.)

In *L. perenne* ssp. *multiflorum*, the Trp-2027-Leu amino acid substitution conferred resistance to FOPs but not DIMs or DEN (Kaundun *et al.* 2021). The Ile-1781-Leu mutation in *L. perenne* ssp. *multiflorum* conferred resistance to all G1 herbicides, except clethodim at the labeled rate (120 g ha⁻¹) in Europe (Délye *et al.* 2008; Scarabel *et al.* 2011). The Trp-1999-Ser mutation in a different *L. perenne* ssp. *multiflorum* population conferred high levels of resistance to pinoxaden and FOPs and partial resistance to sethoxydim and cycloxydim while being sensitive to tepraloxym and clethodim (Kaundun *et al.* 2013).

In Australia, heterozygous *L. rigidum* plants carrying the mutant Ile-1781-Leu allele were killed by clethodim (60 g ai ha⁻¹), while most homozygous individuals survived (Yu *et al.* 2007a, 2007b). In an *L. perenne* population, metabolic resistance affected the efficacy of pinoxaden but not clethodim (Ghanizadeh *et al.* 2022). Metabolic resistance is typically favored under low-dose selection, especially for the less potent G1 herbicides such as diclofop-methyl (Neve and Powles 2005). In cool-season grasses, enhanced metabolism affects predominantly cereal- and dicot-selective G1 herbicides, such as diclofop, fenoxaprop, clodinafop, tralkoxydim, and pinoxaden; in contrast, dicot only-selective cycloxydim, sethoxydim, and clethodim are less affected (Kaundun 2014). For example, enhanced metabolism identified in the *L. rigidum* population SLR31 affected most cereal- and dicot-selective FOP and DIM herbicides but not sethoxydim (Vila-Aiub *et al.* 2005). A similar observation was made for NTSR *L. perenne* ssp. *multiflorum* populations from the United Kingdom surviving diclofop, clodinafop, and tralkoxydim but remaining sensitive to cycloxydim and pinoxaden (Hull *et al.* 2014). Furthermore, a *L. perenne* ssp. *multiflorum* population with individuals showing high levels of NTSR to FOPs, partial resistance to pinoxaden and cycloxydim, and sensitivity to tepraloxym and clethodim has been documented (Kaundun *et al.* 2021). In Australia, despite a



Figure 1. Control of *Digitaria sanguinalis* with quizalofop-*p*-ethyl (left) and clethodim (right) in a field in Ontario, Canada.

high frequency of resistance to FOP herbicides, clethodim remains widely used to control *L. rigidum* (Broster et al. 2022).

Wild Oat (*Avena fatua* L.)

The Ile-2041-Asn mutation in *A. fatua* from Mexico conferred resistance to FOPs and DIMs but not pinoxaden (Cruz-Hipolito et al. 2011). In contrast, the Asp-2078-Gly mutation in *A. fatua* from Chile conferred cross-resistance to all three ACCase families. Lower resistance indices for DIMs and DEN in *A. fatua* could be explained by a ploidy and dilution effect (i.e., due to homoeologous ACCase genes) of the TSR mechanisms in this species (Yu et al. 2013). In *A. fatua*, ACCase genes from all three genomes are expressed and, for example, a single Ile-2041-Asn mutation may not be sufficient to endow resistance to DIMs and pinoxaden.

Large Crabgrass [*Digitaria sanguinalis* (L.) Scop.]

In greenhouse and field trials conducted in Ontario, Canada, *D. sanguinalis* was resistant to all G1 herbicides (FOPs, DIMs, and DEN) with the exception that clethodim (DIM) was still effective (Figure 1). Group 1 resistance in this *D. sanguinalis* population is thus active ingredient-specific within the DIM herbicides; preliminary unpublished research indicates resistance is due to gene overexpression (M Laforest, personal communication).

Other Examples of G1 Resistance

In Japanese foxtail (*Alopecurus japonicus* Steud.), the Trp-2027-Cys amino acid substitution conferred resistance to fenoxaprop, clodinafop-propargyl, fluazifop-*P*-butyl, quizalofop-*P*-ethyl, haloxyfop-*R*-methyl, cyhalofop-butyl, metamifop, and pinoxaden but not clethodim and sethoxydim (Xu et al. 2013). In slough grass [*Beckmannia syzigachne* (Steud.) Fernald], the Trp-2027-Cys amino acid substitution conferred resistance to the FOPs and DEN but not pinoxaden (Li et al. 2014; Petit et al. 2010). The Trp-1999-Cys mutation affected the efficacy of fenoxaprop in sterile oat (*Avena sterilis* L.), but plants were sensitive to clodinafop-propargyl and sethoxydim (Liu et al. 2007). Resistance to cyhalofop-butyl has been detected at a low frequency (3% or 12%, depending on the survey) in *Echinochloa* spp. in Arkansas rice fields (Rouse et al. 2018). In a barnyardgrass [*Echinochloa crus-galli* (L.) P. Beauv.] population from China, a TSR mechanism via amino acid substitution (Asp-2078-Glu) conferred resistance to FOP and DEN herbicides but not metamifop (Fang et al. 2020). In two *E. crus-galli* populations collected from the U.S. Midsouth, an NTSR mechanism conferred resistance to FOPs (Hwang et al. 2022).

Summary and Implications for Future Weed Management

Group 1 herbicides are far from being a homogeneous group with respect to herbicide resistance. Phenotypes of plants displaying TSR to G1 herbicides frequently depend on herbicide family, active ingredient, target-site amino acid substitution, ploidy level, and number of mutant ACCase alleles. Metabolic resistance is often unpredictable in conferring cross-resistance in weeds (Jugulam and Shyam 2019) and can be broad, class specific, or even active ingredient specific, depending on the species, resistance genes/enzymes involved and occasionally environmental conditions (Matzrafi et al. 2016; Refatti et al. 2019). The unpredictable nature of metabolic resistance in weeds may also be due to the mostly unknown substrate specificity, or lack of specificity (Atkins 2020; Brazier-Hicks et al. 2022), of Phase I or II herbicide-metabolizing enzymes or Phase III parent herbicide/herbicide-metabolite transporters (Jugulam and Shyam 2019; Kreuz et al. 1996; Yu and Powles 2014); these areas clearly warrant additional physiological research.

Group 2-Resistant Weeds

Acetolactate synthase (ALS)-inhibiting herbicides (G2), also known as acetohydroxyacid synthase inhibitors, are the largest herbicide site-of-action group based on number of active ingredients (HRAC 2024). This group comprises six chemical families: imidazolinones (IMIs), pyrimidinyl benzoates (PTBs), sulfonanilides, sulfonyleureas (SUs), triazolones (SCTs), and Type 1 and Type 2 triazolopyrimidines (TPs), which collectively contain 58 active ingredients (HRAC 2024). The ALS enzyme occurs in the biosynthetic pathway of the three branched-chain amino acids in plants (Yu and Powles 2014). Inhibition of ALS by G2 herbicides slowly deprives plant meristems of these essential amino acids and proteins required for plant growth and development, resulting in plant death (Kishore and Shah 1988).

Resistance to G2 herbicides can evolve in weeds after fewer than 10 applications (Beckie and Tardif 2012). Since G2 herbicides were introduced in 1982, a total of 174 weed species have evolved resistance to G2 herbicides globally, including 106 dicots and 68 monocots (Heap 2024). The sheer number of documented cases of G2 resistance demonstrates this enzyme is more prone to resistance evolution compared with other herbicide targets, largely due to the uncompetitive inhibition kinetics of G2 herbicides and the ALS enzyme resulting in no fitness penalty in most cases of weed resistance (Powles and Yu 2010; Yu and Powles 2014). The most prevalent cause of G2 resistance is a TSR mechanism, with approximately 30 amino acid substitutions identified at eight sites

in ALS. Among these substitutions, Pro-197 is the most common, followed by substitutions at Trp-574 (Tranel et al. 2024). Enhanced metabolism, an NTSR mechanism, confers G2 resistance in some weed species. The following examples demonstrate that G2 resistance is complex and cannot be captured fully by simply stating “G2-resistant weeds.” This complexity stems from the various mechanisms in which weeds evolve resistance to G2 herbicides, such as mutations in the ALS enzyme or through enhanced metabolism and rapid herbicide detoxification in resistant populations (Yu and Powles 2014).

Barnyardgrass (Echinochloa crus-galli)

Echinochloa crus-galli populations have evolved resistance to G2 herbicides via an altered target site, either an Ala-122-Val or Ala-122-Thr substitution (Riar et al. 2013). One population (Ala-122-Val) was resistant to IMIs but sensitive to PTBs and TPs. Conversely, the other *E. crus-galli* population (Ala-122-Thr) was resistant to IMIs and TPs but sensitive to PTBs. A separate study documented the Ala-122-Asn amino acid substitution in the ALS gene, which conferred significant cross-resistance to each G2 herbicide (IMI, PTB, TP, and SU) (Panozzo et al. 2017).

Common Ragweed (Ambrosia artemisiifolia L.)

A study conducted in Illinois reported imazamox (IMI) resistance was greater than cloransulam-methyl (TP) resistance in *A. artemisiifolia* populations (Zheng et al. 2005). The study revealed that only 54% of the imazamox-resistant plants contained one or more Leu-574 ALS alleles, and the presence of a Leu-574 allele contributing to imazamox resistance depended on the population. Leu-574 alleles were not identified in plants from populations resistant to imazamox but sensitive to cloransulam-methyl, indicating these populations had a different mechanism of G2 resistance. In contrast, the Leu-574 ALS allele was determined to be the primary factor for cloransulam-methyl resistance in *A. artemisiifolia*.

Downy Brome (Bromus tectorum L.)

A population of *B. tectorum* from Montana exhibited 5-fold resistance (low level) to pyroxsulam (TP), 14-fold resistance (moderate) to propoxycarbazone-sodium (SCT), and 110-fold resistance (high) to imazamox (IMI) (Kumar and Jha 2017). Sequence analysis revealed a single target-site mutation, Ser-653-Asn, in resistant plants. Interestingly, this population remained sensitive to the SU herbicide, sulfosulfuron. In a study conducted in Oregon, a *B. tectorum* population exhibited high resistance to the SU herbicides, primisulfuron-methyl and sulfosulfuron, and the SCT herbicide, propoxycarbazone-sodium, but was sensitive to the IMI herbicide, imazamox. Resistance was attributed to a Pro-197-Ser mutation (Park and Mallory-Smith 2004).

Eastern Black Nightshade (Solanum ptycanthum Dunal)

Solanum ptycanthum populations from Illinois, Indiana, and Wisconsin displayed high levels of resistance (>100-fold) to IMI herbicides in the greenhouse, but either lacked cross-resistance to other G2 herbicides (Milliman et al. 2003) or displayed low-level resistance to the sulfonylurea herbicide, primisulfuron-methyl (5.9-fold; Volenberg et al. 2000). In the populations from Illinois and Indiana, a single base pair mutation in the ALS gene led to an Ala-122-Thr substitution (Milliman et al. 2003), which is known to confer IMI-specific resistance (Powles and Yu 2010).

Mayweed Chamomile (Anthemis cotula L.)

Studies were conducted to characterize resistance of six *A. cotula* populations collected across the U.S. Pacific Northwest to three classes of G2 herbicides: SUs, IMIs, and TPs (Intanon et al. 2011). The findings revealed cross-resistance to thifensulfuron + tribenuron/chlorsulfuron (SUs), imazethapyr (IMI), and cloransulam-methyl (TP), albeit with varying degrees of resistance within each herbicide class and population. Resistance was solely attributed to mutations in ALS1, as mutations were not found in ALS2. The amino acid substitutions at Pro-197 differed among the resistant populations, and multiple mutations were detected within a single resistant population. This study highlights genotypic variation associated with cross-resistance to G2 herbicides both within and among populations.

Amaranthus spp.

Waterhemp (Amaranthus tuberculatus [Moq.] Sauer) and Palmer amaranth (Amaranthus palmeri [S. Watson])

Two *A. tuberculatus* populations from Illinois were resistant to imazethapyr (IMI) but sensitive to chlorimuron (SU) (Patzoldt and Tranel 2007). Imazethapyr-resistant plants from both populations exhibited amino acid substitutions at position 653 of ALS (either Asn or Thr). Another *A. tuberculatus* population from Illinois (McLean County-resistant [MCR]) with NTSR to G5 (triazines) and G27 herbicides also exhibited resistance to G2 herbicides (Guo et al. 2015). This population contained plants with the Trp-574-Leu mutation, but other plants without ALS mutations exhibited a different phenotype via NTSR (presumably a P450-based mechanism). The TSR plants displayed a high level of resistance to G2 herbicides (>100-fold), while plants from an MCR subpopulation with NTSR exhibited moderate to low resistance or reduced sensitivity to: imazethapyr (IMI; R/S = 19), imazapyr (IMI; R/S = 8.9), primisulfuron-methyl (SU; R/S = 11), sulfometuron (SU; R/S = 5.8), cloransulam-methyl (TP; R/S = 90), propoxycarbazone-sodium (SCT; R/S = 3.1), and pyriithiobac (PTB; R/S = 2.8) (Guo et al. 2015).

A G2-resistant population of *A. palmeri* from Kansas resistant to chlorsulfuron (SU) was also resistant to thifensulfuron (SU), propoxycarbazone-sodium (SCT), and pyriithiobac (PTB), but not imazamox (IMI). Further investigations revealed the presence of TSR (Pro-197-Ser in ALS), while pretreatment with the plant P450 inhibitor, malathion, also indicated enhanced metabolism (NTSR) in this population (Nakka et al. 2017b). Malathion can be used as a herbicide synergist to investigate metabolism-based resistance in weeds, because cytochrome P450 enzymes often play a role in the metabolism of herbicides within plants (Nandula et al. 2019). These enzymes are responsible for the detoxification of numerous herbicides, wherein increased P450 activity or expression often leads to evolved herbicide resistance in weeds (Dimaano and Iwakami 2021).

Rigid ryegrass (Lolium rigidum)

The first occurrence of G2-resistant *L. rigidum* was documented in Australia in 1982 (Heap 2024). In Western Australia, researchers identified six ALS mutations in *L. rigidum* that contribute to resistance: Pro-197-Ala, Pro-197-Arg, Pro-197-Gln, Pro-197-Leu, Pro-197-Ser, and Trp-574-Leu (Yu et al. 2008). Each Pro-197 mutation was associated with sulfometuron (SU) resistance, while the Trp-574-Leu mutation conferred resistance to sulfometuron (SU) and imazapyr (IMI).

Wild Radish (*Raphanus raphanistrum* L.)

In Western Australia, researchers identified five G2 resistance-conferring mutations (Pro-197-Ala, Pro-197-Thr, Pro-197-Ser, Asp-376-Glu, and Trp-574-Leu) in *R. raphanistrum* (Yu et al. 2012). Plants carrying homozygous ALS mutations at Pro-197 exhibited cross-resistance to SU and TP herbicides. Similarly, plants homozygous for the Trp-574-Leu mutation demonstrated resistance to SU, TP, and IMI herbicide families. *Raphanus raphanistrum* plants homozygous for Asp-376-Glu displayed high resistance to chlorsulfuron (SU; R/S = 172) and metosulam (TP; R/S >110). In contrast, these plants had moderate resistance to imazamox (IMI; R/S = 3) and imazethapyr (IMI; R/S = 8), while remaining sensitive to imazapyr (IMI; R/S = 0.76).

Other Examples of G2 Resistance

Amino acid substitutions at position Pro-197 in ALS1 conferred G2 resistance in common groundsel (*Senecio vulgaris* L.) from France (Délye et al. 2016). A Pro-197-Leu substitution conferred resistance to all SU herbicides tested, as well as imazamox and thiencazabone, but not florasulam. However, a Pro-197-Ser substitution conferred resistance to all SU herbicides tested as well as florasulam and thiencazabone, but not imazamox. A Pro-197-Gln substitution in common chickweed [*Stellaria media* (L.) Vill.] from the United Kingdom was associated with resistance to metsulfuron (SU), but not florasulam (TP), whereas a Trp-574-Leu substitution conferred resistance to both herbicides (Marshall et al. 2010).

Negative Cross-Resistance to Other G2 Herbicides

Negative cross-resistance occurs when a weed population resistant to a herbicide becomes more sensitive to other herbicides; these herbicides may have the same or different sites of action (Poston et al. 2002). An understanding of negative cross-resistance is crucial for weed management, because it reveals alternative herbicides that could still control resistant weeds. It also highlights the need to diversify herbicide use and employ integrated weed management strategies to reduce herbicide resistance.

Smooth pigweed (*Amaranthus hybridus* L.)

In greenhouse bioassays, IMI-resistant *A. hybridus* showed a low level of cross-resistance to chlorimuron (SU), but greater sensitivity to thifensulfuron (SU), pyrithiobac (PTB), and cloransulam-methyl (TP) (Poston et al. 2000). Enzyme activity assays with ALS determined resistant *A. hybridus* populations exhibited greater than 10-fold resistance to IMI compared with the sensitive populations due to altered levels of ALS enzyme inhibition (Poston et al. 2002). However, the resistance ratios for chlorimuron (SU) and pyrithiobac (PTB) in the IMI-resistant populations were less than 1. It was later confirmed that G2 resistance in the populations studied (Poston et al. 2000, 2002) was conferred by an Ala-122-Thr substitution (Whaley et al. 2006). A Ser-653-Asn substitution was identified in four different *A. hybridus* populations (Whaley et al. 2006), which showed 261- to 537-fold resistance to imazethapyr (IMI), 29- to 88-fold resistance to pyrithiobac (PTB), and reduced sensitivity to thifensulfuron and chlorimuron (SUs) by 10- to 25-fold and 2- to 14-fold, respectively. However, one of these resistant populations (R2) displayed increased sensitivity to cloransulam-methyl (TP; R/S = 0.08), while the other three displayed reduced sensitivity (R/S = 3 to 10) (Whaley et al. 2006). The increased sensitivity to

cloransulam-methyl in population R2 resulted from a 25-fold more sensitive ALS enzyme (i.e., lower 50% inhibition value) *in vitro* compared with a sensitive population, rather than any alterations in cloransulam-methyl absorption, translocation, or metabolism rates (Poston et al. 2001).

