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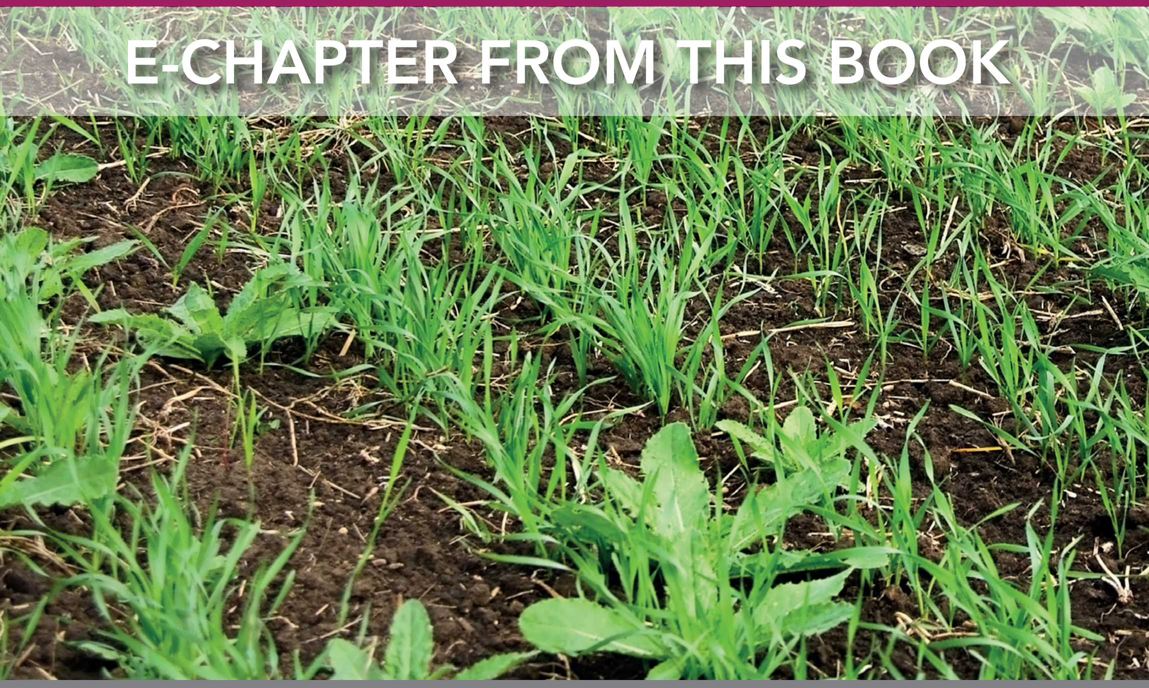

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The role of herbicide-resistant crops in integrated weed management

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1 Introduction

Chemical weed control began with the use of 2,4-D in the mid-1940s. Since then, a wide array of herbicides has been commercialized and that has greatly contributed to increased crop yields. Herbicide use in 21 major crops in the United States increased over 13-fold from 16 million kg in 1960 to 217 million kg in 1981. By 1980, over 90% of the corn, cotton and soybean areas were treated with herbicides compared to less than 10% of these crops planted in 1952 (Fernandez-Cornejo et al. 2014). With the introduction of several new, more specific and more effective herbicides, the cost of weed control with herbicides decreased relative to other control practices (labour, fuel and machinery). These benefits of lower production costs, higher crop yields and quality, and increased profit margins for farmers resulted in over-dependence on herbicides for weed management. Use of the same herbicide year after year has led to evolution of herbicide-resistant (HR) weeds. Development of herbicide resistance in weeds is widely recognized as a result of adaptive evolution of weed populations to repetitive use of same herbicide or class of herbicides (Jasieniuk et al. 1996). In response to selection pressure exerted by herbicides, weed populations change in genetic composition by selection of genes already present or arisen newly through mutation resulting in evolution of resistance (Délye et al. 2013; Jasieniuk et al. 1996). The first case of resistance to triazines was reported in 1968 (Ryan 1970). Since then, there has been an alarming increase in evolution and spread of HR weeds. As of 2017, globally, 252 weed species (147 dicots and 105 monocots) have evolved resistance

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to 161 different herbicides representing 23 of the 26 known herbicide sites of action (SOA) in 91 crops in 68 countries (Heap 2017).

