

## REVIEW ARTICLE

# UNDERSTANDING HERBICIDE RESISTANCE IN WEEDS: HISTORICAL EMERGENCE, GENETICS, MECHANISMS, AND SUSTAINABLE MANAGEMENT STRATEGIES

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## ABSTRACT

Herbicide resistance in weed species poses a significant threat to global food security by reducing crop yields and complicating weed management strategies. Since the introduction of synthetic herbicides in the mid-20th century, resistant weed populations have increasingly emerged due to the widespread and repeated use of herbicides, particularly systemic types like glyphosate. We're in a difficult spot globally when it comes to managing weeds. A growing number of weeds are developing resistance to multiple herbicides simultaneously, meaning many of our current herbicides are becoming ineffective. Resistance arises through genetic mutations, categorized mainly as target-site or non-target-site mechanisms. The evolution of "superweeds" and the rapid increase in resistance cases highlight the urgent need for integrated weed management (IWM) approaches. However, economic, labor, and practical constraints, alongside a focus on major crops, limit the adoption of sustainable management practices. This review explores the history, mechanisms, and challenges of herbicide resistance and discusses the importance of diversified weed control tactics.

### KEYWORDS

Herbicide resistance, glyphosate, target-site resistance, non-target site resistance, integrated weed management, superweeds

## 1. INTRODUCTION

Weeds that have gained the innate capacity to endure and procreate after being sprayed with a pesticide dose that would typically kill weeds of the same kind are said to be herbicide resistant (Keshtkar et al., 2019). According to the United Nations Department of Economic and Social Affairs, the global population is projected to reach approximately 8.5 billion by 2030 and increase further to 9.7 billion by 2050. Weeds present a major challenge to global food security, causing considerable economic losses in agriculture. They reduce crop harvests by competing with cultivated plants for vital resources such as sunlight, nutrients, and water (Oerke, 2006). Ongoing herbicide use in food production has resulted in the rapid emergence of resistance among many weed species (Chen et al., 2021). Over the last four decades, modern herbicides have largely replaced traditional weed control methods such as manual labor, animal use, and mechanical tools, significantly contributing to increased agricultural productivity across the globe. Nevertheless, weeds have not been entirely eradicated despite the widespread use of herbicides (Powles and Yu, 2010). When herbicides kill weeds that are easily affected, the few weeds that are naturally resistant get an advantage. These resistant weeds survive and pass on their ability to resist the herbicide to their offspring, meaning future generations will also be unaffected by the same type of herbicide (Ward et al., 2014a). Herbicides have become the most widely used type of pesticide worldwide, with their usage rising significantly. Although intensive agriculture is crucial for meeting global food demands, it often relies heavily on chemical inputs such as pesticides (Ward et al., 2014a).

## 2. HISTORY

Herbicide-resistant weed populations began to appear following the

introduction of synthetic herbicides in the late 1940s. In the initial twenty years after their use began, reports of herbicide resistance were relatively rare (Shaner, 2014). When researchers noticed that some weed populations might resist herbicide treatments that had previously been successful in controlling them, they began to identify herbicide resistance in the early 1950s (Heap, 2022). The earliest cases of developed herbicide resistance were observed in wild carrot (*Daucus carota* L.), which acquired resistance to the auxin analog group of herbicides following multiple consecutive seasons of 2,4-D application (Switzer, 1957). In 1968, the first major case of herbicide resistance was observed in common groundsel (*Senecio vulgaris* L.), which had become resistant to simazine and atrazine, making those herbicides useless (Ryan, 1970). Although guidelines for managing herbicide resistance were in place, the issue continued to intensify. The release of glyphosate-resistant crops in 1995 provided a temporary relief, with farmers quickly embracing the simple and effective glyphosate-based weed control strategy. Nevertheless, concerns raised by researchers and certain companies about the long-term viability of this method were mostly overlooked (Shaner, 2014). Glyphosate-resistant weed populations rapidly increased in the 1990s as a result of the extensive usage of glyphosate and the widespread adoption of glyphosate-resistant crops (Duke and Powles, 2011). The initial international conference on herbicide resistance took place in Cordoba, Spain, in 1995 (DePrado, Jorrín, and García-Torres, 1997).