G2 Resistance and Negative Cross-Resistance to G14 and G27 Herbicides

Kochia [*Bassia scoparia* (L.) A.J. Scott]

Bassia scoparia with resistance to G2 herbicides was reported first in the United States in 1987 (Primiani et al. 1990). In western Canada, 85% of fields where *B. scoparia* was surveyed in 2007 exhibited G2 resistance (Beckie et al. 2012b), which increased to 100% in surveys during the past decade (Beckie et al. 2019). A total of 16 different single-nucleotide polymorphisms in the ALS gene sequences were identified among 24 G2-resistant *B. scoparia* populations (Warwick et al. 2008), 5 of which resulted in amino acid substitutions at positions Pro-197, Asp-376, and Trp-574. The Trp-574-Leu substitution was most common, followed by Pro-197 (multiple different substitutions), Asp-376-Glu, and Trp-574-Arg. Plants from one *B. scoparia* population with a Trp-574 substitution showed negative cross-resistance to carfentrazone (G14; R/S = 0.5), mesotrione (G27; R/S = 0.4), and pyrasulfotole (G27; R/S = 0.2) (Beckie et al. 2012a). Therefore, negative cross-resistance to G14 and G27 herbicides in this *B. scoparia* population may be a pleiotropic effect associated with ALS substitutions at position Trp-574. However, further research is needed to investigate this theory and determine the mechanism by which putative negative cross-resistance is conferred.

Summary and Implications for Future Weed Management

Resistance to G2 herbicides can evolve in weeds after relatively few applications. Several TSR (ALS mutations) and NTSR-based mechanisms confer resistance to the G2 herbicides. The level of resistance and cross-resistance to other G2 herbicides can vary among the resistance mechanisms present in weed populations. This variation underscores the complexity of managing G2-resistant weeds and the critical information that is often lost due to generalization across the six ALS-inhibiting herbicide families and 58 active ingredients. Additionally, occasional negative cross-resistance to other G2 or G14 and G27 herbicides indicates the need for a detailed understanding of resistance mechanisms to effectively address G2 resistance issues.

Group 3-Resistant Weeds

The G3 herbicides are inhibitors of microtubule polymerization or microtubule assembly and consist of five chemical families (HRAC 2024): dinitroanilines (largest group; including trifluralin, pendimethalin, and ethalfluralin), pyridines (dithiopyr and thiazopyr), phosphoramidates (butamifos and DMPA), benzoic acid (DCPA), and benzamide (pronamide). The mechanism of action is best understood for the dinitroanilines: the herbicide binds to the α -tubulin subunit (Vaughan and Vaughn 1988), which prevents heterodimerization of α/β -tubulin subunits. The α -tubulin-herbicide complex is added to the extending end of microtubules, blocking further addition of α/β -tubulin subunits (Anthony and Hussey 1999; Morrissette et al. 2004). Because microtubules are dynamic structures that continuously depolymerize from the minus end (i.e., constantly degrading), the result is shortened and eventual depletion of microtubules, resulting in lack of cell division



Figure 2. Emergence of *Lolium rigidum* populations collected randomly from crop fields in southeastern South Australia. Each population was treated with the Group 3 herbicides, trifluralin and pronamide, preemergence. These findings demonstrate resistance to trifluralin but not pronamide in the field-collected populations above. Untreated (left); treated with 800 g ha⁻¹ trifluralin (middle); treated with 500 g ha⁻¹ pronamide (right). Each tray contains samples collected from 20 fields with the sample from an individual field sown in a single cell. The same 20 populations are planted in each tray. Each herbicide rate used represents the lowest labeled rate for weed management in no-till grain crop production in Australia.

and cell wall formation (Vaughan and Vaughn 1988). These herbicides are typically applied preplant, preplant incorporated (PPI), or preemergence to control emerging weed seedlings.

To date, 12 weed species have evolved resistance to the G3 herbicides. These are 10 grass weeds and two broadleaf species (*A. palmeri* and narrow-leaved fumitory [*Fumaria densiflora* DC]) (Heap 2024). Most species have evolved resistance to the dinitroaniline herbicides; however, two species (*A. fatua* and annual bluegrass [*Poa annua* L.]) have evolved resistance to pronamide, and *P. annua* is also resistant to dithiopyr (Heap 2024). Three known mechanisms of resistance to G3 herbicides have been identified in weeds. TSR mutations in α -tubulin have been identified in several weed species (Yamamoto et al. 1998), and mutations occur at several sites within the α -tubulin gene (Chen et al. 2021). In addition, NTSR via enhanced metabolism confers resistance in *A. myosuroides* and *L. rigidum* and decreased translocation in *P. annua*. It is possible for both TSR and NTSR mechanisms to coexist in the same plant or population; this combination of mechanisms is consistent with variation in responses to G3 herbicides among species and even populations within a species, as described in the following sections.

Blackgrass (*Alopecurus myosuroides*)

Alopecurus myosuroides populations from the United Kingdom display large variations in resistance among the G3 (dinitroaniline) herbicides. One population (Peldon) has a high level of resistance to pendimethalin and lower resistance to oryzalin and butralin, but is sensitive to trifluralin, ethalfluralin, and isopropalin (Moss 1990). This population was presumed to have NTSR to the dinitroaniline herbicides. Further studies showed this population was resistant to dinitroanilines with a ring-methyl substitution but sensitive to those containing a 4-trifluoromethyl group (James et al. 1995). It was postulated that resistance was the result of enhanced metabolism of dinitroaniline herbicides at the 4-methyl position. In contrast, some TSR mutations provide broad cross-resistance to the dinitroaniline herbicides (Chen et al. 2021).

Rigid ryegrass (*Lolium rigidum*)

Lolium rigidum in Australia has evolved resistance to trifluralin through TSR and NTSR mechanisms. A population (SLR31)

without TSR (Fleet et al. 2018) had higher resistance (8- to 15-fold) to trifluralin, pendimethalin, and ethalfluralin, but lower resistance (2- to 4-fold) to oryzalin and isopropalin (McAlister et al. 1995). This population was subsequently shown to be resistant due to enhanced metabolism of trifluralin by P450s (Chen et al. 2018). Populations of *L. rigidum* with TSR have higher levels of trifluralin resistance than those with only NTSR (Chen et al. 2020; Fleet et al. 2018). An *L. rigidum* population with Val-202-Phe and Thr-239-Ile mutations in α -tubulin had 30-fold resistance to trifluralin and oryzalin, but only 12-fold resistance to pendimethalin and ethalfluralin (Chen et al. 2020). However, populations of *L. rigidum* with both TSR and NTSR to the dinitroaniline herbicides occur and tend to have higher levels of resistance to trifluralin (Chen et al. 2020, 2022).

Significantly, most *L. rigidum* populations in Australia remain sensitive to pronamide. Random collections of field populations from South Australia identified high frequencies of resistance to trifluralin; however, all populations were completely controlled by pronamide (Figure 2). This finding indicates that none of the mechanisms present in populations selected with trifluralin confer field-effective cross-resistance to pronamide in *L. rigidum*. The lack of cross-resistance to pronamide has led to this herbicide being frequently used to control *L. rigidum* populations resistant to trifluralin in pulse crops in southern Australia (Brunton et al. 2018).

Poa annua and Goosegrass [*Eleusine indica* (L.) Gaertn.]

Poa annua has evolved resistance to prodiamine, dithiopyr, and pronamide (McCullough et al. 2017). Little is known about resistance mechanisms to prodiamine or dithiopyr in *P. annua*. In some pronamide-resistant populations, mutations have not been identified in α - or β -tubulin (Barua et al. 2020; Singh et al. 2021). Resistance to pronamide is associated with reduced herbicide translocation in some populations (Igles et al. 2023; McCullough et al. 2017). A Thr-239-Ile mutation in α -tubulin was identified in several *P. annua* populations with pronamide resistance (Igles et al. 2023). However, this mutation was identified in a sensitive population, indicating the Thr-239-Ile mutation is not the sole factor for resistance. This conclusion is supported by a dinitroaniline-resistant *E. indica* population containing a Thr-239-Ile

mutation in α -tubulin, which had high resistance to trifluralin and oryzalin but sensitivity to pronamide (Anthony et al. 1998).

Summary and Implications for Future Weed Management

As considerable variation exists in the mechanisms and levels of resistance to individual G3 herbicides in resistant weeds, this variability provides an opportunity to use some G3 herbicides in the short term to control weed populations that are resistant to other members of the G3 group. For example, the lack of cross-resistance to pronamide has led to this herbicide being frequently used to control *L. rigidum* populations resistant to trifluralin in pulse crops in southern Australia (Brunton et al. 2018). However, we acknowledge that the ability of outcrossing weed species (such as *L. rigidum* and *A. myosuroides*) to accumulate resistance alleles through cross-pollination means these strategies may need to be monitored and altered as necessary to control more complex G3 resistance patterns that may evolve in the future.

Group 4-Resistant Weeds

The G4 herbicides are the first mode of action commercialized in agriculture and have been used for more than seven decades (Peterson et al. 2016). These herbicides selectively control broadleaf weeds in grasses and hence are used widely in corn (*Zea mays* L.) and cereal crop production, turfgrass, and pastures (Sterling and Hall 1997). The selectivity of synthetic auxins is bestowed primarily by the natural ability of tolerant grasses to metabolize and detoxify these herbicides rapidly, irreversibly, and permanently (reviewed by Grossman 2010; Mithila et al. 2011). Synthetic auxin herbicides are so named because they mimic several plant physiological responses to indole-3-acetic acid, a natural plant growth hormone (Grossman 2010). Based on the position of the carboxylic acid moiety and type of aromatic group, these herbicides have been classified into seven herbicide subfamilies (HRAC 2024): benzoates, phenoxy-carboxylates, phenyl-carboxylates, pyridine-carboxylates, pyridyloxy-carboxylates, pyrimidine-carboxylates, and quinoline-carboxylates. Evolved resistance to the quinoline-carboxylate subfamily of G4 herbicides, which primarily control grass weeds selectively in tolerant grasses (turf and cereals), will not be covered in this section, because one main active ingredient (quinclorac) is commonly used (Grossman 2010) and, as a result, cross-resistance within G4 is difficult to ascertain in grass species. Upon treatment with G4 herbicides, sensitive (dicot) plants exhibit a complex cascade of biochemical and physiological events, leading to abnormal growth (epinasty) via overproduction of the two phytohormones, abscisic acid and ethylene, as well as an accumulation of reactive oxygen species (Grossman 2010; Mithila et al. 2011). The following paragraphs discuss the evolution of resistance to G4 herbicides in dicot weed species as well as corresponding cross-resistance patterns that complicate weed management strategies.

Amaranthaceae Family: *Amaranthus tuberculatus*, *Amaranthus palmeri*, and *Bassia scoparia*

Waterhemp (*Amaranthus tuberculatus*) and Palmer amaranth (*Amaranthus palmeri*)

Several *Amaranthus* weed species (monoecious and dioecious) have evolved resistance to G4 herbicides. Cross-resistance patterns are complex, and the underlying mechanisms of resistance (when known) appear to contribute to this complexity (Shergill et al.

2018). For example, an *A. tuberculatus* population from Nebraska is approximately 10-fold and 2- to 3-fold resistant to 2,4-D and dicamba, respectively (Bernards et al. 2012). Subsequently, it was reported that these 2,4-D-resistant *A. tuberculatus* plants metabolize 2,4-D seven times faster than sensitive plants (Figueiredo et al. 2018), but the mechanism conferring reduced sensitivity to dicamba in this population is unknown. Another *A. tuberculatus* population from Illinois was resistant to five HRAC groups, including G4 (2,4-D), despite no synthetic auxin herbicide field-use history (Evans et al. 2019). Subsequently, ineffective control of the same *A. tuberculatus* population with dicamba was reported (Bobadilla et al. 2022). A 9.5-fold resistance factor to 2,4-D was initially reported (Evans et al. 2019), while the dicamba resistance level was 5- to 10-fold (Bobadilla et al. 2022) in this population.

Several *A. palmeri* populations have evolved resistance to G4 herbicides. A 2,4-D-resistant *A. palmeri* population from Kansas was found in a field with a prolonged history of 2,4-D use, but this population is sensitive to dicamba (Shyam et al. 2021). However, the first case of dicamba-resistant *A. palmeri* was identified in Tennessee in a field with extensive dicamba use, although cross-resistance to 2,4-D is unknown (Foster and Steckel 2022). Additionally, fold-resistance levels to 2,4-D in *A. palmeri* vary among populations, ranging from 3-fold (Kumar et al. 2019b) to 7-fold (Hwang et al. 2023) to 12-fold (Shyam et al. 2022). This variation may have resulted from different sensitive populations being used for comparison among studies. Recent research has shown the 2,4-D-resistant *A. palmeri* population from Kansas exhibits low (~3.5-fold) cross-resistance to MCPA, another phenoxy carboxylic acid, via rapid metabolism (Singh et al. 2023).

Kochia (Bassia scoparia)

Bassia scoparia is a problem weed in the U.S. and Canadian Great Plains. Resistance to G4 herbicides is widespread in this species (Heap 2024). In particular, resistance to dicamba is prevalent in many *B. scoparia* populations across the Great Plains and western United States (Kumar et al. 2019a; Westra et al. 2019). Several *B. scoparia* populations exhibit cross-resistance to other G4 herbicides, including dicamba, 2,4-D and/or fluroxypyr, as well as glyphosate (Heap 2024), although dicamba- and glyphosate-resistant *B. scoparia* populations from Colorado were not cross-resistant to fluroxypyr (Westra et al. 2019). Several *B. scoparia* populations with 2.9- to 15-fold or 3.8-fold resistance to dicamba and fluroxypyr, respectively, were found in western Kansas with a history of preemergence and postemergence applications of G4 herbicides in corn (Kumar et al. 2019a). Additionally, these Kansas populations are resistant to glyphosate (Kumar et al. 2019a).

Group 4-resistant *B. scoparia* populations in Canada were identified in small grain cereal crops with a history of prolonged use of these herbicides (Geddes et al. 2023). Approximately 44% of field sites surveyed in Alberta, Canada, had *B. scoparia* populations with resistance to fluroxypyr (pyridyloxy carboxylic acid) compared with 28% with dicamba (benzoic acid) resistance (Geddes et al. 2023). Resistance factors (R/S) ranged up to 6.5-fold for dicamba and 52-fold for fluroxypyr based on visual estimates of control (28 d after foliar treatment), or up to 3.7- and 73-fold to dicamba and fluroxypyr, respectively, based on plant survival (Geddes et al. 2022b). Among the G4-resistant *B. scoparia* populations sampled, 52% were resistant to fluroxypyr but not dicamba, while 24% showed the opposite pattern, and only a small percentage of these populations were resistant to both herbicides (Geddes et al. 2023). In western Canada, dicamba and fluroxypyr

are generally applied separately, but growers often rotate between these herbicides in small grain crop production (Anonymous 2023). These results and usage patterns indicate that resistance to dicamba or fluroxypyr in these *B. scoparia* populations is likely due to separate, currently undefined mechanisms (Geddes et al. 2022a, 2022b, 2023).

Brassicaceae Family: Wild Mustard (*Sinapis arvensis* L.), Raphanus raphanistrum, and Oriental Mustard (*Sisymbrium orientale* L.)

Weed species in the Brassicaceae family have evolved resistance to G4 herbicides in Canada and Australia (Heap 2024). An *S. arvensis* population found in a wheat (*Triticum aestivum* L.)/barley (*Hordeum vulgare* L.) field with prolonged history of G4 herbicide use in Canada was cross-resistant to 2,4-D, dicamba and picloram (Peniuk et al. 1993). Several *R. raphanistrum* populations in Australia have evolved resistance to 2,4-D and MCPA (Heap 2024). Although both herbicides belong to the phenoxy subclass of G4 herbicides, resistance mechanisms to these herbicides are not the same (Goggin et al. 2016, 2018; Jugulam et al. 2013) but likely involve alterations in auxin signaling pathways as well as cellular transport and whole-plant translocation. Two *S. orientale* populations from southern Australia are resistant to 2,4-D (Dang et al. 2017); these two populations display a high level of 2,4-D resistance (67- to 81-fold), although cross-resistance to other G4 herbicides was not reported. Both TSR and NTSR mechanisms were found in this population (Dang et al. 2017, 2018; Figueiredo et al. 2022).

Compositae Family: Yellow Starthistle (*Centaurea solstitialis* L.) and Tall Fleabane [*Conyza sumatrensis* (Retz.) E. Walker]

A population of *C. solstitialis* resistant to picloram was discovered in Washington State in 1988 following 10 years of repeated picloram treatments in a pasture (Callihan et al. 1990). This population displayed cross-resistance to foliar-applied clopyralid, fluroxypyr, and dicamba, but not triclopyr or 2,4-D (Fuerst et al. 1996). Interestingly, this population is >3.5-fold more resistant to clopyralid than picloram, although both herbicides belong to the pyridine-carboxylate subfamily (Fuerst et al. 1996). Furthermore, inheritance studies indicate that clopyralid resistance in *C. solstitialis* is controlled by a single nuclear recessive gene (Sabba et al. 2003). It was postulated that pyridine-carboxylate-specific resistance may be due to alterations in specific binding site(s) of these herbicides (Sabba et al. 2003; Walsh et al. 2006), which is discussed in more detail in the “Summary and Implications for Future Weed Management” for Group 4.

Erigeron sumatrensis

An *Erigeron* (syn.: *Conyza*) *sumatrensis* population with resistance to 2,4-D was recently reported in Brazil in a field with a history of repeated use of 2,4-D, glyphosate, paraquat plus diuron, and saflufenacil (dos Santos Souza et al. 2023). The resistance mechanism is complex and atypical compared with most G4-resistant dicots (dos Santos Souza et al. 2023). For example, 2,4-D-resistant plants exhibit necrotic leaf tissue immediately after application of 2,4-D, followed by rapid defoliation. However, plants recover and grow normally within 2 wk after treatment. Although this is not a common resistance mechanism for G4 herbicides, such rapid cell death followed by tissue necrosis was previously reported in glyphosate-resistant giant ragweed (*Ambrosia trifida* L.) (Moretti et al. 2018). This glyphosate-resistance mechanism does not confer cross-resistance to G4

herbicides (Van Horn et al. 2018). It is not yet known whether this 2,4-D-resistance mechanism in *E. sumatrensis* confers cross-resistance to any other herbicides.

Corn Poppy (*Papaver rhoeas* L.)

Intense selection pressure from 2,4-D and tribenuron-methyl (a G2 herbicide; SU) resulted in the evolution of 2,4-D- and tribenuron-methyl-resistant *P. rhoeas* in Spain (Rey-Caballero et al. 2016; Torra et al. 2017). Cross-resistance to other G4 herbicides is not common in the populations studied to date, although two 2,4-D-resistant *P. rhoeas* populations exhibited resistance to dicamba and aminopyralid (Rey-Caballero et al. 2016). The level of 2,4-D resistance in *P. rhoeas* varied from 7- to 40-fold, depending on population (Rey-Caballero et al. 2016; Torra et al. 2017). Reduced translocation and rapid 2,4-D metabolism were reported resistance mechanisms (Rey-Caballero et al. 2016; Torra et al. 2017, 2021).