HR crops, both transgenic (created through integration of transgene) and non-transgenic (created through traditional plant breeding or mutagenesis) as shown in Tables 1 and 2, have been widely grown in several countries since their commercialization in the early 1980s to mid-1990s (Green 2012; Powles 2008; Reddy and Jha 2016). HR crop technology was a blessing for growers as it provided simple, flexible, effective and economical weed management options. Each specific HR crop (viz., glyphosate-resistant, glufosinate-resistant, imidazolinone-tolerant) provided a unique opportunity to manage specific weeds. Furthermore, HR crops offered simplicity and flexibility to manage a broad spectrum of weeds and weeds resistant to other herbicides. For example, use of glyphosate in glyphosate-resistant (GR) crops offered a tremendous advantage to manage weeds resistant to other herbicides such as ALS inhibitors, acetyl CoA carboxylase (ACCase) inhibitors, dinitroanilines and organo-arsenicals. Among all HR crops, GR crops offered farmers more simplicity and flexibility to manage weeds. The rapid adoption of GR crops by growers was mainly because of weed-free fields, increased yields with less input, and increased profit per unit area (Castle et al. 2006). The high rate of adoption of GR soybean, cotton and corn in North America resulted in unprecedented impact because glyphosate was often the sole herbicide used over large production areas. Its use was accompanied by a drastic decline in mechanical and cultural methods to manage weed seed banks (Green 2011; Jha et al. 2017; Owen and Zelaya 2005; Shaw et al. 2009). Ultimately, over-reliance on glyphosate, especially in conservation tillage systems, resulted in evolution of GR weeds. There are now 37 GR weed species globally (Heap 2017).

Table 1 Commercially available transgenic herbicide-resistant (HR) crops (Adapted from Green and Castle 2010; Green 2012)

Crop	Resistance trait	Trait gene(s)	Year available
Canola	Glufosinate	*pat*	1995
Canola	Glyphosate	*cp4 epsps, gox v247*	1996
Corn	Glufosinate	*pat*	1996
Corn	Glyphosate	Multiple *zm-2mepsps*	1998
		Two *cp4 epsps* cassettes	2001
Soybean	Glyphosate	*cp4 epsps*	1996
Soybean	Glufosinate	*pat*	2009
Cotton	Glyphosate	*cp4 epsps*	1997
		Two *cp4 epsps*	2006
		zm-2mepsps	2009
Cotton	Glufosinate	*bar*	2005
Rice	Glufosinate	*bar*	2006
Sugar beet	Glyphosate	*cp4 epsps*	2007
Alfalfa	Glyphosate	Two *cp4 epsps*	2011*

* Glyphosate-resistant alfalfa was first released in 2006, but got legal clearance for sale in 2011.

Table 2 Commercially available non-transgenic herbicide-resistant (HR) crops (Adapted from Green and Castle 2010; Green 2012)

Crop	Resistance trait	Selection method	Year available
Soybean	Triazine	Tissue culture	1981
	Sulfonylureas	Seed mutagenesis	1994
Canola	Triazine	Whole plant	1984
	Imidazolinone	Microspore selection	1997
Corn	Imidazolinone	Pollen mutagenesis/tissue culture	1993
	Cyclohexanediones (sethoxydim)	Tissue culture	1996
Wheat	Imidazolinone	Seed mutagenesis	2002
Rice	Imidazolinone	Seed mutagenesis	2002
Sunflower	Imidazolinone	Transfer from weedy relative	2003
	Sulfonylureas	Transfer from weedy relative	2006
Sorghum	Sulfonylureas	Transfer from weedy relative	2013