Since the late 1980s, no completely new types of herbicides were made. Instead, companies kept using the same herbicides in different ways. They did this by making crops like soybean, maize, and cotton able to survive these herbicides, even if used together (this is called stacked traits). But now, companies are starting to look for new kinds of herbicides again because the old ones aren't working as well anymore (Green and Owen, 2011).

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### 3. DIFFERENT HERBICIDES

Glyphosate is among the most widely used non-selective systemic herbicides, capable of controlling a broad range of weed species by blocking the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), which is essential for the production of aromatic amino acids in plants. Despite its potent weed control capabilities, glyphosate is considered to have low toxicity and poses minimal environmental risks (Duke and Powles, 2008). Paraquat is a non-selective herbicide that induces swift drying of green plant tissues by interfering with electron

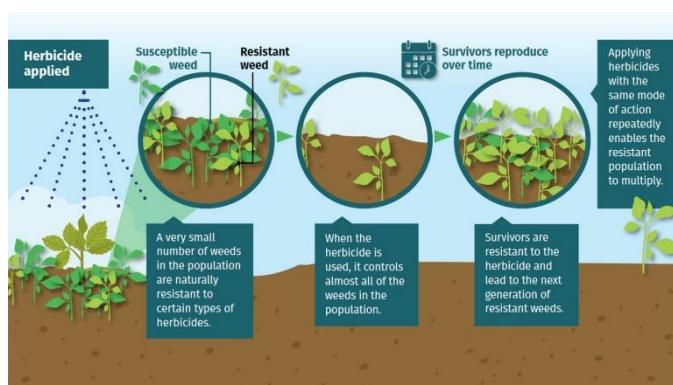
transport in photosystem I, which results in the generation of reactive oxygen species (Hess, 2000). Glufosinate is a non-selective contact herbicide that blocks the activity of glutamine synthetase, leading to a buildup of ammonia in plant tissues and interference with the photosynthetic process (Avila-Garcia and Mallory-Smith, 2011). 2,4-Dichlorophenoxyacetic acid (2,4-D) is a synthetic auxin that specifically affects broadleaf weeds in cereal fields and turf by interfering with their normal patterns of cell growth and division (Grossmann, 2010). Pendimethalin is a pre-emergence herbicide that disrupts microtubule assembly, consequently hindering the process of cell division in plants (Senseman, 2007).

Type of Herbicide	Example(s)	Mode of Action	Selectivity	Reference
Contact Herbicides	Paraquat, Diquat	Destroy plant tissue on contact, usually by disrupting cell membranes.	Non-selective	Ross and Lembi, 2009
Systemic Herbicides	Glyphosate, 2,4-D	Translocated through the plant to inhibit essential biochemical pathways (e.g., amino acid synthesis).	Glyphosate: Non-selective, 2,4-D: Selective (broadleaf)	Devine et al., 1993
Pre-emergent Herbicides	Pendimethalin, Atrazine	Inhibit seed germination or seedling growth by affecting root or shoot development.	Selective or Non-selective depending on the chemical	Zimdahl, 2013
Post-emergent Herbicides	Fluazifop, Dicamba	Absorbed through foliage and translocated to growing points, disrupting growth processes.	Fluazifop: Selective (grasses), Dicamba: Selective (broadleaf)	Green, 2014
Residual Herbicides	Imazapyr, Simazine	Remain active in the soil for extended periods, preventing growth of new weeds.	Selective or Non-selective depending on application	Senseman, 2007
Selective Herbicides	2,4-D, MCPA	Target specific types of plants without harming the crop.	Selective	Tu et al., 2001
Non-selective Herbicides	Glyphosate, Glufosinate	Kill most or all plant types.	Non-selective	Duke and Powles, 2008