Summary and Implications for Future Weed Management

Despite more than seven decades of commercial use of G4, evolution resistance to this group has been relatively low (44 species total) compared with, for example, resistance in the G1, G2, and G5 groups. Both TSR and NTSR mechanisms have been reported (Figueiredo et al. 2018, 2022; Goggin et al. 2018; Leclere et al. 2018; Shyam et al. 2022). Levels of resistance or cross-resistance patterns to G4 herbicides within and among dicot species and populations is complicated, in part because multiple target-site proteins (six TIR1/AFBs) have been identified in *Arabidopsis* (Walsh et al. 2006), although the precise number of target sites in most weed species is unknown. The relatively large number of potential G4 herbicide target sites, which display either specific or overlapping binding properties with G4 herbicide families in *Arabidopsis* (Walsh et al. 2006), contributes to the complexity of cross-resistance within G4 compared with single site-of-action HRAC groups (i.e., G2, G9, and G27). For example, multiple alleles conferring resistance could evolve for each TIR1/AFB gene homologue in the same population or plant (Mithila et al. 2011; Peterson et al. 2016).

Cross-resistance levels and patterns of resistance to G4 herbicides also depend on weed species or population and mechanism of resistance (TSR, NTSR, or a combination of both), which may be exacerbated by widespread use of G4 herbicides in numerous cropping systems (Geddes et al. 2023). However, potential fitness costs resulting from TSR mechanisms or impaired auxin signaling in response to G4 herbicides (Figueiredo et al. 2022), combined with the recessive nature of some G4 resistance traits (Mithila et al. 2011; Sabba et al. 2003), may limit the evolution and spread of additional G4-resistant species and populations.

Group 5—Resistant Weeds

The G5 herbicides are classified as photosystem II (PSII) inhibitors; more specifically as “serine 264-binders.” The G5 herbicides include seven herbicide families (amides, phenylcarbamates, pyridazinones, triazines, triazinones, triazolinones, uracils, and ureas) and more than 70 active ingredients (HRAC 2024). Globally, 87 weed species have evolved resistance to G5 herbicides, including 53 dicots and 34 monocots (Heap 2024). The most common basis for G5 resistance is a TSR mechanism via mutations in the *psbA* gene, which result in the following amino acid substitutions of the encoded D1 protein: Val-219-Ile, Ala-251-Val, Phe-255-Ile, Ser-264-Gly (most common), Ser-264-Thr, and



Figure 3. Control of *Amaranthus tuberculatus* with metribuzin (560 g ai ha⁻¹) with Group 5 resistance due to enhanced metabolism (left) and an altered target site (right) from two fields in Ontario, Canada.

Asn-266-Thr (Powles and Yu 2010). Almost all target-site mutations responsible for resistance to PSII inhibitors occur in a region ranging from amino acid residues Phe-211 to Leu-275 in the D1 protein (Powles and Yu 2010). TSR to G5 herbicides is unique, because *psbA* is encoded by a plastid gene; therefore, TSR is maternally inherited (Murphy and Tranel 2019). No reports indicate that a single TSR mutation in *psbA* confers resistance to all G5 herbicides. Enhanced metabolism, a NTSR mechanism often resulting in reduced translocation, confers G5 resistance in some weed species (Jugulam and Shyam 2019). This section will focus on G5-resistant weeds, often referred to as “triazine- or PSII-resistant weeds” to highlight that resistance is complex and is not captured entirely by merely stating “G5-resistant weeds.”

Groundsel (*Senecio vulgaris*)

The first weed to evolve resistance to the G5 herbicides was *S. vulgaris* in 1968 (Ryan 1970). This *S. vulgaris* population evolved resistance to atrazine and simazine (triazines) applied preemergence or postemergence (0% control with both herbicides at 6.7 kg ai ha⁻¹); in contrast, this population was sensitive to chloroxuron and fluometuron (ureas) applied postemergence (100% control). This seminal research on G5 resistance concluded that this *S. vulgaris* population evolved resistance to triazines but not ureas.

Jimsonweed (*Datura stramonium* L.)

A population of *D. stramonium* that evolved resistance to atrazine and simazine (triazines) was sensitive to prometryn (triazine), metribuzin (triazinone), and terbacil (uracil) (Yerkes 1995). Resistance in this population was influenced by the herbicide family (triazine vs. triazinone and uracil) and active ingredient within the triazine family (resistant to atrazine and simazine but sensitive to prometryn).

Common Lambsquarters (*Chenopodium album* L.)

The first documented case of G5-resistant *C. album* was in Ontario, Canada, in 1974 (Bandeem and McLaren 1976). This population evolved resistance to atrazine, cyanazine, simazine, and cyprazine (triazines) but was sensitive to metribuzin (triazinone) and linuron, metobromuron, and chlorbromuron (ureas). The authors concluded this G5-resistant *C. album* population was chemical family specific; it was resistant to triazines but sensitive to triazinones and ureas. The mechanism of resistance in this biotype has not been elucidated. In contrast, a *C. album* population from eastern Canada with the Ser-264-Gly mutation evolved resistance

to the G5 herbicide metribuzin (triazinone) but was sensitive to linuron (urea) (McKenzie-Gopsill et al. 2020). A *C. album* population from Germany with a Leu-218-Val substitution evolved resistance to the triazinones but was sensitive to terbuthylazine (triazine) (Thiel and Varrelmann 2014); all *C. album* populations tested were more resistant to metribuzin than metamitron, both triazinone herbicides. Thus, G5-resistant *C. album* varies by population. The Ontario population is resistant to the triazine herbicides but sensitive to triazinone and urea herbicides; the eastern Canada population is resistant to triazinones but sensitive to linuron; and the population from Germany is the opposite of the Ontario population, resistant to triazinones but sensitive to triazines. These research findings clearly demonstrate it is an oversimplification to merely refer to G5-resistant *C. album*.

Amaranthus spp.

Waterhemp (*Amaranthus tuberculatus*) and Palmer amaranth (*Amaranthus palmeri*)

There is an effect of mechanism of G5 resistance in Ontario *A. tuberculatus* populations (Westerveld et al. 2021). For example, the calculated metribuzin rates applied preemergence for 50% control of *A. tuberculatus* populations with NTSR (enhanced metabolism) and TSR (Ser-264-Gly) were 350 and 7,868 g ai ha⁻¹, respectively. This research concluded the *A. tuberculatus* population with NTSR was sensitive to metribuzin (triazinone) (Figure 3) but resistant to atrazine (triazine). In contrast, the G5-resistant population with TSR (Ser-264-Gly) was resistant to atrazine (triazine) and metribuzin (triazinone) (Figure 3). Similarly, Vennapusa et al. (2018) reported higher efficacy of metribuzin (triazinone) than atrazine (triazine) for control of numerous Nebraska *A. tuberculatus* populations. Metribuzin (560 g ai ha⁻¹) applied preemergence or postemergence controlled these Nebraska *A. tuberculatus* populations, whereas atrazine (1,345 g ai ha⁻¹) did not control most populations evaluated. Similar to the Ontario populations, sequence analysis of the *psbA* gene did not identify D1 mutations conferring atrazine resistance; however, the G5-resistant populations conjugated atrazine with glutathione via glutathione S-transferase (GST) activity faster than the known sensitive population. Greenhouse research conducted with two *A. tuberculatus* populations from Illinois with metabolic atrazine resistance (Ma et al. 2013) demonstrated that only atrazine applied preemergence controlled the Adams County-resistant (ACR) population, but neither atrazine applied preemergence nor postemergence controlled the Mclean County-resistant (MCR)

population (Ma et al. 2016). The research described demonstrates that metabolism-based mechanisms in *A. tuberculatus* confer resistance to atrazine (triazine) but do not confer cross-resistance to metribuzin (triazinone) (O'Brien et al. 2018; Vennapusa et al. 2018; Westerveld et al. 2021) and that in some *A. tuberculatus* populations (MCR vs. ACR), metabolic atrazine resistance is affected by application timing (Ma et al. 2016).

A Wisconsin *A. palmeri* population sensitive to metribuzin (triazinone) was resistant to atrazine (triazine) (Faleco et al. 2022). Similarly, another population of *A. palmeri* from Kansas revealed metabolic resistance (possibly via GST activity) to atrazine with 100% survival, but only 36% of plants survived metribuzin application (Shyam et al. 2021). In contrast, an Arkansas *A. palmeri* population was controlled with atrazine but resistant to metribuzin (Schwartz-Lazaro et al. 2017). It appears that the GST-mediated metabolism of atrazine in *A. tuberculatus* and *A. palmeri* does not affect metribuzin, most likely because atrazine metabolism by GSTs proceeds via C-Cl bond displacement by reduced glutathione, but the corresponding methylthio group in metribuzin apparently blocks this reaction in *Amaranthus* spp.

Wild radish (*Raphanus raphanistrum*)

A population of *R. raphanistrum* in Australia evolved resistance to atrazine and simazine (triazines) and metribuzin (triazinone) but was sensitive to diuron (urea) (Hashem et al. 2001; Walsh et al. 2004). Further research by Lu et al. (2019) determined metribuzin resistance was conferred by TSR (Ser-264-Gly) and NTSR (enhanced metabolism resulting in reduced translocation). The level of resistance in *R. raphanistrum* is amino acid substitution-specific; populations possessing the Ser-264-Gly substitution exhibit a higher level of resistance compared with populations possessing the Phe-274-Val substitution (Lu et al. 2018).

Shepherd's Purse [*Capsella bursa-pastoris* (L.) Medik.]

Capsella bursa-pastoris evolved TSR to G5 herbicides via a Phe-255-Ile substitution in the D1 protein (Perez-Jones et al. 2009). This substitution conferred resistance to hexazinone (triazinone) but not atrazine (triazine), terbacil (uracil), and diuron (urea) in *C. bursa-pastoris*; the authors concluded resistance was chemical family or active ingredient specific (Perez-Jones et al. 2009).

Velvetleaf (*Abutilon theophrasti* Medik.)

Resistance in *A. theophrasti* to atrazine (triazine) was confirmed in populations from Maryland (Ritter 1986) and Wisconsin (Gray et al. 1995) collected in 1986 and 1990, respectively. The mechanism of resistance was enhanced metabolism via GST activity (Gray et al. 1995). Resistance factors for these populations were: atrazine, ≥ 99 ; simazine, ≥ 100 ; ametryne, ≤ 1.6 ; cyanazine, ≤ 1.1 ; metribuzin, ≤ 1.1 ; linuron, ≤ 1.0 ; and terbacil, ≤ 0.8 . Group 5 resistance in *A. theophrasti* is thus active ingredient (within chemical family) specific (triazines: atrazine and simazine vs. ametryne and cyanazine) as well as chemical family specific (triazine vs. triazinone, urea, and uracil) (Gray et al. 1995).

Other Examples of G5 Resistance

A population of *S. orientale* with a Ser-264-Gly amino acid substitution in D1 was resistant to atrazine (triazine) (≥ 300 -fold) but sensitive to diuron (urea) (Dang et al. 2017). A *S. arvensis* population evolved resistance to atrazine (triazine) but was sensitive

to diuron (urea) (Ali et al. 1986). An *A. hybridus* population with the Ser-264-Gly substitution in D1 was 1,000-fold resistant to atrazine (triazine) but sensitive to diuron (urea) (Gronwald 1994). A silvergrass [*Vulpia bromoides* (L.) Gray] population from western Australia with the Ser-264-Gly substitution in D1 evolved resistance to atrazine and simazine (triazines) (594-fold) and metribuzin (triazinone) but was sensitive to diuron (urea) (Ashworth et al. 2016). Collectively, these research findings demonstrate G5 resistance is chemical family (triazine or triazinone vs. urea) specific or active ingredient (atrazine vs. diuron) specific.

G5 Resistance and Negative Cross-Resistance to G6 Herbicides

Kochia (*Bassia scoparia*)

Group 5-resistant *B. scoparia* evolved resistance to tebuthiuron (16-fold), diuron (16-fold), and metribuzin (4-fold) but exhibited negative cross-resistance to the G6 ("histidine 215-binder")-inhibiting herbicide bromoxynil. The resistance ratios for tebuthiuron, diuron, metribuzin, and bromoxynil were 38, 7, 4, and 0.2, respectively. This population was sensitive to bromoxynil at 50% of the field use rate (Mengistu et al. 2005). Interestingly, negative cross-resistance did not occur with bentazon, another G6 herbicide. This research indicates that negative cross-resistance in *B. scoparia* is specific to herbicide family (benzothiadiazole vs. benzonitrile) and active ingredient (bentazon vs. bromoxynil).

Summary and Implications for Future Weed Management

The G5 herbicides are important for annual broadleaf weed control in numerous crops. The chemical family/active ingredient cross-resistance patterns within G5 herbicides allows knowledgeable weed management practitioners to exploit this knowledge for the benefit of crop producers globally. For example, G5-resistant *C. album* in Ontario, Canada, can be successfully controlled in soybean [*Glycine max* (L.) Merr.] with metribuzin but not atrazine (Bandein and McLaren 1976); in contrast, G5-resistant *C. album* in Prince Edward Island, ON, Canada, can be successfully controlled in potato (*Solanum tuberosum* L.) with linuron, a G5 herbicide, but not metribuzin (McKenzie-Gopsill et al. 2020). Precise knowledge of the cross-resistance patterns within a group can result in improved weed control, reduced weed seed return to the soil, and delayed evolution of herbicide resistance.

Group 9-Resistant Weeds

Background on the Evolution of Glyphosate Resistance in Weeds

The G9 consists of one herbicide family (glycine) and one active ingredient (glyphosate) (HRAC 2024). Glyphosate was commercialized in 1974 and is a systemic, nonselective herbicide (Jaworski 1972). The precise mechanism of action of glyphosate is competitive inhibition of phosphoenolpyruvate in the binary complex of shikimate-3-phosphate: 3-phosphoshikimate-1-carboxyvinyltransferase, EPSP synthase (EPSPS; EC 2.5.1.19) (Kishore and Shah 1988). Compared with other single site-of-action herbicides, glyphosate was initially considered a low-risk compound with respect to evolved weed resistance (Bradshaw et al. 1997), primarily because it is poorly metabolized by plants and binds tightly to a few conserved amino acids in EPSPS (Duke and Powles 2008; Sammons et al. 2007). Consequently, TSR due to EPSPS mutations was deemed unlikely as it would incur a severe fitness cost. However, glyphosate resistance is

now documented in 28 dicot and 31 grass weeds and is third-most in terms of number of species (Heap 2024). The unprecedented pressure exerted by extensive use of glyphosate has selected for the most diverse types of resistance mechanisms (TSR and NTSR) compared with other herbicides (Gaines et al. 2020), as discussed in the following sections.

Glyphosate resistance due to single, double, and triple TSR mutations has been identified in 20 weed species (Heap 2024). The most common EPSPS mutation is the Pro-106-Ser mutation, followed by the Pro-106-Arg, Pro-106-Thr, and Pro-106-Leu. The Pro-106-Ser mutation has been documented in *E. indica*, *A. palmeri*, horseweed [*E. canadensis* (L.) Cronquist], and sourgrass [*Digitaria insularis* (L.) Mez ex Ekman], among others (Beres et al. 2020; Kaundun et al. 2008, 2019a, 2019b). Another rare mutation conferring glyphosate resistance is the Thr-102-Ser change found in a coatbuttons (*Tridax procumbens* L.) population (Li et al. 2018). Additionally, double Thr-102-Ile/Pro-106-Ser mutations in *E. indica* and hairy beggarticks (*Bidens pilosa* L.) and double Thr-102-Ile/Pro-106-Thr mutations in greater beggar's ticks (*Bidens subalternans* DC) endow TSR to glyphosate (Alcántara-de la Cruz et al. 2016; Takano et al. 2020). Recently, a triple Thr-102-Ile/Ala-103-Val/Pro-106-Ser mutant was associated with glyphosate resistance in smooth pigweed (*Amaranthus hybridus* L.), although the precise role of the Ala-103-Val mutation is yet to be established (Perotti et al. 2019). In contrast to weed populations with single Pro-106-Ser/Thr/Ala/Leu and Thr-102-Ser mutations that confer relatively low levels of glyphosate resistance (<10-fold), weed populations containing the double Thr-102-Ile/Pro-106-Ser, Thr-102-Ile/Pro-106-Thr or triple Thr-102-Ile/Ala-103-Val/Pro-106-Ser mutations confer high resistance levels (Baek et al. 2021).

An additional and unusual TSR mechanism to glyphosate consists of EPSPS gene overexpression (Gaines et al. 2020). This mechanism was first identified in *A. palmeri* (Gaines et al. 2010) and is now documented in three other dicot and six grass species, including *A. tuberculatus*, *B. scoparia*, *L. perenne* ssp. *multiflorum*, and Australian fingergrass (*Chloris truncata* R. Br.) (Baek et al. 2021). Other NTSR mechanisms consist of reduced uptake and impaired transport. Reduced glyphosate absorption has been detected in several species, including *B. pilosa*, *A. palmeri*, johnsongrass [*Sorghum halepense* (L.) Pers.], tall windmill grass (*Chloris elata* Desv.), and Judd's grass [*Leptochloa virgata* (L.) P. Beauv.] (Alcántara-de la Cruz et al. 2016; Brunharo et al. 2016; de Carvalho et al. 2012; Dominguez-Valenzuela et al. 2017; Michitte et al. 2007; Vila-Aiub et al. 2012). Reduced glyphosate absorption alone typically does not result in control failures. Impaired transport was identified in the second glyphosate-resistant *L. rigidum* sample collected from Australia (Powles et al. 1998) and can endow low, moderate, or high levels of glyphosate resistance. In most instances, the precise genetic basis underlying impaired transport remains undetermined.

Different glyphosate-resistance mechanisms can occur in the same populations and plants, especially when one mechanism is not sufficient to confer significant levels of glyphosate resistance (González-Torralva et al. 2012). For example, low levels of EPSPS overexpression combined with mutations at codon 106 act in concert to endow significant glyphosate resistance in junglerice [*Echinochloa colona* (L.) Link] (Alarcón-Reverte et al. 2015) and *E. indica* (Gherekhloo et al. 2017). Reduced translocation and the Pro-106-Ser mutation endow resistance to *A. tuberculatus* and narrowleaf plantain (*Plantago lanceolata* L.) populations (Nandula et al. 2013; Ndou et al. 2021). Similarly, EPSPS overexpression and the Pro-106-Ser mutation act additively to confer glyphosate

resistance in an *A. palmeri* population from Argentina (Kaundun et al. 2019a). Reduced absorption and translocation, EPSPS mutation at codon 106, and low levels of glyphosate metabolism, each conferring low levels of glyphosate resistance, have been identified in a *D. insularis* population from Brazil (de Carvalho et al. 2012).

Because glyphosate is the only G9 member, characterizing resistance to this HRAC group should theoretically be straightforward compared with other herbicide groups consisting of structurally diverse active ingredients with distinct binding sites and NTSR profiles (e.g., G1 and G2). However, complexity arises because phenotypic expression and fold resistance to glyphosate can depend on herbicide rate, plant growth stage, environmental conditions, heterozygosity at EPSPS (codon 106), and ploidy of the species, especially for weed populations characterized by low-to-moderate resistance levels, as discussed in the following sections for several weed species.