The increasing number of HR weeds led to development and commercialization of several multiple HR (stacked-trait) crops as tools to manage weeds that had become difficult-to-control or resistant to glyphosate and other herbicides (Duke 2005; Owen 2008; Reddy and Jha 2016). However, diversification of weed control methods is critical to future use of HR technology, otherwise, shifts in weed populations related to ecological adaptation, natural tolerance or evolved resistance (Owen and Zelaya 2005), will continue to pose an economic threat to production agriculture. Lessons need to be learnt and integrated weed management (IWM) programmes need to be implemented to maintain sustainability of GR and other HR crop technologies (Powles 2008). This chapter provides an outlook on major HR crops (commercialized or under development), their benefits and pitfalls, and outlines a direction forward for growers to manage weeds, regardless of herbicide resistance.

2 Glyphosate-resistant crops

Commercialization of HR crops, particularly GR crops, has created a paradigm change in weed management tactics adopted by growers on their farms. GR soybean, cotton and canola were introduced in 1996 and corn in 1998. By 2016, 94% of soybean, 89% of cotton and 89% of corn areas were planted with GR cultivars in the United States (USDA 2016). Globally, 83% of soybean, 75% of cotton, 29% of corn and 24% of canola areas were planted with GR cultivars in 2015 (James 2015). The rapid adoption of GR crop technology was attributed to the effective, easy-to-use, economical and safe use of glyphosate for broad-spectrum weed control. Agronomic advantages such as early planting and conservation tillage also facilitated rapid adoption and commercial success of GR crops to enhance global food security (Green 2012; Powles 2008). Conservation tillage (particularly no tillage) in GR crop systems is considered more environmentally sustainable, compared with the conventional tillage systems, with regard to soil erosion and water quality (Cerdeira and Duke 2006; Price et al. 2011). Anecdotal evidence suggests that corn, soybean and cotton growers valued consistency in weed control and protection against yield loss as important reasons for adopting GR crop technology. At the outset, the GR crops (viz. corn, cotton and soybean) offered a tremendous opportunity to manage weeds resistant to other herbicides (ALS inhibitors, ACCase inhibitors, dinitroanilines and organo-arsenicals) (Green 2012). Prudent use of GR crops could have increased herbicide diversity for weed control by enabling use of herbicide tank mixtures, herbicide rotations or sequential herbicide programmes. Instead, the simplicity and convenience of glyphosate-based GR cropping systems has been over-exploited, with growers often relying on glyphosate only for weed control in GR corn, soybean and cotton (Bayliss 2000; Duke 2005; Gianessi 2005; Green 2011). This situation could partially be attributed to the common perception that GR weeds would never evolve, since no weeds developed resistance to glyphosate even after more than two decades (prior to 1996) of non-selective glyphosate use in non-crop situations (Bradshaw et al. 1997).

One of the major consequences of this unprecedented change following the rapid adoption of GR crops has been a greater selection pressure on the weed community (Duke 2005). There has been a decline in number of herbicides used to manage weeds. 'The number of herbicide active ingredients used on at least 10% of the US soybean area declined from 11 in 1995 to only 1, glyphosate, in 2002' (Green and Owen 2011). This lack of diversity in weed control tactics resulted in weed population shifts to species that have natural tolerance to or have evolved resistance to glyphosate (Duke 2005; Owen 2008). With an increase in land area under GR soybean, corn and cotton production in the United States, weed species such as pigweeds (*Amaranthus* spp.), horseweed (*Conyza canadensis* (L.) Cronq.), common lambsquarters (*Chenopodium album* L.), velvetleaf (*Abutilon theophrasti* Medik.), Asiatic dayflower (*Commelina communis* L.) and tropical spiderwort (*Commelina benghalensis* L.) well adapted to no-till systems and/or difficult to control with glyphosate, became dominant in the weed community (Culpepper 2006; Hilgenfeld et al. 2001; Owen 2008; Scursoni et al. 2007).