Goosegrass (*Eleusine indica*)

Glyphosate rate dependency for phenotypic resistance expression was noted in two *E. indica* populations, one from Tennessee and one from the Philippines, with the Pro-106-Ser mutation in EPSPS (Huffman et al. 2016; Kaundun et al. 2008). Resistance indices associated with the single target-site mutation were low (2.1- to 3.4-fold) in homozygous resistant SS106 versus wild-type PP106 genotypes derived from the same parental populations in both studies. At a glyphosate rate (1.0 kg ae ha⁻¹) that completely killed a PP106 subpopulation, 72% of homozygous mutant SS106 *E. indica* plants (13-cm tall) survived glyphosate (Kaundun et al. 2008). Compared with heterozygous PS106 individuals, a larger proportion of homozygous resistant SS106 mutant plants survived and accumulated greater dry biomass following a discriminating glyphosate rate of 350 g ae ha⁻¹ in the greenhouse (Huffman et al. 2016).

Palmer amaranth (*Amaranthus palmeri*)

A similar observation was made for a unique *A. palmeri* population from Argentina characterized by the Pro-106-Ser mutation coupled with a low level (1.8-fold) of EPSPS overexpression, but surprisingly in the absence of EPSPS gene duplication (Kaundun et al. 2019a). Approximately 75% of heterozygous PS106 and 88% homozygous SS106 plants survived a reduced rate of glyphosate-potassium (400 g ai ha⁻¹). However, survivorship of PS106 and SS106 individuals decreased to 40% and 73%, respectively, at the recommended glyphosate use rate of 800 g ai ha⁻¹ (Kaundun et al. 2019a).

Effect of Plant Growth Stage, Environmental Factors, and Ploidy Level on Glyphosate Resistance

Horseweed (*Erigeron canadensis*)

Plant growth stage was an important parameter in a *E. canadensis* population from California, whereby a direct relationship was identified between glyphosate efficacy and plant phenology. Sensitive and resistant *E. canadensis* plants at the 5- to 8-leaf stages were controlled with glyphosate at 2 to 4 kg ae ha⁻¹, whereas plants at the 11-leaf stage and onward survived glyphosate application (Shrestha et al. 2007). A similar observation was made on glyphosate-resistant *E. canadensis* populations from different U.S. states with impaired glyphosate translocation and EPSPS overexpression (1.8- to 3.1-fold). Plants from the sensitive and

resistant populations at the 2-leaf stage were equally controlled by glyphosate, while a 3-fold resistance index was calculated for plants at the rosette stage (Dinelli et al. 2006).

Giant ragweed (Amaranthus trifida)

Temperature is an important determinant for the efficacy of glyphosate on sensitive and resistant weeds. In some studies, greater control was achieved at higher temperatures, while other studies reported the inverse, depending on the mechanism of resistance and specific weed population (McWhorter et al. 1980; Vila-Aiub et al. 2013). For example, the efficacy of glyphosate on both sensitive and resistant *A. trifida* populations increased at 29/17 C day/night compared with 20/11 C day/night due to increases in herbicide absorption and translocation (Ganie et al. 2017).

In most instances, however, glyphosate is more efficacious at controlling resistant populations at lower temperatures in *E. indica*, *S. halepense*, *L. rigidum*, *E. colona*, *B. scoparia*, and *E. canadensis* (Kleinman et al. 2016; Nguyen et al. 2016; Ou et al. 2018; Vila-Aiub et al. 2013), possibly by altering biokinetic factors affecting glyphosate-induced phytotoxicity mechanisms. Lowering the temperature at application from 30 to 19 C in *S. halepense* and 19 to 8 C in *L. rigidum* reduced survival and aboveground biomass in glyphosate-resistant plants (Vila-Aiub et al. 2013). An *E. indica* population was 8.9-fold more resistant to glyphosate than a sensitive population at 30/20 C but 3.1-fold at 20/15 C (Guo et al. 2023). A glyphosate-resistant *E. canadensis* population with vacuolar sequestration (Ge et al. 2010, 2011) was sensitive to glyphosate when maintained at 11 C, which was attributed to a lower ability to sequester glyphosate in the vacuole. In a similar manner, an *L. perenne* population appeared to lose glyphosate resistance when treated and grown under cooler conditions (Ghanizadeh et al. 2015).

The ploidy level of a weed species combined with temperature at time of application can also affect the phenotypic expression of glyphosate resistance. This is exemplified by *E. colona* (a hexaploid, warm-season C₄ grass) populations characterized by Pro-106-Thr or Pro-106-Leu mutations in EPSPS (Han et al. 2016). These populations did not survive a field use rate of glyphosate (450 g ae ha⁻¹) applied at moderate temperatures (25/20 C), likely due to dilution effects caused by allohexaploidy (i.e., homoeologous copies of EPSPS) and expression of several other EPSPS alleles that confer glyphosate sensitivity. However, control of most resistant plants (68%) was achieved when glyphosate was applied during high temperatures (35/30 C), and both R and S plants showed a 2.5-fold increase in LD₅₀ values (Han et al. 2016).

Summary and Implications for Future Weed Management

Although investigations of cross-resistance are not possible, because glyphosate is the only G9 herbicide member, it is clear that the magnitude and diversity of glyphosate resistance within a species, population, or individual plant is affected by numerous TSR and NTSR mechanisms as well as plant growth stage, environmental conditions, and genetics (zygosity and ploidy). Resistant weed populations evolved relatively quickly during the past 30 yr due to the intense selection pressure exerted by widespread glyphosate use in glyphosate-resistant cropping systems, combined with fewer applications of preemergence and postemergence herbicides from other HRAC groups (Landau et al. 2023). Management of glyphosate-resistant biotypes is influenced by glyphosate rate, growth stage of the weed, and temperature at the time of application.

Group 14-Resistant Weeds

The G14 herbicides (protoporphyrinogen oxidase [PPO or Protox] inhibitors) include five herbicide families (diphenyl ethers, *N*-phenyl-imides, *N*-phenyl-oxadiazolones, *N*-phenyl-triazolinones, and phenylpyrazoles) and at least 30 active ingredients (HRAC 2024). Before commercialization of glyphosate-resistant crops, G14 herbicides were widely used for preemergence and post-emergence control of broadleaf weeds (Falk et al. 2006). Today, 16 species have evolved resistance to this site of action (Barker et al. 2023; Heap 2024).

Waterhemp (Amaranthus tuberculatus) and Palmer amaranth (Amaranthus palmeri)

Multiple TSR and NTSR mechanisms have been identified in several *Amaranthus* species that confer resistance to the G14 herbicides applied postemergence (Barker et al. 2023). Relatively few G14-resistance mechanisms have been identified in *Amaranthus tuberculatus*, with ΔGly210 and/or the Arg-128-Gly/Ile as the only TSR mechanisms elucidated (Nie et al. 2019; Patzoldt et al. 2006). NTSR (presumably metabolism-based, but not studied directly) to carfentrazone-ethyl postemergence in *A. tuberculatus* has been noted, but plants remained sensitive to other G14 herbicides postemergence (Obenland et al. 2019). Conversely, G14 resistance in *A. palmeri* is considerably more complex, with the presence of multiple target-site mutations identified in the target protein PPO2: ΔGly210, Arg-128-Gly/Met, Gly-399-Ala, and the recently detected Val-361-Ala mutation (Nie et al. 2023) conferring cross-resistance to nearly all postemergence G14 herbicides, except trifludimoxazin (Porri et al. 2023). Metabolism-based NTSR (Varanasi et al. 2018) and enhanced PPO2 expression have also been discovered alone or in combination with various TSR mutations (Rangani et al. 2023), further complicating and contributing to G14 resistance post-emergence. From a practical standpoint, TSR mutations such as ΔGly210, Gly-399-Ala, and Arg-128-Gly/Met have been discovered in the same population, plant, and even in the same PPO2 allele (Noguera et al. 2021), thus creating new challenges for resistance management recommendations.

Resistance to preemergence G14 herbicides is more nuanced. In numerous greenhouse trials, research investigating control of G14-resistant *Amaranthus* has demonstrated that R/S ratios for fomesafen are much lower preemergence (when using field soil or a mixture of field soil, peat, and sand) compared with postemergence (Lillie et al. 2020; Wuerffel et al. 2015a). Field trials conducted on G14-resistant *A. tuberculatus* with the ΔGly210 mutation demonstrated that commercially acceptable control can be achieved when G14 herbicides, including diphenyl ethers such as fomesafen, are applied preemergence (Falk et al. 2006; Houston et al. 2021; Wuerffel et al. 2015b). Research on *A. palmeri* has concluded that preemergence fomesafen may not adequately control G14-resistant populations (regardless of the mechanism), but if a preemergence G14 herbicide is desired, then flumioxazin, sulfentrazone, or saflufenacil provides the greatest levels of control (Rangani et al. 2023; Schwartz-Lazaro et al. 2017; Umphres et al. 2018). Although growers applying G14 herbicides preemergence may achieve acceptable control depending on the species and G14 herbicide used, selection pressure still occurs as the herbicide concentration decreases in the soil, thereby shortening the length of residual control (Lillie et al. 2020; Wuerffel et al. 2015b).

Interestingly, G14 herbicides applied preemergence are seemingly less effective for G14-resistant *A. palmeri* compared

with *A. tuberculatus*, possibly due to the greater number of resistance mechanisms, and combinations thereof, present in *A. palmeri*. Furthermore, Rangani et al. (2023) noted that individual TSR mutations in *PPO2* are necessary, but alone may not be sufficient, to overcome soil-applied G14 herbicides in resistant *Amaranthus* populations. Multiple “small-effect” TSR mechanisms, such as increased *PPO2* overexpression and combinations of target-site mutations in an individual plant or *PPO2* allele (Porri et al. 2022), and/or NTSR mechanisms such as enhanced metabolism (Borgato et al. 2024; Varanasi et al. 2018), may lead to increased chances of seedling survival to preemergence-applied G14 herbicides (Rangani et al. 2023). For example, populations of *A. palmeri* heterozygous for the Δ Gly210 mutation were more sensitive than individuals homozygous for the Δ Gly210 mutation or heterozygous for the Δ Gly210 and Gly-399-Ala mutations in *PPO2* (mutations most likely in different alleles; Carvalho-Moore et al. 2021). This finding provides further support of the hypothesis that combinations of multiple G14-resistance mechanisms (TSR and/or NTSR) likely reduce efficacy of preemergence G14 herbicides in certain *A. palmeri* populations.

Summary and Implications for Future Weed Management

Evolved resistance to G14 herbicides has become more complex in recent years, especially in *Amaranthus* species, in which several TSR and NTSR mechanisms have been identified in the same individual, and even the same allele, consequently conferring greater levels of G14 resistance compared with a single G14-resistance mechanism (Barker et al. 2023; Noguera et al. 2021). Known G14-resistance mechanisms in *Amaranthus* confer cross-resistance to all G14 herbicides applied postemergence, with the exception of new, highly active G14 herbicides like trifludimoxazin (Porri et al. 2023) or unknown NTSR mechanism(s) conferring carfentrazone-ethyl-specific resistance in *A. tuberculatus* (Obenland et al. 2019). Generally, G14 herbicides applied preemergence provide acceptable control of *A. tuberculatus* (Falk et al. 2006; Wuerffel et al. 2015b); however, multiple research groups have found this not to be the case in several *A. palmeri* populations (Schwartz-Lazaro et al. 2017; Umphres et al. 2018), possibly due to the greater number and diversity of TSR and NTSR G14-resistance mechanisms (Rangani et al. 2023). In summary, it is clear that simply stating “G14 resistance” in *Amaranthus* spp. is inaccurate and misleading due to the active ingredient- and application timing-specific resistance profiles described.

Group 15-Resistant Weeds

The G15 herbicides are preemergence residual herbicides that control small-seeded annual monocots, some small-seeded dicots, and sedges (Fuerst 1987; Hager et al. 2002; Hay et al. 2018; Soltani et al. 2019; Strom et al. 2022; Symington et al. 2023; Vyn et al. 2006). The G15 herbicides are very-long-chain fatty-acid elongase (VLCFAE) inhibitors (Tanetani et al. 2009), which are a family of enzymes located in membranes of the endoplasmic reticulum (Böger et al. 2000; Krähmer et al. 2019). The G15 herbicides include eight herbicide families (azoly-carboxamides, benzofurans, isoxazolines, oxiranes, thiocarbamates, α -chloroacetamides, α -oxyacetamides, and α -thioacetamides) and more than 40 active ingredients (HRAC 2024). Resistance to G15 herbicides has been relatively slow to evolve compared with other herbicide groups (Jhala et al. 2024); to date, only 13 species (11 monocots and 2 dicots) have evolved resistance to G15 herbicides (Heap 2024) despite more than 60 yr of usage in field crops.

Wild oats (*Avena fatua*)

Several *A. fatua* populations were classified as resistant to G15 herbicides (specifically, triallate) in the late 1980s and 1990s in North America (Heap 2024). Triallate resistance in *A. fatua* has been associated with low resistance levels ($R/S < 3$) to the G15 herbicide, pyroxasulfone, and G14 herbicide, sulfentrazone, despite this population lacking exposure to either herbicide (Mangin et al. 2016). It was theorized that triallate, G1 herbicides, and/or G2 herbicides selected for cross-resistance to pyroxasulfone and sulfentrazone via enhanced metabolism (Mangin et al. 2016).

Rigid ryegrass (*Lolium rigidum*)

The first weed population with reported resistance to G15 herbicides (specifically, metolachlor and triallate) was an *L. rigidum* population in Southern Australia in 1982 (Heap 2024). Resistance to pyroxasulfone and other G15 herbicides was subsequently discovered in *L. rigidum* as well (Brunton et al. 2018, 2019; Burnet et al. 1994; Busi et al. 2014). A pyroxasulfone-resistant *L. rigidum* population displayed cross-resistance to prosulfocarb and triallate (Busi and Powles 2013), which could be selected for by either herbicide (Busi and Powles 2016). Varying levels of resistance (between 8- and 66-fold) to the G15 herbicides triallate, EPTC, prosulfocarb, thiobencarb, S-metolachlor, metazachlor, and pyroxasulfone, as well as the G3 herbicide, trifluralin, have also been reported in *L. rigidum* from Australia (Brunton et al. 2018, 2019). Despite G15 resistance, certain mixtures containing two different herbicides, such as pyroxasulfone plus triallate, applied PPI improved *L. rigidum* control and wheat yield compared with a single PPI herbicide (Brunton et al. 2020).

Echinochloa Complex: *Echinochloa crus-galli*, Early Barnyardgrass [*Echinochloa oryzoides* (Ard.) Fritsch], and Rice Barnyardgrass [*Echinochloa phyllopogon* (Stapf) Koso-Pol.]

Resistance to the G15 herbicide, butachlor, has been reported in *E. crus-galli* in China (Heap 2024), and several *E. crus-galli* populations resistant to butachlor and propanil (a PSII inhibitor) were identified in Asia (Juliano et al. 2010). Thiocarbamate-resistant *E. phyllopogon* and *E. oryzoides* populations discovered in rice fields in California were resistant to multiple herbicides, including G1, G2, G4 (quinclorac), and G13 (clomazone), but were not resistant to propanil, glyphosate, or glufosinate (Busi 2014; Fischer et al. 2000). Interestingly, the addition of thiobencarb to bispyribac-sodium in a tank mixture led to synergistic control of bispyribac-sodium-resistant and bispyribac-sodium-sensitive *E. phyllopogon* populations (Fischer et al. 2004).

Recent molecular-genetic studies of multiple-resistant *E. phyllopogon* (Dimaano et al. 2022) indicated distinct enzymes confer resistance to G1 and G2 versus G15 herbicides. For example, transgenic *Arabidopsis* plants expressing the *CYP81A12/21* genes demonstrated this P450 enzyme likely provides cross-resistance to G1 and G2 herbicides, but not the G15 herbicide, thiobencarb, implying that resistance in *E. phyllopogon* may involve a combination of cross- and multiple-resistance traits (Dimaano et al. 2022).

Amaranthus spp.

Waterhemp (*Amaranthus tuberculatus*) and Palmer amaranth (*Amaranthus palmeri*)

Two *A. tuberculatus* populations resistant to G15-inhibiting herbicides have been characterized in Illinois: one population



Figure 4. Representative images of variable Group 15 (G15) herbicide efficacy for controlling a G15-resistant *Amaranthus tuberculatus* population (CHR) and a sensitive (Urbana, IL) population, 28 d after treatment. Figure 4 was reproduced directly without changes from Strom et al. (2022).

from McLean County (MCR or SIR; Strom et al. 2019) and one population from Champaign County (CHR; Evans et al. 2019). Both resistant populations exhibited reduced control in the field with G15 herbicides from the isoxazoline and α -chloroacetamide chemical families (HRAC 2024); however, the greatest decline in efficacy (relative to sensitive populations) occurred with *S*-metolachlor, while acetochlor was affected the least (Strom et al. 2019, 2022). In greenhouse studies, resistance to *S*-metolachlor ranged from 18- to 64-fold in the MCR and CHR populations (Strom et al. 2019). The primary mechanism of resistance to *S*-metolachlor in both populations is enhanced oxidative metabolism mediated by P450 activity (Strom et al. 2021), although rapid glutathione conjugation likely plays a secondary role (Strom et al. 2020, 2021). However, the reason acetochlor remains most effective compared with other active ingredients in G15 for controlling these G15-resistant populations (Figure 4) has not been determined but warrants further research, including comparative metabolism studies and *in vitro* enzyme assays.

Resistance to G15 herbicides in two *A. palmeri* populations has been reported in Arkansas (Brabham et al. 2019) as well as in several populations collected in the U.S. Midsouth (Kouame et al. 2022). Greenhouse studies demonstrated 8- to 10-fold resistance to *S*-metolachlor in the two resistant populations from Arkansas compared with sensitive populations (Brabham et al. 2019). Although cross-resistance to other G15 herbicides was not detected, the resistant *A. palmeri* populations from Arkansas displayed reduced sensitivity to acetochlor, dimethenamid-*p*, and pyroxasulfone (Brabham et al. 2019).

Summary and Implications for Future Weed Management

Resistance to G15 herbicides has been slow to evolve compared with other herbicide groups (Heap 2024). Several reasons have been posited concerning why resistance has been slow to evolve to the G15 herbicides, including the complexity and possible redundancy of VLCFAE enzymes in plants and potential fitness costs associated with TSR mechanisms (Beckie 2006; Böger 2003; Busi 2014; Jhala et al. 2024). All reported resistant weed

populations to date with known G15-resistance mechanisms have exhibited rapid metabolic detoxification rates (with the exception of triallate-resistant *A. fatua*, in which lack of bioactivation confers resistance; Kern et al. 1996) due to oxidative and/or glutathione-mediated reactions compared with sensitive populations of the same species (Busi 2014; Busi et al. 2018; Strom et al. 2020). However, until specific Phase I or II genes and enzymes are discovered and biochemically characterized, we can only speculate that differential herbicide substrate specificities or expression patterns of these Phase I/II enzymes underlies the unique active ingredient-specific patterns of cross-resistance in weeds.

Group 27-Resistant Weeds

The G27 herbicides are classified as 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitors (Hawkes et al. 2019; Jhala et al. 2023). This HRAC group includes three herbicide families (isoxazoles, pyrazoles, and triketones) and at least 14 active ingredients (HRAC 2024). Globally, five weed species (*A. palmeri*, *A. retroflexus*, *A. tuberculatus*, *R. raphanistrum*, and Chinese sprangletop [*Leptochloa chinensis* (L.) Nees ex]) have evolved resistance to the G27 herbicides. Group 27 resistance is a multigenic trait (Huffman et al. 2015; Kohlhasse et al. 2018; Oliveira et al. 2018; Shyam et al. 2021) conferred predominantly by metabolic mechanisms, including enhanced herbicide oxidation and/or glutathione conjugation via GSTs (Concepcion et al. 2021; Ju et al. 2023). However, HPPD gene overexpression, a TSR mechanism, has been reported in *A. palmeri* (Nakka et al. 2017a) and other NTSR mechanisms, such as impaired whole-plant or subcellular transport, remain possible (Ma et al. 2013). In dioecious *Amaranthus* populations examined, NTSR to G27 and G5 herbicides has always been associated (Hamberg et al. 2023; Jacobs et al. 2020).

Waterhemp (*Amaranthus tuberculatus*)

Amaranthus tuberculatus has evolved resistance to G27 herbicides from three herbicide families: pyrazoles (topramezone), isoxazoles

(isoxaflutole), and triketones (mesotrione, tembotrione, and syncarpic acid-3) applied postemergence (Concepcion et al. 2021; Evans et al. 2019; Hausman et al. 2011; McMullan and Green 2011; O'Brien et al. 2018; Oliveira et al. 2017; Shergill et al. 2018). The resistance level to G27 herbicides is active ingredient specific. This specificity is exemplified by varying levels of resistance to mesotrione, tembotrione, and topramezone of 18-, 5-, and 2-fold, respectively (Oliveira et al. 2017). Variable results are corroborated by Evans et al. (2019), who reported the relative order of *A. tuberculatus* control and biomass reductions following postemergence field use rates was topramezone > tembotrione > mesotrione. However, the field use history of G27 herbicides may also play a significant role in determining cross-resistance (both levels and patterns) in *A. tuberculatus*. For example, the Nebraska population (NEB) was exposed to mesotrione and tembotrione (both triketones), while the Illinois population (MCR or SIR) was treated with mesotrione, tembotrione, and topramezone (Hausman et al. 2011; Kaundun et al. 2017). The NEB population is resistant to topramezone, which implies that triketone G27 herbicides can select for cross-resistance to pyrazole G27 herbicides.

Control of G27-resistant *A. tuberculatus* can be influenced by application timing. Resistance levels calculated with mesotrione were 9- or 13-fold applied preemergence (depending on the population or subpopulation used) and 10- or 35-fold applied postemergence (depending on the sensitive population used) for comparison (Hausman et al. 2011, 2013, 2016), and 2.4- or 45-fold for preemergence or postemergence, respectively (Kaundun et al. 2017). Early postemergence (5 cm; 4 to 5 true leaves) isoxaflutole and mesotrione treatments led to 10- and 32-fold resistance levels, respectively, in the Illinois SIR population and 4- and 7-fold resistance levels, respectively, in the NEB population compared with a G27-sensitive *A. tuberculatus* population (O'Brien et al. 2018). Group 27 resistance in *A. tuberculatus* can thus be affected by active ingredient (mesotrione vs. topramezone vs. tembotrione), application timing (preemergence vs. postemergence), and populations examined.

Wild radish (*Raphanus raphanistrum*)

Raphanus raphanistrum is resistant to triketones (mesotrione and tembotrione), isoxazole (isoxaflutole), and pyrazoles (topramezone and pyrasulfotole) (Busi et al. 2022; Lu et al. 2023). Busi et al. (2022) reported 50%, 60%, and 100% survival with the recommended postemergence field rates of mesotrione, topramezone, and pyrasulfotole, respectively, in two *R. raphanistrum* populations. Differences among *R. raphanistrum* populations in their responses to pyrasulfotole were also reported; populations 86-2020 and 91-2020 had resistance indices of 5.3 and 8.4, respectively (Busi et al. 2022). Furthermore, population 86-2020 was more resistant to postemergence mesotrione (triketone) and topramezone (pyrazole) + MCPA, while population 91-2020 was more resistant to pyrasulfotole (pyrazole) + bromoxynil. Interestingly, mesotrione (triketone) preemergence controlled *R. raphanistrum* >99%, while pyrasulfotole (pyrazole) + bromoxynil and topramezone (pyrazole) + bromoxynil postemergence provided <90% control in the field (Busi et al. 2022). Mesotrione preemergence controlled one G27-resistant *R. raphanistrum* population (91-2020) in the field, but this population was resistant to postemergence mesotrione in the greenhouse (Busi et al. 2022).

Summary and Implications for Future Weed Management

Herbicides in G27 were commercialized in the late 1990s (Jhala et al. 2023) and thus have had a relatively "brief" time period to select for G27-resistant weed populations compared with all other HRAC groups. It is currently unknown whether weed resistance to G27 herbicides evolved solely due to selection pressure from G27 herbicides or whether previous usage patterns of other herbicides (before 1998) may have contributed to the magnitude and patterns of G27 resistance. Despite a noncommercial class of G27 herbicides (e.g., syncarpic acids) having known sites of oxidative metabolism chemically blocked, effective control of G27-resistant *A. tuberculatus* populations was not obtained with the herbicide, syncarpic acid-3 (Concepcion et al. 2021) due to a previously unknown metabolic pathway involving Phase I (enzymes not yet characterized) and Phase II (GST) enzymes acting in concert. This unexpected metabolic capacity revealed an incredible, adaptive response possessed by some multiple-herbicide resistant *A. tuberculatus* populations to display cross-resistance, via detoxification, of compounds to which they had not been previously exposed. With the anticipated introduction of G27-resistant soybean cultivar technology (Siehl et al. 2014) in the future, resistance and cross-resistance to G27 herbicides (current or in development) may be exacerbated unless proper stewardship of active ingredients is practiced. In summary, patterns and magnitude of G27 resistance in weeds can be population specific (as in *R. raphanistrum*), active ingredient specific (as in *A. tuberculatus* and *R. raphanistrum*), and application timing specific (as in *A. tuberculatus* and *R. raphanistrum*).

Conclusions and Future Directions

This review has highlighted that differences in the magnitude and patterns of resistance exist within many herbicides' sites-of-action groups for numerous weed species and populations based on the active ingredient investigated. Importantly, a recent genomics study reported several alleles of *ALS*, *EPSPS*, and *PPO2* genes conferring TSR were major drivers that shaped the evolution of *A. tuberculatus* as a species during the past 50 yr, during which herbicide selection pressures were intense in row crops (Kreiner et al. 2022). Other factors, such as temperature and application timing, can also influence resistance levels and cross-resistance patterns in weed populations. Some variability within HRAC groups is due to specific target-site mutations only conferring resistance to some chemical classes within an HRAC group, such as G3 and G5, or to only some members of a chemical class, such as with G1, G2, and G14 herbicides. NTSR mechanisms further complicate these patterns, as NTSR can provide sporadic, unpredictable resistance within an HRAC group as well as cross-resistance to herbicides in different groups. As a result, resistance to one active ingredient does not always result in resistance across an HRAC group, emphasizing that resistance is much more complex than stating a weed is resistant to a single HRAC group.

One possible benefit of understanding underlying factors that cause differences in resistance patterns is for developing new "resistance breaking" chemistries that avoid TSR or NTSR mechanisms (Barker et al. 2023; Kaundun 2021; Porri et al. 2023; Scutt et al. 2024). Such herbicides would greatly aid in management of resistant populations, particularly where multiple

resistance mechanisms are present. Another way that understanding resistance patterns can be exploited is when mechanisms do not provide broad resistance to all herbicides within a group or across all environmental conditions at the time of application. In such cases, other herbicides within the group (or the same herbicide, as with G9) can be used to control resistant weeds, at least in the short term, as utilized with certain G1, G3, G5, and G9 herbicides. Alternatively, preemergence G14 herbicides with residual activity typically control G14-resistant *Amaranthus* populations, although the mechanistic basis for this discrepancy is still unknown.

However, using such approaches more widely presents some risk and requires specific information about the sensitivity of individual herbicide-resistant populations (Leon 2024). This task could be achieved by testing populations to determine herbicides that are still efficacious and thereby extend their effective use. For example, utilizing clethodim to control FOP-resistant grass populations or metribuzin to control metabolic triazine-resistant *Amaranthus* may provide effective short-term solutions for weed management. Alternatively, it is difficult to predict whether new TSR and/or NTSR mechanisms will evolve and render these short-term solutions ineffective. For example, it is possible that currently known or unknown fitness costs (Baucom 2019; Park and Mallory-Smith 2005; Vila-Aiub 2019; Vila-Aiub et al. 2005) associated with certain resistance mechanisms may prevent widespread resistance to some active ingredients in certain weed species. As a result, an urgent need exists to employ diverse management practices to complement herbicides as useful tools to optimize weed control. Harvest weed seed destruction (Geddes and Davis 2021) and integration and stewardship of effective chemicals (Landau et al. 2023) with nonchemical strategies (Schreier et al. 2022) should be utilized for promoting sustainable weed management in the future.

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References

- Alarcón-Reverte R, García A, Watson SB, Abdallah I, Sabaté S, Hernández MJ, Dayan FE, Fischer AJ (2015) Concerted action of target-site mutations and high EPSPS activity in glyphosate-resistant junglerice (*Echinochloa colona*) from California. *Pest Manag Sci* 71:996–1007
- Alcántara-de la Cruz R, Fernández-Moreno PT, Ozuna CV, Rojano-Delgado AM, Cruz-Hipólito HE, Domínguez-Valenzuela JA, Barro F, De Prado R (2016) Target and non-target site mechanisms developed by glyphosate-resistant hairy beggarticks (*Bidens pilosa* L.) populations from Mexico. *Front Plant Sci* 7:1492
- Ali A, McLaren RD, Machado VS (1986) Chloroplastic resistance to triazine herbicides in *Sinapis arvensis* L. (wild mustard). *Weed Res* 26:39–44
- Anonymous (2023) The Blue Book: Alberta's Crop Protection Guide 2023. Calgary: Alberta Wheat Commission. 700 p
- Anthony RG, Hussey PJ (1999) Dinitroaniline herbicide resistance and the microtubule cytoskeleton. *Trends Plant Sci* 4:112–116
- Anthony RG, Waldin TR, Ray JA, Bright SW, Hussey PJ (1998) Herbicide resistance caused by spontaneous mutation of the cytoskeletal protein tubulin. *Nature* 393:260–263
- Ashworth MB, Han H, Knell G, Powles SB (2016) Identification of triazine-resistant *Vulpia bromoides*. *Weed Technol* 30:456–463
- Atkins WM (2020) Mechanisms of promiscuity among drug metabolizing enzymes and drug transporters. *FEBS J* 287:1306–1322
- Baek YS, Bobadilla LK, Giacomini DA, Montgomery JS, Murphy BP, Tranel PJ (2021) Evolution of glyphosate-resistant weeds. Pages 93–128 in Knaak JB, ed. *Reviews of Environmental Contamination and Toxicology*. Volume 255, Glyphosate. Springer International Publishing, Cham, Switzerland
- Bandeén JD, McLaren RD (1976) Resistance of *Chenopodium album* to triazine herbicides. *Can J Plant Sci* 56:411–412
- Barker AL, Pawlak J, Duke SO, Beffa R, Tranel PJ, Wuerffel J, Young B, Porri A, Liebl R, Aponte R, Findley D, Betz M, Lerchl J, Culpepper S, Bradley K, Dayan FE (2023) Discovery, mode of action, resistance mechanisms, and plan of action for sustainable use of Group 14 herbicides. *Weed Sci* 71:173–188
- Barua R, Boutsalis P, Malone J, Gill G, Preston C (2020) Incidence of multiple herbicide resistance in annual bluegrass (*Poa annua*) across southeastern Australia. *Weed Sci* 68:340–347
- Baucom RS (2019) Evolutionary and ecological insights from herbicide-resistant weeds: what have we learned about plant adaptation, and what is left to uncover? *New Phytol* 223:68–82
- Beckie HJ (2006) Herbicide-resistant weeds: management tactics and practices. *Weed Technol* 20:793–814
- Beckie HJ, Hall LM, Shirriff SW, Martin E, Leeson JY (2019) Triple-resistant kochia [*Kochia scoparia* (L.) Schrad.] in Alberta. *Can J Plant Sci* 99:281–285
- Beckie HJ, Johnson EN, Légère A (2012a) Negative cross-resistance of acetolactate synthase inhibitor-resistant kochia (*Kochia scoparia*) to protoporphyrinogen oxidase- and hydroxyphenylpyruvate dioxygenase-inhibiting herbicides. *Weed Technol* 26:570–574
- Beckie HJ, Tardif FJ (2012) Herbicide cross resistance in weeds. *Crop Prot* 35:15–28
- Beckie HJ, Warwick SI, Sauder CA, Lozinski C, Shirriff S (2012b) Occurrence and molecular characterization of acetolactate synthase (ALS) inhibitor-resistant kochia (*Kochia scoparia*) in western Canada. *Weed Technol* 25:170–175
- Beres ZT, Giese LA, Mackey DM, Owen MDK, Page ER, Snow AA (2020) Target-site EPSPS Pro-106-Ser mutation in *Conyza canadensis* biotypes with extreme resistance to glyphosate in Ohio and Iowa. *USA Sci Rep* 10:7577
- Bernards ML, Crespo RJ, Kruger GR, Gaussoin R, Tranel PJ (2012) A waterhemp (*Amaranthus tuberculatus*) population resistant to 2,4-D. *Weed Sci* 60:379–384
- Bobadilla LK, Giacomini DA, Hager AG, Tranel PJ (2022) Characterization and inheritance of dicamba resistance in a multiple-resistant waterhemp (*Amaranthus tuberculatus*) population from Illinois. *Weed Sci* 70:4–13
- Böger P (2003) Mode of action for chloroacetamides and functionally related compounds. *J Pestic Sci* 28:324–329
- Böger P, Matthes B, Schmalfuß J (2000) Towards the primary target of chloroacetamides: new findings pave the way. *Pest Manag Sci* 56:497–508
- Borgato EA, Thiagarayaselvam A, Peterson DE, Hay MM, Dille JA, Jugulam M (2024) Metabolic resistance to protoporphyrinogen oxidase-inhibitor herbicides in a Palmer amaranth population from Kansas. *J Agric Food Chem* 72:5122–5132
- Brabham C, Norsworthy JK, Houston MM, Varanasi VK, Barber T (2019) Confirmation of S-metolachlor resistance in Palmer amaranth (*Amaranthus palmeri*). *Weed Technol* 33:720–726
- Bradshaw L, Padgett S, Kimball S, Well B (1997) Perspectives on glyphosate resistance. *Weed Technol* 11:189–198
- Brazier-Hicks M, Franco-Ortega S, Watson P, Rougemont B, Cohn J, Dale R, Hawkes TR, Goldberg-Cavalleri A, Onkokesung N, Edwards R (2022) Characterization of cytochrome P450s with key roles in determining herbicide selectivity in maize. *ACS Omega* 7:17416–17431
- Broster J, Boutsalis P, Gill GS, Preston C (2022) The extent of herbicide resistance in *Lolium rigidum* Gaud. (annual ryegrass) across south-eastern Australia as determined from random surveys. *Crop Pasture Sci* 73:1308–1317
- Brunharo CA, Patterson EL, Carrizo DR, de Melo MS, Nicolai M, Gaines TA, Nissen SJ, Christoffoleti PJ (2016) Confirmation and mechanism of glyphosate resistance in tall windmill grass (*Chloris elata*) from Brazil. *Pest Manag Sci* 72:1758–1764
- Brunton DJ, Boutsalis P, Gill G, Preston C (2018) Resistance to multiple PRE herbicides in a field-evolved rigid ryegrass (*Lolium rigidum*) population. *Weed Sci* 66:581–585