With the first discovery of GR rigid ryegrass (*Lolium rigidum* Gaudin) in Australia in 1996 (Powles et al. 1998), by 2017, 37 weed species were resistant to glyphosate globally (Heap 2017). In the United States, 17 weed species evolved resistance to glyphosate mostly in GR cropping systems (Heap 2017). Of particular significance is GR Palmer amaranth (*Amaranthus palmeri* S. Watson) that first appeared in GR cotton in Georgia in 2008, and has now become a threat to the conservation tillage system in corn, soybean and cotton crops across south-eastern, Midsouth and Midwestern USA (Price et al. 2011). Other economically significant weed species that evolved glyphosate resistance with the massive adoption of GR crops over large areas in the United States include common ragweed (*Ambrosia artemisiifolia* L.), giant ragweed (*Ambrosia trifida* L.) and various *Conyza* and *Lolium* spp. Likewise, the rapid adoption of GR soybean in Argentina and Brazil resulted in field-evolved GR biotypes of johnsongrass (*Sorghum halepense* L. Pers) and wild poinsettia (*Euphorbia heterophylla* L.), respectively (Vila-Aiub et al. 2007; Vidal et al. 2007).

Because of rapid reproduction potential and spread of these GR weeds, growers have to face drastic crop yield reductions and have to change their crop production and weed control practices, which in most cases, are cost prohibitive (Shaw et al. 2011). For instance, herbicide input costs to manage GR Palmer amaranth in cotton in Georgia, USA, have more than doubled due to complex and expensive weed control programmes required for successful management (Sosnoskie and Culpepper 2014). A recent survey suggests that nearly 50% of US growers are now dealing with GR weeds in their fields (Fraser 2013). Therefore, weed management practices must integrate other herbicide SOAs, if this novel, once-in-a-century herbicide (glyphosate), and GR crop technology, are to be sustained for future use.

3 Glufosinate-resistant crops

Glufosinate-resistant corn, cotton and soybean were commercialized in 1997, 2004 and 2009, respectively, a similar time frame as their GR counterparts. Glufosinate resistance trait has provided US cotton and soybean growers a valuable tool to manage GR weeds, such as Palmer amaranth (Norsworthy et al. 2008). Stacked-trait cultivars of soybean, corn and cotton that confer resistance to both glufosinate and glyphosate are now commercially available and allow growers to diversify their weed management programmes. Greater cost, narrow spectrum of weeds and more restrictive timing of application (effective mostly on smaller weeds) are the major factors contributing to the slower adoption of glufosinate versus glyphosate (Green and Owen 2011). Furthermore, glufosinate is not very effective on grasses and perennial weeds. Three weed species goosegrass (*Eleusine indica* L.), perennial ryegrass (*Lolium perenne* L. ssp. perenne) and Italian ryegrass (*Lolium perenne* L. ssp. *multiflorum*) have already evolved resistance to glufosinate (Heap 2017), which may impede the long-term utility of this HR crop technology if not used as a component of IWM.

4 Imidazolinone and sulphonylurea-tolerant crops

Imidazolinone (IMI) herbicides including imazapyr, imazapic, imazethapyr, imazamox, imazamethabenz and imazaquin control weeds by inhibiting the acetohydroxyacid synthase (AHAS) or acetolactate synthase (ALS) enzyme, thereby disrupting the biosynthesis of branched chain amino acids in plants (Tan et al. 2005). These herbicides are used for broad-spectrum grass and broadleaf control in IMI-tolerant crops. The IMI-tolerance trait, also referred as the Clearfield™ trait, was commercialized in corn in 1993, followed by canola (1997), wheat (2002), rice (2002) and sunflower (2003). IMI herbicides are effective for control of certain difficult-to-control weeds such as shattercane [*Sorghum bicolor* (L) Moench] and johnsongrass [*Sorghum halepense* (L) Pers] in IMI-tolerant corn, red rice (*Oryza sativa* var. *sylvatica*) in IMI-tolerant rice, wild mustard [*Brassica kaber* (DC) LC Wheeler] and stinkweed [*Pluchea camphorata* (L) DC] in IMI-tolerant oilseed rape, and downy brome (*Bromus tectorum* L.), jointed goatgrass (*Aegilops cylindrica* Host) and Italian ryegrass in IMI-tolerant wheat (Tan et al. 2005).