- Brunton DJ, Boutsalis P, Gill G, Preston C (2019) Resistance to very-long-chain fatty-acid (VLCFA)-inhibiting herbicides in multiple field-selected rigid ryegrass (*Lolium rigidum*) populations. *Weed Sci* 67:267–272
- Brunton DJ, Boutsalis P, Gill G, Preston C (2020) Control of thiocarbamate-resistant rigid ryegrass (*Lolium rigidum*) in wheat in southern Australia. *Weed Technol* 34:19–24
- Burnet MW, Barr AR, Powles SB (1994) Chloroacetamide resistance in rigid ryegrass (*Lolium rigidum*). *Weed Sci* 42:153–157
- Busi R (2014) Resistance to herbicides inhibiting the biosynthesis of very-long-chain fatty acids. *Pest Manag Sci* 70:1378–1384
- Busi R, Gaines TA, Vila-Aiub MM, Powles SB (2014) Inheritance of evolved resistance to a novel herbicide (pyroxasulfone). *Plant Sci* 217:127–134
- Busi R, Porri A, Gaines TA, Powles SB (2018) Pyroxasulfone resistance in *Lolium rigidum* is metabolism-based. *Pestic Biochem Physiol* 148:74–80
- Busi R, Powles SB (2013) Cross-resistance to prosulfocarb and triallate in pyroxasulfone-resistant *Lolium rigidum*. *Pest Manag Sci* 69:1379–1384
- Busi R, Powles SB (2016) Cross-resistance to prosulfocarb + S-metolachlor and pyroxasulfone selected by either herbicide in *Lolium rigidum*. *Pest Manag Sci* 72:1664–1672
- Busi R, Zhang B, Goggin D, Bryant G, Beckie HJ (2022) Identification of field resistance to HPPD-inhibiting herbicides in wild radish (*Raphanus raphanistrum*). *Weed Sci* 70:529–536
- Callihan RH, Schirman RW, Northam FE (1990) Picloram resistance in yellow starthistle. *West Soc Weed Sci Abstr* 30:31
- Carvalho-Moore P, Rangani G, Heiser J, Findley D, Bowe SJ, Roma-Burgos N (2021) PPO2 mutations in *Amaranthus palmeri*: implications on cross-resistance. *Agriculture* 11:760
- Chen J, Chu Z, Han H, Goggin DE, Yu Q, Sayer C, Powles SB (2020) A Val-202-Phe α -tubulin mutation and enhanced metabolism confer dinitroaniline resistance in a single *Lolium rigidum* population. *Pest Manag Sci* 76:645–652
- Chen J, Goggin D, Han H, Busi R, Yu Q, Powles S (2018) Enhanced trifluralin metabolism can confer resistance in *Lolium rigidum*. *J Agric Food Chem* 66:7589–7596
- Chen J, Yu Q, Owen M, Han H, Patterson E, Sayer C, Powles S (2022) Target-site resistance to trifluralin is more prevalent in annual ryegrass populations from Western Australia. *Pest Manag Sci* 78:1206–1212
- Chen J, Yu Q, Patterson E, Sayer C, Powles S (2021) Dinitroaniline herbicide resistance and mechanisms in weeds. *Front Plant Sci* 12:634018
- Concepcion JCT, Kaundun SS, Morris JA, Hutchings S-J, Strom SA, Lygin AV, Riechers DE (2021) Resistance to a nonselective 4-hydroxyphenylpyruvate dioxygenase-inhibiting herbicide via novel reduction-dehydration-glutathione conjugation in *Amaranthus tuberculatus*. *New Phytol* 232:2089–2105
- Cruz-Hipolito H, Osuna MD, Dominguez-Valenzuela JA, Espinoza N, De Prado R (2011) Mechanism of resistance to ACCase-inhibiting herbicides in wild oat (*Avena fatua*) from Latin America. *J Agric Food Chem* 59:7261–7267
- Dang HT, Malone JM, Boutsalis P, Gill G, Preston C (2017) Identification of a target-site mutation conferring resistance to triazine herbicides in oriental mustard (*Sisymbrium orientale* L.) from Australia. *Weed Biol Manag* 17:153–160
- Dang HT, Malone JM, Boutsalis P, Krishnan M, Gill G, Preston C (2018) Reduced translocation in 2,4-D-resistant oriental mustard populations (*Sisymbrium orientale* L.) from Australia. *Pest Manag Sci* 74:1524–1532
- de Carvalho LB, Alves PLdCA, González-Torralva F, Cruz-Hipolito HE, Rojano-Delgado AM, De Prado R, Gil-Humanes J, Barro F, Luque de Castro MD (2012) Pool of resistance mechanisms to glyphosate in *Digitaria insularis*. *J Agric Food Chem* 60:615–622
- Délye C, Causse R, Michel S (2016) Genetic basis, evolutionary origin and spread of resistance to herbicides inhibiting acetolactate synthase in common groundsel (*Senecio vulgaris*). *Pest Manag Sci* 72:89–102
- Délye C, Matějček A, Michel S (2008) Cross-resistance patterns to ACCase-inhibiting herbicides conferred by mutant ACCase isoforms in *Alopecurus myosuroides* Huds. (black-grass), re-examined at the recommended herbicide field rate. *Pest Manag Sci* 64:1179–1186
- Devine MD, Eberlein CV (1997) Physiological, biochemical and molecular aspects of herbicide resistance based on altered target sites. Pages 159–185 in Roe RM, Burton JD, Kuhr RJ, eds. *Herbicide Activity: Toxicology, Biochemistry and Molecular Biology*. Amsterdam: IOS
- Dimaano NG, Iwakami S (2021) Cytochrome P450-mediated herbicide metabolism in plants: current understanding and prospects. *Pest Manag Sci* 77:22–32
- Dimaano NG, Tominaga T, Iwakami S (2022) Thiobencarb resistance mechanism is distinct from CYP81A-based cross-resistance in late water-grass (*Echinochloa phyllopogon*). *Weed Sci* 70:160–166
- Dinelli G, Marotti I, Bonetti A, Minelli M, Catizone P, Barnes J (2006) Physiological and molecular insight on the mechanisms of resistance to glyphosate in *Conyza canadensis* (L.) Cronq. biotypes. *Pestic Biochem Physiol* 86:30–41
- Dominguez-Valenzuela JA, Gherekhloo J, Fernández-Moreno PT, Cruz-Hipolito HE, Alcántara-de la Cruz R, Sánchez-González E, De Prado R (2017) First confirmation and characterization of target and non-target site resistance to glyphosate in Palmer amaranth (*Amaranthus palmeri*) from Mexico. *Plant Physiol Biochem* 115:212–218
- dos Santos Souza A, Leal JFL, Montgomery JS, Ortiz MF, Araujo ALS, Morran S, Figueiredo MRA, Langaro AC, Zobiolo LHS, Nissen SJ, Gaines TA, de Pinho CF (2023) Nontarget site resistance due to rapid physiological response in 2,4-D-resistant *Conyza sumatrensis*: reduced 2,4-D translocation and auxin-induced gene expression. *Pest Manag Sci* 79:3581–3592
- Duke S, Powles S (2008) Glyphosate: a once-in-a-century herbicide. *Pest Manag Sci* 64:319–325
- Evans CM, Strom SA, Riechers DE, Davis AS, Tranel PJ, Hager AG (2019) Characterization of a waterhemp (*Amaranthus tuberculatus*) population from Illinois resistant to herbicides from five site of action groups. *Weed Technol* 33:400–410
- Faleco FA, Oliveira MC, Arneson NJ, Renz M, Stoltenberg DE, Werle R (2022) Multiple resistance to imazethapyr, atrazine, and glyphosate in a recently introduced Palmer amaranth (*Amaranthus palmeri*) accession in Wisconsin. *Weed Technol* 36:344–351
- Falk JS, Shoup DE, Al-Khatib K, Peterson DE (2006) Protox-resistant common waterhemp (*Amaranthus rudis*) response to herbicides applied at different growth stages. *Weed Sci* 54:793–799
- Fang J, He Z, Liu T, Li J, Dong L (2020) A novel mutation Asp-2078-Glu in ACCase confers resistance to ACCase herbicides in barnyardgrass (*Echinochloa crus-galli*). *Pestic Biochem Physiol* 168:104634
- Figueiredo MR, Leibhart LJ, Reicher ZJ, Tranel PJ, Nissen SJ, Westra P, Bernards ML, Kruger GR, Gaines TA, Jugulam M (2018) Metabolism of 2,4-dichlorophenoxyacetic acid contributes to resistance in a common waterhemp (*Amaranthus tuberculatus*) population. *Pest Manag Sci* 74:2356–2362
- Figueiredo MRD, Küpper A, Malone JM, Petrovic T, Figueiredo ABTD, Campagnola G, Gaines TA (2022) An in-frame deletion mutation in the degran tail of auxin coreceptor IAA2 confers resistance to the herbicide 2,4-D in *Sisymbrium orientale*. *Proc Natl Acad Sci USA* 119:1–9
- Fischer AJ, Ateh CM, Bayer DE, Hill JE (2000) Herbicide-resistant *Echinochloa oryzoides* and *E. phyllopogon* in California *Oryza sativa* fields. *Weed Sci* 48:225–230
- Fischer AJ, Cheatham DP, Vidotto F, De Prado R (2004) Enhanced effect of thiobencarb on bispyribac-sodium control of *Echinochloa phyllopogon* (Stapf) Koss. in California rice (*Oryza sativa* L.). *Weed Biol Manag* 4:206–212
- Fleet B, Malone J, Preston C, Gill G (2018) Target-site point mutation conferring resistance to trifluralin in rigid ryegrass (*Lolium rigidum*). *Weed Sci* 66:246–253
- Focke M, Lichtenthaler HK (1987) Inhibition of the acetyl-CoA carboxylase of barley chloroplasts by cycloxydim and sethoxydim. *Z Naturforsch C* 42:1361–1363
- Foster DC, Steckel LE (2022) Confirmation of dicamba-resistant Palmer amaranth in Tennessee. *Weed Technol* 36:777–780
- Fuerst EP (1987) Understanding the mode of action of the chloroacetamide and thiocarbamate herbicides. *Weed Technol* 1:270–277
- Fuerst EP, Sterling TM, Norman MA, Prather TS, Irzyk GP, Wu Y, Lownds NK, Callihan RH (1996) Physiological characterization of picloram resistance in yellow starthistle. *Pestic Biochem Physiol* 56:149–161
- Gaines T, Duke SO, Morran S, Rigon CAG, Tranel PJ, Küpper A, Dayan FE (2020) Mechanisms of evolved herbicide resistance. *J Biol Chem* 295:10307–10330
- Gaines T, Zhang W, Wang D, Bukuna B, Chisholm S, Shaner D, Nissen S, Patzoldt W, Tranel P, Culpepper A, Grey T, Webster T, Vencill W, Sammons

- R, Jiang J, *et al.* (2010) Gene amplification confers glyphosate resistance in *Amaranthus palmeri*. *Proc Natl Acad Sci USA* 107:1029–1034
- Ganie ZA, Jugulam M, Jhala AJ (2017) Temperature influences efficacy, absorption, and translocation of 2,4-D or glyphosate in glyphosate-resistant and glyphosate-susceptible common ragweed (*Ambrosia artemisiifolia*) and giant ragweed (*Ambrosia trifida*). *Weed Sci* 65:588–602
- Ge X, d'Avignon DA, Ackerman JJ, Duncan B, Spaur MB, Sammons RD (2011) Glyphosate-resistant horseweed made sensitive to glyphosate: low-temperature suppression of glyphosate vacuolar sequestration revealed by ³¹P NMR. *Pest Manag Sci* 67:1215–1221
- Ge X, d'Avignon DA, Ackerman JJ, Sammons RD (2010) Rapid vacuolar sequestration: the horseweed glyphosate resistance mechanism. *Pest Manag Sci* 66:345–348
- Geddes CM, Davis AS (2021) The critical period for weed seed control: a proposed framework to limit weed seed return. *Weed Res* 61:282–287
- Geddes CM, Ostendorf TE, Owen ML, Leeson JY, Sharpe SM, Shirriff SW, Beckie HJ (2022a) Fluroxypyr-resistant kochia [*Bassia scoparia* (L.) AJ Scott] confirmed in Alberta. *Can J Plant Sci* 102:437–441
- Geddes CM, Owen ML, Ostendorf TE, Leeson JY, Sharpe SM, Shirriff SW, Beckie HJ (2022b) Herbicide diagnostics reveal multiple patterns of synthetic auxin resistance in kochia (*Bassia scoparia*). *Weed Technol* 36:28–37
- Geddes CM, Pittman MM, Hall LM, A. Topinka K, Sharpe SM, Leeson JY, Beckie HJ (2023) Increasing frequency of multiple herbicide-resistant kochia (*Bassia scoparia*) in Alberta. *Can J Plant Sci* 103:233–237
- Ghanizadeh H, Buddenhagen CE, Harrington KC, Griffiths AG, Ngow Z (2022) Pinoxaden resistance in *Lolium perenne* L. is due to both target-site and non-target-site mechanisms. *Pestic Biochem Physiol* 184:105103
- Ghanizadeh H, Harrington KC, James TK (2015) Glyphosate-resistant population of *Lolium perenne* loses resistance at winter temperatures. *New Zeal J Agric Res* 58:423–431
- Gherekhloo J, Fernández-Moreno PT, Alcántara-de la Cruz R, Sanchez-Gonzalez E, Cruz-Hipolito HE, Dominguez-Valenzuela JA, De Prado R (2017) Pro-106-Ser mutation and EPSPS overexpression acting together simultaneously in glyphosate-resistant goosegrass (*Eleusine indica*). *Sci Rep* 7:6702
- Goggin DE, Cawthray GR, Powles SB (2016) 2,4-D resistance in wild radish: reduced herbicide translocation via inhibition of cellular transport. *J Exp Bot* 67:3223–3235
- Goggin DE, Kaur P, Owen MJ, Powles SB (2018) 2,4-D and dicamba resistance mechanisms in wild radish: subtle, complex and population specific? *Ann Bot* 122:627–640
- González-Torralva F, Gil-Humanes J, Barro F, Brants I, De Prado R (2012) Target site mutation and reduced translocation are present in a glyphosate-resistant *Lolium multiflorum* Lam. biotype from Spain. *Plant Physiol Biochem* 58:16–22
- Gray JA, Stoltenberg DE, Balke NE (1995) Absence of herbicide cross-resistance in two atrazine-resistant velvetleaf (*Abutilon theophrasti*) biotypes. *Weed Sci* 43:352–357
- Gronwald JW (1994) Resistance to photosystem II-inhibiting herbicides. Pages 27–60 in Powles SB, Holtum JAM, eds. *Herbicide Resistance in Plants: Biology and Biochemistry*. Boca Raton, FL: Lewis
- Grossmann K (2010) Auxin herbicides: current status of mechanism and mode of action. *Pest Manag Sci* 66:113–120
- Guo J, Riggins CW, Hausman NE, Hager AG, Riechers DE, Davis AS, Tranel PJ (2015) Nontarget-site resistance to ALS inhibitors in waterhemp (*Amaranthus tuberculatus*). *Weed Sci* 63:399–407
- Guo W, Zhang C, Wang S, Zhang T, Tian X (2023) Temperature influences glyphosate efficacy on glyphosate-resistant and -susceptible goosegrass (*Eleusine indica*). *Front Plant Sci* 14:1024
- Hager AG, Wax LM, Bollero GA, Simmons FW (2002) Common waterhemp (*Amaranthus rudis* Sauer) management with soil-applied herbicides in soybean (*Glycine max* (L.) Merr.). *Crop Prot* 21:277–283
- Hamberg RC, Yadav R, Dixon PM, Licht MA, Owen MDK (2023) Monitoring the temporal changes in herbicide-resistant *Amaranthus tuberculatus*: a landscape-scale probability-based estimation in Iowa. *Pest Manag Sci* 79:4819–4827
- Han H, Yu Q, Widderick MJ, Powles SB (2016) Target-site EPSPS Pro-106 mutations: sufficient to endow glyphosate resistance in polyploid *Echinochloa colona*? *Pest Manag Sci* 72:264–271
- Hashem A, Dhammu HS, Powles SB, Bowran DG, Piper TJ, Cheam AH (2001) Triazine resistance in a biotype of wild radish (*Raphanus raphanistrum*) in Australia. *Weed Technol* 15:636–641
- Hausman NE, Singh S, Tranel PJ, Riechers DE, Kaundun SS, Polge ND, Thomas DA, Hager AG (2011) Resistance to HPPD-inhibiting herbicides in a population of waterhemp (*Amaranthus tuberculatus*) from Illinois, United States. *Pest Manag Sci* 67:258–261
- Hausman NE, Tranel PJ, Riechers DE, Hager AG (2016) Responses of a waterhemp (*Amaranthus tuberculatus*) population resistant to HPPD-inhibiting herbicides to foliar-applied herbicides. *Weed Technol* 30:106–115
- Hausman NE, Tranel PJ, Riechers DE, Maxwell DJ, Gonzini LC, Hager AG (2013) Responses of an HPPD inhibitor-resistant waterhemp (*Amaranthus tuberculatus*) population to soil-residual herbicides. *Weed Technol* 27:704–711
- Hawkes TR, Langford MP, Viner R, Blain RE, Callaghan FM, Mackay EA, Hogg BV, Singh S, Dale RP (2019) Characterization of 4-hydroxyphenylpyruvate dioxygenases, inhibition by herbicides and engineering for herbicide tolerance in crops. *Pestic Biochem Physiol* 156:9–28
- Hay MM, Shoup DE, Peterson DE (2018) Palmer amaranth (*Amaranthus palmeri*) and common waterhemp (*Amaranthus rudis*) control with very-long-chain fatty acid inhibiting herbicides. *Crop For Turf Manag* 4:1–9
- Heap I (2024) The International Herbicide-Resistant Weed Database. www.weedscience.org. Accessed: May 2, 2024
- [HRAC] Herbicide Resistance Action Committee (2024) HRAC Mode of Action Classification, 2024. <https://hracglobal.com/tools/2024-hrac-global-herbicide-moa-classification>. Accessed: June 18, 2024
- Houston MM, Barber LT, Norsworthy JK, Roberts TL (2021) Evaluation of PRE herbicide programs for control of protoporphyrinogen oxidase-resistant *Amaranthus palmeri* in soybean. *Int J Agron* 2021:6652382
- Huffman J, Hausman NE, Hager AG, Riechers DE, Tranel PJ (2015) Genetics and inheritance of nontarget-site resistances to atrazine and mesotrione in a waterhemp (*Amaranthus tuberculatus*) population from Illinois. *Weed Sci* 63:799–809
- Huffman JL, Riggins CW, Steckel LE, Tranel PJ (2016) The EPSPS Pro106Ser substitution solely accounts for glyphosate resistance in a goosegrass (*Eleusine indica*) population from Tennessee, United States. *J Integr Agric* 15:1304–1312
- Hull R, Tatnell L, Cook S, Beffa R, Moss S (2014) Current status of herbicide-resistant weeds in the UK. Pages 261–272 in *Crop Production in Southern Britain, Precision Decisions for Profitable Cropping*. Wellesbourne, Warwick, UK: Association of Applied Biologists
- Hwang J-I, Norsworthy JK, González-Torralva F, Piveta LB, Barber LT, Butts TR (2022) Cross-resistance of barnyardgrass [*Echinochloa crus-galli* (L.) P. Beauv.] to aryloxyphenoxypropionate herbicides. *Pestic Biochem Physiol* 184:105089
- Hwang JI, Norsworthy JK, Piveta LB, Souza MCD, Barber LT, Butts TR (2023) Metabolism of 2,4-D in resistant *Amaranthus palmeri* S. Wats. *Crop Prot* 165:1–6
- Ignes M, McCurdy JD, McElroy JS, Castro EB, Ferguson JC, Meredith AN, Rutland CA, Stewart BR, Tseng TMP (2023) Target-site and non-target site mechanisms of pronamide resistance in annual bluegrass (*Poa annua*) populations from Mississippi golf courses. *Weed Sci* 71:206–216
- Intanon S, Perez-Jones A, Hulting AG, Mallory-Smith CA (2011) Multiple Pro₁₉₇ ALS substitutions endow resistance to ALS inhibitors within and among mayweed chamomile populations. *Weed Sci* 59:431–437
- Jacobs KE, Butts-Wilmsmeyer CJ, Ma R, O'Brien SR, Riechers DE (2020) Association between metabolic resistances to atrazine and mesotrione in a multiple-resistant waterhemp (*Amaranthus tuberculatus*) population. *Weed Sci* 68:358–366
- James EH, Kemp MS, Moss SR (1995) Phytotoxicity of trifluoromethyl- and methyl-substituted dinitroaniline herbicides on resistant and susceptible populations of black-grass (*Alopecurus myosuroides*). *Pestic Sci* 43:273–277