Similarly, the sulphonylurea-tolerant (ST) trait in crops provides increased tolerance to chlorimuron and other compounds in the sulphonylurea family of ALS inhibitors applied post-emergence for weed control (Reddy and Whiting 2000). The ST soybean offers additional flexibility to growers in double crop situations (soybean after wheat) by mitigating herbicide carryover injury concerns in soybean from soil residual sulphonylurea herbicides applied in wheat.

Because these non-transgenic, HR traits, are incorporated in crops using traditional breeding techniques (mutagenesis and selection), regulatory barriers related to commercialization are significantly less than the transgenic HR traits. These IMI/ST traits are often stacked with other HR trait(s) to allow use of herbicide mixtures because of the widespread distribution of ALS-resistant weeds (Green and Owen 2011; Heap 2017). Reports of gene flow from IMI-tolerant crops to closely related weed species such as red rice, wild sunflower (*Helianthus annuus* L.) and jointed goatgrass (Tan et al. 2005) are other classical examples of why diversity and stewardship programmes are needed for using these HR crops in future.

5 New HR crop technologies

Unfortunately, over-reliance on HR crop technology over the past two decades has led to rapid evolution of HR weeds because of massive selection pressure (Duke and Powles 2009). Evolution of weed resistance to glyphosate has diminished the utility of glyphosate considerably. As a solution to this problem, the development of a new generation of multiple HR crops has been pursued vigorously by several agrochemical industries. Currently, Monsanto, Dow, Bayer, Syngenta and BASF are developing new stacked-trait crops in combination with the GR trait. They are glyphosate-glufosinate (soybean, corn, cotton), glyphosate-ALS inhibitors (soybean, corn, canola), glyphosate-glufosinate-2,4-D (soybean, cotton), glyphosate-glufosinate-dicamba (soybean, corn, cotton), glyphosate-glufosinate-HPPD inhibitors (soybean and cotton), glyphosate-glufosinate-2,4-D-ACCase inhibitors (corn) and glufosinate-dicamba (wheat) (Green 2014). Transgenic, protoporphyrinogen oxidase (PPO)-resistant corn has also been developed (Green and Owen 2011). The relatively new HR traits (Table 3) when used in stacked-trait crops will provide new options with existing herbicides and can potentially be used to control GR- and ALS inhibitor-resistant weeds. However, these stacked-trait crops will not be a total weed management solution because several weeds have already evolved resistance to these herbicides. For example, 87 weeds resistant to various ALS inhibitors, 48 weeds resistant to ACCase inhibitors and 34 weeds resistant to synthetic auxins have already evolved (Heap 2017). Furthermore, PPO-resistant *Amaranthus* species have been documented in Midwestern and Southern US states, including multiple-resistant biotypes of Palmer amaranth (resistant to glyphosate and PPO inhibitors) and common waterhemp (resistant to glyphosate/2, 4-D, ALS, PS II, HPPD and PPO inhibitors) (Heap 2017). Therefore, the utility of stacked-trait crops depends on the specific weed problem to be addressed and requires knowledge of the herbicide SOA to match the specific HR weed problem (Green and Owen 2011; Shaner and Beckie 2014). Improved formulation and application technologies for using 2,4-D (2,4-D choline) and dicamba (DGA salt) will provide growers much-needed tools to manage GR broadleaf weeds in stacked-trait crops, with reduced off-target herbicide drift and injury to sensitive broadleaf plants (Green and Owen 2011). Multiple HR crops will continue to evolve, thereby allowing growers to use new herbicide mixtures with multiple SOAs, but there is an urgent need to use this technology more pragmatically and judiciously to maintain the long-term sustainability of existing herbicides.