- Jaworski EG (1972) Mode of action of *N*-phosphonomethylglycine. Inhibition of aromatic amino acid biosynthesis. *J Agric Food Chem* 20:1195–1198
- Jhala AJ, Kumar V, Yadav R, Jha P, Jugulam M, Williams MM II, Hausman NE, Dayan FE, Burton PM, Dale RP, Norsworthy JK (2023) 4-Hydroxyphenylpyruvate dioxygenase (HPPD)-inhibiting herbicides: past, present, and future. *Weed Technol* 37:1–14
- Jhala AJ, Singh M, Shergill L, Singh R, Jugulam M, Riechers DE, Ganie ZA, Selby TP, Werle R, Norsworthy JK (2024) Very long chain fatty acid-inhibiting herbicides: current uses, site of action, herbicide-resistant weeds, and future. *Weed Technol* 38:e1. doi: [10.1017/wet.2023.90](https://doi.org/10.1017/wet.2023.90)
- Ju B, Liu M, Fang Y, Liu L, Pan L (2023) First report on resistance to HPPD herbicides mediated by nontarget-site mechanisms in the grass *Leptochloa chinensis*. *J Agric Food Chem* 71:17669–17677
- Jugulam M, DiMeo N, Veldhuis LJ, Walsh M, Hall JC (2013) Investigation of MCPA (4-chloro-2-ethylphenoxyacetate) resistance in wild radish (*Raphanus raphanistrum* L.). *J Agric Food Chem* 61:12516–12521
- Jugulam M, Shyam C (2019) Non-target-site resistance to herbicides: recent developments. *Plants* 8:417
- Juliano LM, Casimero MC, Llewellyn R (2010) Multiple herbicide resistance in barnyardgrass (*Echinochloa crus-galli*) in direct-seeded rice in the Philippines. *Int J Pest Manag* 56:299–307
- Kaundun S, Jackson L, Hutchings S-J, Galloway J, Marchegiani E, Howell A, Carlin, McIndoe E, Tuesca D, Moreno R (2019a) Evolution of target-site resistance to glyphosate in an *Amaranthus palmeri* population from Argentina and its expression at different plant growth temperatures. *Plants* 8:512
- Kaundun SS (2014) Resistance to acetyl-CoA carboxylase-inhibiting herbicides. *Pest Manag Sci* 70:1405–1417
- Kaundun SS (2021) Syngenta's contribution to herbicide resistance research and management. *Pest Manag Sci* 77:1564–1571
- Kaundun SS, Dale R, Zelaya I, Dinelli G, Maroti I, McIndoe E, Cairns A (2011) A novel P106L mutation in the EPSPS and an unknown mechanism(s) act additively to confer resistance to glyphosate in a South African *Lolium rigidum* population. *J Agric Food Chem* 59:3227–3233
- Kaundun SS, Downes J, Jackson LV, Hutchings S-J, McIndoe E (2021) Impact of a novel W2027L mutation and non-target site resistance on acetyl-CoA carboxylase-inhibiting herbicides in a French *Lolium multiflorum* population. *Genes* 12:1838
- Kaundun SS, Hutchings SJ, Dale RP, Howell A, Morris JA, Kramer VC, Shivrain VK, McIndoe E (2017) Mechanism of resistance to mesotrione in an *Amaranthus tuberculatus* population from Nebraska. *USA PLoS ONE* 29:12:e0180095
- Kaundun SS, Marchegiani E, Hutchings S-J, Baker K (2019b) Derived polymorphic amplified cleaved sequence (dPACS): a novel PCR-RFLP procedure for detecting known single nucleotide and deletion-insertion polymorphisms. *Int J Mol Sci* 20:3193
- Kaundun SS, Zelaya I, Dale RP, Lycett AJ, Carter P, Sharples KR, McIndoe E (2008) Importance of the P106S target site mutation in conferring resistance to glyphosate in an *Eleusine indica* biotype from the Philippines. *Weed Sci* 56:637–646
- Kern AJ, Peterson DM, Miller EK, Colliver CC, Dyer WE (1996) Triallate resistance in *Avena fatua* L. is due to reduced herbicide activation. *Pestic Biochem Physiol* 56:163–173
- Kishore GM, Shah DM (1988) Amino acid biosynthesis inhibitors as herbicides. *Annu Rev Biochem* 57:627–663
- Kleinman Z, Ben-Ami G, Rubin B (2016) From sensitivity to resistance—factors affecting the response of *Conyza* spp. to glyphosate. *Pest Manag Sci* 72:1681–1688
- Kohlhase DR, Edwards JW, Owen MDK (2018) Inheritance of 4-hydroxyphenylpyruvate dioxygenase inhibitor herbicide resistance in an *Amaranthus tuberculatus* population from Iowa. *USA Plant Sci* 274:360–368
- Kouame KBJ, Bertucci MB, Savin MC, Bararpour T, Steckel LE, Butts TR, Willett CD, Machado FG, Burgos NR (2022) Resistance of Palmer amaranth (*Amaranthus palmeri*) to S-metolachlor in the Midsouthern United States. *Weed Sci* 70:380–389
- Krämer H, Dücker R, Beffa R, Babczinski P (2019) Herbicides disturbing the synthesis of very-long-chain fatty acids. Pages 351–363 in Jeschke P, Witschel M, Krämer W, Schirmer U, eds. *Modern Crop Protection Compounds*. 3rd ed. Weinheim, Germany: Wiley-VCH Verlag
- Kreiner J, Latorre SM, Burbano HM, Stinchcombe HR, Otto SP, Weigel D, Wright CI (2022) Rapid weed adaptation and range expansion in response to agriculture over the past two centuries. *Science* 378:1079–1085
- Kreuz K, Tommasini R, Martinoia E (1996) Old enzymes for a new job. Herbicide detoxification in plants. *Plant Physiol* 111:349–353
- Kumar V, Currie RS, Jha P, Stahlman PW (2019a) First report of kochia (*Bassia scoparia*) with cross-resistance to dicamba and fluroxypyr in western Kansas. *Weed Technol* 33:335–341
- Kumar V, Liu R, Boyer G, Stahlman PW (2019b) Confirmation of 2,4-D resistance and identification of multiple resistance in a Kansas Palmer amaranth (*Amaranthus palmeri*) population. *Pest Manag Sci* 75:2925–2933
- Kumar V, Jha P (2017) First report of Ser653Asn mutation endowing high-level resistance to imazamox in downy brome (*Bromus tectorum* L.). *Pest Manag Sci* 73:2585–2591
- Landau C, Bradley K, Burns B, Flessner M, Gage K, Hager A, Ikley J, Jha P, Jhala A, Johnson PO, Johnson W, Lancaster S, Legleiter T, Lingenfelter D, Loux M, et al. (2023) The silver bullet that wasn't: rapid agronomic weed adaptations to glyphosate in North America. *PNAS Nexus* 2:pgad338
- LeClere S, Wu C, Westra P, Sammons RD (2018) Cross-resistance to dicamba, 2,4-D, and fluroxypyr in *Kochia scoparia* is endowed by a mutation in an AUX/IAA gene. *Proc Natl Acad Sci USA* 115:2911–2920
- Leon RG (2024) Resistance or tolerance: distinction without a difference. *Weed Sci* 72:113–116
- Li J, Peng Q, Han H, Nyporko A, Kulynych T, Yu Q, Powles S (2018) Glyphosate resistance in *Tridax procumbens* via a novel EPSPS Thr-102-Ser substitution. *J Agric Food Chem* 66:7880–7888
- Li L, Du L, Liu W, Yuan G, Wang J (2014) Target-site mechanism of ACCase-inhibitors resistance in American sloughgrass (*Beckmannia syzigachne* Steud.) from China. *Pestic Biochem Physiol* 110:57–62
- Lillie KJ, Giacomini DA, Tranel PJ (2020) Comparing responses of sensitive and resistant populations of Palmer amaranth (*Amaranthus palmeri*) and waterhemp (*Amaranthus tuberculatus* var. *rudis*) to PPO inhibitors. *Weed Technol* 34:140–146
- Liu W, Harrison DK, Chalupska D, Gornicki P, O'Donnell CC, Adkins SW, Haselkorn R, Williams RR (2007) Single-site mutations in the carboxyl-transferase domain of plastid acetyl-CoA carboxylase confer resistance to grass-specific herbicides. *Proc Natl Acad Sci USA* 104:3627–3632
- Lu H, Liu Y, Li M, Han H, Zhou F, Nyporko A, Yu Q, Qiang S, Powles S (2023) Multiple metabolic enzymes can be involved in cross-resistance to 4-hydroxyphenylpyruvate-dioxygenase-inhibiting herbicides in wild radish. *J Agric Food Chem* 71:9302–9313
- Lu H, Yu Q, Han H, Owen MJ, Powles SB (2018) A novel *psbA* mutation (Phe274-Val) confers resistance to PSII herbicides in a wild radish (*Raphanus raphanistrum*). *Pest Manag Sci* 75:144–151
- Lu H, Yu Q, Han H, Owen MJ, Powles SB (2019) Metribuzin resistance in a wild radish (*Raphanus raphanistrum*) population via both *psbA* gene mutation and enhanced metabolism. *J Agric Food Chem* 67:1353–1359
- Ma R, Evans AF, Riechers DE (2016) Differential responses to PRE and POST atrazine in two atrazine-resistant waterhemp populations. *Agron J* 108:1196–1202
- Ma R, Kaundun SS, Tranel PJ, Riggins CW, McGinness DL, Hager AG, Hawkes T, McIndoe E, Riechers DE (2013) Distinct detoxification mechanisms confer resistance to mesotrione and atrazine in a population of waterhemp. *Plant Physiol* 163:363–377
- Mangin AR, Hall LM, Beckie HJ (2016) Triallate-resistant wild oat (*Avena fatua* L.): unexpected resistance to pyrooxasulfone and sulfentrazone. *Can J Plant Sci* 97:20–25
- Marshall R, Hull R, Moss SR (2010) Target site resistance to ALS inhibiting herbicides in *Papaver rhoeas* and *Stellaria media* biotypes from the UK. *Weed Res* 50:621–630
- Matzrafi M, Seiwert B, Reemtsma T, Rubin B, Peleg Z (2016) Climate change increases the risk of herbicide-resistant weeds due to enhanced detoxification. *Planta* 244:1217–1227
- McAlister FM, Holtum JA, Powles SB (1995) Dintroaniline herbicide resistance in rigid ryegrass (*Lolium rigidum*). *Weed Sci* 43:55–62

- McCullough PE, Yu J, Czarnota MA (2017) First report of pronamide-resistant annual bluegrass (*Poa annua*). *Weed Sci* 65:9–18
- McKenzie-Gopsill A, Graham G, Laforest M, Ibarra S, Hann S, Wagg C (2020) Occurrence and management of PSII-inhibitor-resistant *Chenopodium album* L. in Atlantic Canadian potato production. *Agronomy* 10:1369
- McMullan PM, Green JM (2011) Identification of a tall waterhemp (*Amaranthus tuberculatus*) biotype resistant to HPPD-inhibiting herbicides, atrazine, and thifensulfuron in Iowa. *Weed Technol* 25:514–518
- McWhorter CG, Jordan TN, Wills GD (1980) Translocation of ¹⁴C-glyphosate in soybeans (*Glycine max*) and Johnsongrass (*Sorghum halepense*). *Weed Sci* 28:113–118
- Mengistu LW, Michael JC, Lym RG (2005) A *psbA* mutation in *Kochia scoparia* (L.) Schrad from railroad rights-of-way with resistance to diuron, tebuthiuron and metribuzin. *Pest Manag Sci* 61:1035–1042
- Michitte P, De Prado R, Espinoza N, Ruiz-Santaella J, Gauvrit C (2007) Mechanisms of resistance to glyphosate in a ryegrass (*Lolium multiflorum*) biotype from Chile. *Weed Sci* 55:435–440
- Milliman LD, Riechers DE, Wax LM, Simmons FW (2003) Characterization of two biotypes of imidazolinone-resistant eastern black nightshade. *Weed Sci* 51:139–144
- Mithila J, Hall JC, Johnson WG, Kelley KB, Riechers DE (2011) Evolution of resistance to auxinic herbicides: historical perspectives, mechanisms of resistance, and implications for broadleaf weed management in agronomic crops. *Weed Sci* 59:445–457
- Moretti ML, Van Horn CR, Robertson R, Segobye K, Weller SC, Young BG, Johnson WG, Douglas Sammons R, Wang D, Ge X, d'Avignon A (2018) Glyphosate resistance in *Ambrosia trifida*: Part 2. Rapid response physiology and non-target-site resistance. *Pest Manag Sci* 74:1079–1088
- Morrisette NS, Mitra A, Sept D, Sibley LD (2004) Dinitroanilines bind α -tubulin to disrupt microtubules. *Mol Biol Cell* 15:1960–1968
- Moss SR (1990) Herbicide cross-resistance in slender foxtail (*Alopecurus myosuroides*). *Weed Sci* 38:492–496
- Murphy BP, Tranel PJ (2019) Target-site mutations conferring herbicide resistance. *Plants* 8:382
- Nakka S, Godar AS, Wani PS, Thompson CR, Peterson DE, Roelofs J, Jugulam M (2017a) Physiological and molecular characterization of hydroxypyruvate dioxygenase (HPPD)-inhibitor resistance in Palmer amaranth (*Amaranthus palmeri* S. Wats.). *Front Plant Sci* 8:555
- Nakka S, Thompson CR, Peterson DE, Jugulam M (2017b) Target site-based and non-target site-based resistance to ALS inhibitors in Palmer amaranth (*Amaranthus palmeri*). *Weed Sci* 65:681–689
- Nandula VK, Ray JD, Ribeiro DN, Pan Z, Reddy KN (2013) Glyphosate resistance in tall waterhemp (*Amaranthus tuberculatus*) from Mississippi is due to both altered target-site and nontarget-site mechanisms. *Weed Sci* 61:374–383
- Nandula VK, Riechers DE, Ferhatoglu Y, Barrett M, Duke SO, Dayan FE, Goldberg-Cavalleri A, Tétard-Jones C, Wortley DJ, Onkokesung N, Brazier-Hicks M, Edwards R, Gaines T, Iwakami S, Jugulam M, Ma R (2019) Herbicide metabolism: crop selectivity, bioactivation, weed resistance, and regulation. *Weed Sci* 67:149–175
- Ndou V, Pieterse PJ, Brand DJ, Vorster A, Louw A, Phiri E (2021) Mechanism(s) of glyphosate resistance in a selected *Plantago lanceolata* (L.) R biotype. *Agronomy* 11:884
- Neve P, Powles SB (2005) Recurrent selection with reduced herbicide rates results in the rapid evolution of herbicide resistance in *Lolium rigidum*. *Theor Appl Genet* 110:1154–1166
- Nguyen TH, Malone JM, Boutsalis P, Shirley N, Preston C (2016) Temperature influences the level of glyphosate resistance in barnyardgrass (*Echinochloa colona*). *Pest Manag Sci* 72:1031–1039
- Nie H, Harre NT, Young BG (2023) A new V361A mutation in *Amaranthus palmeri* PPX2 associated with PPO-inhibiting herbicide resistance. *Plants* 12:1886
- Nie H, Mansfield BC, Harre NT, Young JM, Steppig NR, Young BG (2019) Investigating target-site resistance mechanism to the PPO-inhibiting herbicide fomesafen in waterhemp and interspecific hybridization of *Amaranthus* species using next generation sequencing. *Pest Manag Sci* 75:3235–3244
- Noguera MM, Rangani G, Heiser J, Bararpour T, Steckel LE, Betz M, Porri A, Lerchl J, Zimmermann S, Nichols RL, Roma-Burgos N (2021) Functional PPO2 mutations: co-occurrence in one plant or the same *ppo2* allele of herbicide-resistant *Amaranthus palmeri* in the US Mid-south. *Pest Manag Sci* 77:1001–1012
- Obenland OA, Ma R, O'Brien SR, Lygin AV, Riechers DE (2019) Carfentrazone-ethyl resistance in an *Amaranthus tuberculatus* population is not mediated by amino acid alterations in the PPO2 protein. *PLoS ONE* 14: e0215431
- O'Brien SR, Davis AS, Riechers DE (2018) Quantifying resistance to isoxaflutole and mesotrione and investigating their interactions with metribuzin POST in waterhemp (*Amaranthus tuberculatus*). *Weed Sci* 66:586–594
- Oliveira MC, Gaines TA, Jhala AJ, Knezevic SZ (2018) Inheritance of mesotrione resistance in an *Amaranthus tuberculatus* (var. *rudis*) population from Nebraska. *USA Front Plant Sci* 9:60
- Oliveira MC, Jhala AJ, Gaines T, Irmak S, Amundsen K, Scott JE, Knezevic SZ (2017) Confirmation and control of HPPD-inhibiting herbicide-resistant waterhemp (*Amaranthus tuberculatus*) in Nebraska. *Weed Technol* 31: 67–79
- Ou J, Stahlman P, Jugulam M (2018) Reduced absorption of glyphosate and decreased translocation of dicamba contribute to poor control of kochia (*Kochia scoparia*) at high temperature. *Pest Manag Sci* 74:1134–1142
- Panozzo S, Scarabel L, Rosan V, Sattin M (2017) A new Ala-122-Asn amino acid change confers decreased fitness to ALS-resistant *Echinochloa crus-galli*. *Front Plant Sci* 8:2042
- Park KW, Mallory-Smith CA (2004) Physiological and molecular basis for ALS inhibitor resistance in *Bromus tectorum* biotypes. *Weed Res* 44:71–77
- Park KW, Mallory-Smith CA (2005) Multiple herbicide resistance in downy brome (*Bromus tectorum*) and its impact on fitness. *Weed Sci* 53:780–786
- Patzoldt WL, Hager AG, McCormick JS, Tranel PJ (2006) A codon deletion confers resistance to herbicides inhibiting protoporphyrinogen oxidase. *Proc Natl Acad Sci USA* 103:12329–12334
- Patzoldt WL, Tranel PJ (2007) Multiple ALS mutations confer herbicide resistance in waterhemp (*Amaranthus tuberculatus*). *Weed Sci* 55:421–428
- Peniuk MG, Romano ML, Hall JC (1993) Physiological investigations into the resistance of wild mustard (*Sinapis arvensis* L.) biotype to auxinic herbicide. *Weed Res* 33:431–440
- Perez-Jones A, Intanon S, Mallory-Smith CA (2009) Molecular analysis of hexazinone-resistant shepherd's-purse (*Capsella bursa-pastoris*) reveals a novel *psbA* mutation. *Weed Sci* 57:574–578
- Perotti VE, Larran AS, Palmieri VE, Martinatto AK, Alvarez CE, Tuesca D, Permingeat HR (2019) A novel triple amino acid substitution in the EPSPS found in a high-level glyphosate-resistant *Amaranthus hybridus* population from Argentina. *Pest Manag Sci* 75:1242–1251
- Peterson MA, McMaster SA, Riechers DE, Skelton JJ, Stahlmann PW (2016) 2,4-D past, present, and future: a review. *Weed Technol* 30:303–345
- Petit C, Bay G, Pernin F, Délye C (2010) Prevalence of cross- or multiple resistance to the acetyl-coenzyme A carboxylase inhibitors fenoxaprop, clodinafop and pinoxaden in black-grass (*Alopecurus myosuroides* Huds.) in France. *Pest Manag Sci* 66:168–177
- Porri A, Betz M, Seebrock K, Knapp M, Johnen P, Witschel M, Aponte R, Liebl R, Tranel PJ, Lerchl J (2023) Inhibition profile of trifludimoxazin towards PPO2 target site mutations. *Pest Manag Sci* 79:507–519
- Porri A, Noguera MM, Betz M, Sälinger D, Brändle F, Bowe SJ, Lerchl J, Meyer L, Knapp M, Roma-Burgos N (2022) Can double PPO mutations exist in the same allele and are such mutants functional? *Pest Manag Sci* 78:2258–2264
- Poston DH, Hirata CM, Wilson HP (2002) Response of acetolactate synthase from imidazolinone-susceptible and -resistant smooth pigweed to ALS inhibitors. *Weed Sci* 50:306–311
- Poston DH, Wilson HP, Hines TE (2000) Imidazolinone resistance in several *Amaranthus hybridus* populations. *Weed Sci* 48:508–513
- Poston DH, Wu J, Hatzios KK, Henry PW (2001) Enhanced sensitivity to cloransulam-methyl in imidazolinone-resistant smooth pigweed. *Weed Sci* 49:711–716
- Powles SB, Lorraine-Colwill DF, Dellow JJ, Preston C (1998) Evolved resistance to glyphosate in rigid ryegrass (*Lolium rigidum*) in Australia. *Weed Sci* 46:604–607