Table 3 New transgenic herbicide-resistant (HR) traits stacked with glyphosate- and/or glufosinate resistance trait(s) (Adapted from Green and Castle 2010; Green 2012)

Resistance trait	Trait characteristics	Crop(s)*
2,4-D	Microbial degradation enzyme	Corn, cotton, soybean
Dicamba	*Pseudomonas maltophilia*, *O*-demethylase	Corn, cotton, soybean
HPPD inhibitor	Over-expression, alternate pathway, and increased pathway flux	Soybean, cotton
PPO inhibitors	Resistant microbial and *Arabidopsis thaliana* PPO	Corn
AOPP, ACCase inhibitor and synthetic auxin	Microbial, aryloxyalkanoate dioxygenase	Corn
Multiple herbicides	Glutathione *S*-transferase, *Escherichia coli* P450, *Zea mays*	TBD

* Some of these publicly disclosed HR traits will be commercialized in the near future.
HPPD, 4-hydroxyphenylpyruvate dioxygenase; PPO, protoporphyrinogen oxidase; AOPP, aryloxyphenoxypropionate; ACCase, acetyl CoA carboxylase; TBD, to be determined.

6 HR crops as part of an IWM programme

Herbicides (with or without HR crops) are still essential for weed management in modern cropping systems. HR crop technology alone cannot provide total weed control. HR crops must be integrated with other weed control tactics. It is best regarded as supplementary to other weed control methods that increase the diversity of weed control tactics. There is a greater need for IWM, a holistic approach that integrates different methods of weed control to manage weeds and maintain crop yields (Harker and O'Donovan 2013; Swanton and Murphy 1996). The IWM approach must include use of combinations of mechanical (tillage before planting, in-crop cultivation, hand hoeing, post-harvest tillage), cultural (competitive cultivars, plant densities, row spacing, crop rotation, winter crops in rotation, cover crops), chemical (residual herbicides, herbicide full-labelled rate, tank mixtures at the label rate, sequences, application timing, herbicide rotation with different modes of action), biological tactics where and when available, as well as preventive (weed seed bank management, clean equipment) techniques. Also, use of combinations of different herbicide application methods: post-harvest (fallow seedbed), pre-plant foliar (burndown), pre-plant incorporated, pre-emergence, post-emergence over-the-top, directed-post-emergence and spot treatment is critical to manage weeds. Due to high short-term costs associated with the use of an array of weed control tactics, growers often are reluctant to diversify management tactics. Sustainable weed management requires a longer-term strategy than that of a single-season approach. Herbicide dependence has failed as evident from the severity of the evolution of weeds resistant to 23 of the 26 herbicide SOA. Growers have no choice. They must diversify to achieve sustainable weed management.

7 Summary

The HR (single or stacked-trait) crops represent a revolutionary breakthrough in weed control technology, but they are only one of several weed control tactics. The HR weed management strategies must be diversified in order to curtail or disrupt HR weeds from evolving and spreading, with an ultimate goal of not allowing any weed to survive and set seed. Integration of HR crop technology with cultural, mechanical and chemical (along with biological where available) tactics is critical in the management of herbicide resistance and to ensure sustained food and fibre production. The future weed management tactics look a lot more like the ones used in the past, that is, the pre-HR crop era. HR crops will still not eliminate the need for discovery of new SOA herbicides and other new technologies (robotics and site-specific weed management tools) to manage the 'wicked' nature (Shaw 2016) of the problem of HR weeds.

8 Where to find further information

Additional information on HR (single or stacked-trait) crops and IWM approaches is readily available in the literature and at various websites maintained by state cooperative extension services of land-grant universities and agrochemical companies. Several research articles, reviews and book chapters have been published on various aspects of HR crops and IWM systems. Some of them have been listed (by no means exhaustive) in the following references section and others can be found by diligent search of literature.

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