- Powles SB, Yu Q (2010) Evolution in action: plants resistant to herbicides. *Annu Rev Plant Biol* 61:317–347
- Primiani MM, Cotterman JC, Saari LL (1990) Resistance of kochia (*Kochia scoparia*) to sulfonylurea and imidazolinone herbicides. *Weed Technol* 4:169–172
- Rangani G, Porri A, Salas-Perez RA, Lerchl J, Karaikal SK, Velásquez JC, Roma-Burgos N (2023) Assessment of efficacy and mechanism of resistance to soil-applied PPO inhibitors in *Amaranthus palmeri*. *Agronomy* 13:592
- Refatti JP, de Avila LA, Camargo ER, Ziska LH, Oliveira C, Salas-Perez R, Rouse CE, Roma-Burgos N (2019) High [CO₂] and temperature increase resistance to cyhalofop-butyl in multiple-resistant *Echinochloa colona*. *Front Plant Sci* 10:529
- Rey-Caballero J, Menéndez J, Giné-Bordonaba J, Salas M, Alcántara R, Torra J (2016) Unravelling the resistance mechanisms to 2,4-D (2,4-dichlorophenoxyacetic acid) in corn poppy (*Papaver rhoeas*). *Pestic Biochem Physiol* 133:67–72
- Riar DS, Norsworthy JK, Srivastava V, Nandula V, Bond JA, Scott RC (2013) Physiological and molecular basis of acetolactate synthase-inhibiting herbicide resistance in barnyardgrass (*Echinochloa crus-galli*). *J Agric Food Chem* 61:278–289
- Ritter RL (1986) Triazine resistant velvetleaf and giant foxtail control in no-tillage corn. *Proc Northeast Weed Sci Soc* 40:50–52
- Rouse CE, Roma-Burgos N, Norsworthy JK, Tseng T-M, Starkey CE, Scott RC (2018) *Echinochloa* resistance to herbicides continues to increase in Arkansas rice fields. *Weed Technol* 32:34–44
- Ryan GF (1970) Resistance of common groundsel to simazine and atrazine. *Weed Sci* 18:614–616
- Sabba RP, Ray IM, Lownds N, Sterling TM (2003) Inheritance of resistance to clopyralid and picloram in yellow starthistle (*Centaurea solstitialis* L.) is controlled by a single nuclear recessive gene. *J Hered* 94:523–527
- Sammons R, Heering D, Danicola N, Glick H, Elmore G (2007) Sustainability and stewardship of glyphosate and glyphosate-resistant crops. *Weed Technol* 21:347–354
- Scarabel L, Panozzo S, Varotto S, Sattin M (2011) Allelic variation of the ACCase gene and response to ACCase-inhibiting herbicides in pinoxaden-resistant *Lolium* spp. *Pest Manag Sci* 67:932–941
- Schreier H, Bish M, Bradley KW (2022) The impact of electrocution treatments on weed control and weed seed viability in soybean. *Weed Technol* 36:481–489
- Schwartz-Lazaro LM, Norsworthy JK, Scott RC, Barber LT (2017) Resistance of two Arkansas Palmer amaranth populations to multiple herbicide sites of action. *Crop Prot* 96:158–163
- Scutt JN, Willetts NJ, Campos BF, Oliver S, Hennessy A, Joyce PM, Hutchings S-J, le Goupil G, Colombo WL, Kaundun SS (2024) Metproxybicyclone, a novel carbocyclic aryl-dione acetyl-CoA carboxylase-inhibiting herbicide for the management of sensitive and resistant grass weeds. *J Agric Food Chem* 72:21380–21392
- Shergill LS, Bish MD, Jugulam M, Bradley KW (2018) Molecular and physiological characterization of six-way resistance in an *Amaranthus tuberculatus* var. *rudis* biotype from Missouri. *Pest Manag Sci* 74:2688–2698
- Shrestha A, Hembree KJ, Va N (2007) Growth stage influences level of resistance in glyphosate-resistant horseweed. *Calif Agric* 61:67–70
- Shyam C, Borgato EA, Peterson DE, Dille JA, Jugulam M (2021) Predominance of metabolic resistance in a six-way-resistant Palmer amaranth (*Amaranthus palmeri*) population. *Front Plant Sci* 11:614618
- Shyam C, Peterson DE, Jugulam M (2022) Resistance to 2,4-D in Palmer amaranth (*Amaranthus palmeri*) from Kansas is mediated by enhanced metabolism. *Weed Sci* 70:390–400
- Siehl DL, Tao Y, Albert H, Dong Y, Heckert M, Madrigal A, Lincoln-Cabatu B, Lu J, Fenwick T, Bermudez E, Sandoval M, Horn C, Green JM, Hale T, Pagano P, et al. (2014) Broad 4-hydroxyphenylpyruvate dioxygenase inhibitor herbicide tolerance in soybean with an optimized enzyme and expression cassette. *Plant Physiol* 166:1162–1176
- Singh R, Tardif FJ, Jugulam M (2023) Characterization of MCPA resistance in Palmer amaranth (*Amaranthus palmeri*). *Weed Sci* 71:565–573
- Singh V, Dos Reis FC, Reynolds C, Elmore M, Bagavathiannan M (2021) Cross and multiple herbicide resistance in annual bluegrass (*Poa annua*) populations from eastern Texas golf courses. *Pest Manag Sci* 77:1903–1914
- Soltani N, Brown LR, Sikkema PH (2019) Weed control in corn and soybean with Group 15 (VLCFA inhibitor) herbicides applied PRE. *Intl J Agron* 2019:1–7
- Sterling TM, Hall JC (1997) Mechanism of action of natural auxins and the auxinic herbicides. Pages 111–141 in Roe RM, Burton JD, Kuhr RJ, eds. *Herbicide Activity: Toxicology, Biochemistry and Molecular Biology*. Amsterdam: IOS Press
- Strom SA, Gonzini LC, Mitsdarfer C, Davis AS, Riechers DE, Hager AG (2019) Characterization of multiple herbicide-resistant waterhemp (*Amaranthus tuberculatus*) populations from Illinois to VLCFA-inhibiting herbicides. *Weed Sci* 67:369–379
- Strom SA, Hager AG, Concepcion JCT, Seiter NJ, Davis AS, Morris JA, Kaundun SS, Riechers DE (2021) Metabolic pathways for S-metolachlor detoxification differ between tolerant corn and multiple-resistant waterhemp. *Plant Cell Physiol* 62:1770–1785
- Strom SA, Hager AG, Seiter NJ, Davis AS, Riechers DE (2020) Metabolic resistance to S-metolachlor in two waterhemp (*Amaranthus tuberculatus*) populations from Illinois. *USA Pest Manag Sci* 76:3139–3148
- Strom SA, Jacobs KE, Seiter NJ, Davis AS, Riechers DE, Hager AG (2022) Control of waterhemp (*Amaranthus tuberculatus*) at multiple locations in Illinois with single PRE applications of VLCFA-inhibiting herbicides. *Weed Technol* 36:253–260
- Symington HE, Soltani N, Kaastra AC, Hooker DC, Robinson DE, Sikkema PH (2023) Multiple herbicide-resistant waterhemp control with Group 15 herbicides. *Weed Technol* 37:251–258
- Takano HK, Fernandes VN, Adegas FS, Oliveira RS Jr, Westra P, Gaines TA, Dayan FE (2020) A novel TIPT double mutation in EPSPS conferring glyphosate resistance in tetraploid *Bidens subalternans*. *Pest Manag Sci* 76:95–102
- Takano HK, Ovejero RFL, Belchior GG, Maymone GPL, Dayan FE (2021) ACCase-inhibiting herbicides: mechanism of action, resistance evolution and stewardship. *Sci Agric* 78:e20190102
- Tanetani Y, Kaku K, Kawai K, Fujioka T, Shimizu T (2009) Action of mechanism of a novel herbicide, pyroxasulfone. *Pestic Biochem Physiol* 95:47–55
- Thiel H, Varrelmann M (2014) Identification of a new PSII target site *psbA* mutation leading to D1 amino acid leu218val exchange in the *Chenopodium album* D1 protein and comparison to cross-resistance profiles of known modifications at positions 251 and 264. *Pest Manag Sci* 70:278–285
- Torra J, Rojano-Delgado AM, Menéndez J, Salas M, de Prado R (2021) Cytochrome P450 metabolism-based herbicide resistance to imazamox and 2,4-D in *Papaver rhoeas*. *Plant Physiol Biochem* 160:51–61
- Torra J, Rojano-Delgado AM, Rey-Caballero J, Royo-Esnal A, Salas ML, De Prado R (2017) Enhanced 2,4-D metabolism in two resistant *Papaver rhoeas* populations from Spain. *Front Plant Sci* 8:1584
- Tranel PJ, Wright TR, Heap IM (2024) Mutations in herbicide-resistant weeds to inhibition of acetolactate synthase. <https://weedsociety.org/Pages/MutationDisplayAll.aspx>. Accessed: May 3, 2024
- Umphres AM, Steckel LE, Mueller TC (2018) Control of protoporphyrinogen oxidase-inhibiting herbicide resistant and susceptible Palmer amaranth (*Amaranthus palmeri*) with soil-applied protoporphyrinogen oxidase-inhibiting herbicides. *Weed Technol* 32:95–100
- Van Horn CR, Moretti ML, Robertson RR, Segobye K, Weller SC, Young BG, Johnson WG, Schulz B, Green AC, Jeffery T, Lesperance MA (2018) Glyphosate resistance in *Ambrosia trifida*: Part 1. Novel rapid cell death response to glyphosate. *Pest Manag Sci* 74:1071–1078
- Varanasi VK, Brabham C, Norsworthy JK (2018) Confirmation and characterization of non-target site resistance to fomesafen in Palmer amaranth (*Amaranthus palmeri*). *Weed Sci* 66:702–709
- Vaughan MA, Vaughn KC (1988) Carrot microtubules are dinitroaniline resistant. I. Cytological and cross-resistance studies. *Weed Res* 28:73–83
- Vennapusa AR, Faleco F, Vieira B, Samuelson S, Kruger GR, Werle R, Jugulam M (2018) Prevalence and mechanism of atrazine resistance in waterhemp (*Amaranthus tuberculatus*) from Nebraska. *Weed Sci* 66:595–602

- Vila-Aiub M, Gundel PE, Yu Q, Powles SB (2013) Glyphosate resistance in *Sorghum halepense* and *Lolium rigidum* is reduced at suboptimal growing temperatures. *Pest Manag Sci* 69:228–232
- Vila-Aiub MM (2019) Fitness of herbicide-resistant weeds: current knowledge and implications for management. *Plants* 8:469
- Vila-Aiub MM, Balbi MC, Distéfano AJ, Fernández L, Hopp E, Yu Q, Powles SB (2012) Glyphosate resistance in perennial *Sorghum halepense* (Johnsongrass), endowed by reduced glyphosate translocation and leaf uptake. *Pest Manag Sci* 68:430–436
- Vila-Aiub MM, Neve P, Steadman K, Powles SB (2005) Ecological fitness of a multiple herbicide-resistant *Lolium rigidum* population: dynamics of seed germination and seedling emergence in resistant and susceptible phenotypes. *J Appl Ecol* 42:288–298
- Volenberg DS, Stoltenberg DE, Boerboom CM (2000) *Solanum ptycanthum* resistance to acetolactate synthase inhibitors. *Weed Sci* 48:399–401
- Vyn JD, Swanton CJ, Weaver SE, Sikkema PH (2006) Control of *Amaranthus tuberculatus* var. *rudis* (common waterhemp) with pre and post-emergence herbicides in *Zea mays* L. (maize). *Crop Prot* 25:1051–1056
- Walsh MJ, Powles SB, Beard BR, Parkin BT, Porter SA (2004) Multiple-herbicide resistance across four modes of action in wild radish (*Raphanus raphanistrum*). *Weed Sci* 52:8–13
- Walsh TA, Neal R, Merlo AO, Honma M, Hicks GR, Wolff K, Matsumura W, Davies JP (2006) Mutations in an auxin receptor homolog AFB5 and in SGT1b confer resistance to synthetic picolinate auxins and not to 2,4-dichlorophenoxyacetic acid or indole-3-acetic acid in *Arabidopsis*. *Plant Physiol* 142:542–552
- Warwick SI, Xu R, Sauder C, Beckie HJ (2008) Acetolactate synthase target-site mutations and single nucleotide polymorphism genotyping in ALS-resistant kochia (*Kochia scoparia*). *Weed Sci* 56:797–806
- Wenger J, Niderman T, Mathews C, Wailes (2019) Acetyl-CoA carboxylase inhibitors. Pages 501–528 in Jeschke P, Witschel M, Krämer W, Schirmer U, eds. *Modern Crop Protection Compounds*. 3rd ed. Weinheim, Germany: Wiley-VCH Verlag
- Westerveld DB, Soltani N, Hooker DC, Robinson DE, Tranel PJ, Laforest M, Sikkema, PH (2021) Biologically effective dose of metribuzin applied PRE and POST for the control of waterhemp (*Amaranthus tuberculatus*) with different mechanisms of resistance to photosystem II-inhibiting herbicides. *Weed Sci* 69:631–641
- Westra EP, Nissen SJ, Getts TJ, Westra P, Gaines TA (2019) Survey reveals frequency of multiple resistance to glyphosate and dicamba in kochia (*Bassia scoparia*). *Weed Technol* 33:664–672
- Whaley CM, Wilson HP, Westwood JH (2006) ALS resistance in several smooth pigweed (*Amaranthus hybridus*) biotypes. *Weed Sci* 54:828–832
- Wuerffel RJ, Young JM, Matthews JL, Young BG (2015a) Characterization of PPO-inhibitor-resistant waterhemp (*Amaranthus tuberculatus*) response to soil-applied PPO-inhibiting herbicides. *Weed Sci* 63:511–521
- Wuerffel RJ, Young JM, Tranel PJ, Young BG (2015b) Soil-residual protoporphyrinogen oxidase-inhibiting herbicides influence the frequency of associated resistance in waterhemp (*Amaranthus tuberculatus*). *Weed Sci* 63:529–538
- Xiang S, Callaghan M, Watson K, Tong L (2009) A different mechanism for the inhibition of the carboxyltransferase domain of acetyl-coenzyme A carboxylase by tepraloxym. *Proc Natl Acad Sci USA* 106:20723–20727
- Xu H, Zhu X, Wang H, Li J, Dong L (2013) Mechanism of resistance to fenoxaprop in Japanese foxtail (*Alopecurus japonicus*) from China. *Pestic Biochem Physiol* 107:25–31
- Yamamoto E, Zeng L, Baird WV (1998) α -Tubulin missense mutations correlate with antimicrotubule drug resistance in *Eleusine indica*. *Plant Cell* 10:297–308
- Yerkes CN (1995) Characterization of Atrazine Resistance in Photoautotrophic Cell Cultures and Weed Biotypes. Ph.D. dissertation. West Lafayette, IN: Purdue University. 157 p
- Yu LPC, Kim YS, Tong L (2010) Mechanism for the inhibition of the carboxyltransferase domain of acetyl-coenzyme A carboxylase by pinoxaden. *Proc Natl Acad Sci USA* 107:22072–22077
- Yu Q, Ahmad-Hamdani M, Han H, Christoffers M, Powles S (2013) Herbicide resistance-endowing ACCase gene mutations in hexaploid wild oat (*Avena fatua*): insights into resistance evolution in a hexaploid species. *Heredity* 110:220–231
- Yu Q, Cairns A, Powles S (2007a) Glyphosate, paraquat and ACCase multiple herbicide resistance evolved in a *Lolium rigidum* biotype. *Planta* 225:499–513
- Yu Q, Collavo A, Zheng M-Q, Owen M, Sattin M, Powles SB (2007b) Diversity of acetyl-coenzyme A carboxylase mutations in resistant *Lolium* populations: evaluation using clethodim. *Plant Physiol* 145:547–558
- Yu Q, Han H, Li M, Purba E, Walsh MJ, Powles SB (2012) Resistance evaluation for herbicide resistance-endowing acetolactate synthase (ALS) gene mutations using *Raphanus raphanistrum* populations homozygous for specific ALS mutations. *Weed Res* 52:178–186
- Yu Q, Han H, Powles SB (2008) Mutations of the ALS gene endowing resistance to ALS-inhibiting herbicides in *Lolium rigidum* populations. *Pest Manag Sci* 64:1229–1236
- Yu Q, Powles S (2014) Metabolism-based herbicide resistance and cross resistance in crop weeds: a threat to herbicide sustainability and global crop production. *Plant Physiol* 166:1106–1118
- Zhang H, Tweel B, Tong L (2004) Molecular basis for the inhibition of the carboxyltransferase domain of acetyl-coenzyme-A carboxylase by haloxyfop and diclofop. *Proc Natl Acad Sci USA* 101:5910–5915
- Zheng D, Patzoldt WL, Tranel PJ (2005) Association of the W574L ALS substitution with resistance to cloransulam and imazamox in common ragweed (*Ambrosia artemisiifolia*). *Weed Sci* 53:424–430