### 4. MECHANISM OF HERBICIDE RESISTANCE IN WEEDS

When a particular herbicide or group of herbicides is used, it creates a selective pressure that leads to the development of herbicide-resistant populations. Under this pressure, plants that already possess resistance traits have a significant advantage in survival. While the susceptible plants are killed off, the resistant ones live on and reproduce (Prather and Holt, 2000). Herbicide resistance in weeds is commonly classified into two main types: target-site resistance (TSR) and non-target site resistance (NTSR) mechanisms (Jugulam and Shyam, 2019). Target-site resistance (TSR) arises either from modifications to the herbicide's target site or from increased copies of the target gene. This results in higher levels of the target enzyme, which lessens the herbicide's harmful impact on the plant (Powles and Yu, 2010). Non-target site resistance (NTSR) involves different strategies that allow plants to survive herbicide application without altering the herbicide's specific target. These strategies limit the amount of active herbicide that reaches its intended site of action. This can occur through reduced herbicide retention on the plant surface, decreased uptake by plant tissues, restricted movement within the plant (impaired translocation), increased ability to break down the herbicide (enhanced metabolism), or by isolating the herbicide in specific cell compartments where it cannot be effective (subcellular sequestration) (Gaines et al., 2020; Nandula et al., 2019). Target-site resistance (TSR) and non-target site resistance (NTSR) mechanisms can coexist within the same plant, leading to enhanced herbicide resistance. The diverse range of resistance methods, both the broad-spectrum NTSR and the more specific TSR (as well as some forms of NTSR that have emerged over a relatively short period), highlight the remarkable ability of weed populations to rapidly evolve and withstand intense herbicide pressures (Gaines et al., 2020). Resistance can arise from changes in either a single gene (monogenic) or multiple genes (polygenic), affecting the herbicide's target site (TSR) or other parts of the plant (NTSR). Studies indicate that low herbicide doses may encourage polygenic resistance, whereas high doses are more likely to promote monogenic resistance at the target site (Neve and Powles, 2005). Using herbicides at the recommended field rate can inhibit the accumulation of minor resistance alleles in individual weeds, thereby significantly reducing the likelihood of polygenic non-target site resistance (NTSR) developing. These minor alleles may either be part of the existing genetic variation in the population or may emerge due to stress from sub-lethal doses of herbicides (Gressel, 2010). Weed types that resist herbicides by breaking them down (enhanced metabolism) usually show a lower level of resistance than those with changes at the herbicide's

target site. However, these metabolism-based resistant weeds can develop more quickly when herbicides are used often at lower-than-recommended doses. This repeated low-dose use slowly increases the number of weeds that can better break down the herbicide (Prather and Holt, 2000).



**Figure 1:** How herbicide resistance develops (Manage Resistance Now, 2025)

### 5. GENETICS OF HERBICIDE RESISTANCE

Herbicide resistance in weeds can develop in two ways: from the genetic differences they already have or from changes caused by the stress of being exposed to low, non-lethal amounts of herbicide. This stress can cause changes like DNA mutations, changes in how genes work (epigenetics), changes in which genes are turned on or off, and changes to proteins. These changes can help the weeds survive herbicides but might also cause other side effects (Dyer, 2018). Herbicide resistance in weeds evolves under the influence of several factors, which are examined through population genetic models. These factors include genetic mutations, the initial presence of resistance alleles, modes of inheritance, weed adaptability in environments with or without herbicide application, reproductive strategies, and gene movement between populations. Although mutation rates may be low, intense weed infestations combined with repeated herbicide applications significantly increase the likelihood of resistance emerging (Jasieniuk et al., 1996). When herbicide resistance is controlled by a single, powerful gene, it can spread quickly through a

plant population. However, if resistance depends on multiple genes each having only a small effect, it takes much longer for that resistance to develop and spread (Neve and Powles, 2005). It can take many generations for these genes to accumulate in individual plants, especially if they are rare in the population to begin with. On top of that, each of these genes might contribute to resistance in a different way (Délye et al., 2013). dominant allele increases in frequency within a population more rapidly than a recessive one (Jasieniuk et al., 1996). A dominant resistance gene is always expressed, whether an individual has one or two copies, making it a constant target for natural selection, which slowly eliminates the non-resistant versions of the gene. However, how quickly this dominant resistance gene spreads depends on how strong its dominance is (Christoffers, 1999).

## 6. SUPER WEEDS

Weeds that have evolved resistance to herbicides, commonly known as "superweeds," are problematic plants that can withstand treatment with one or more herbicides. These resistant weeds often arise when genetically modified crops unintentionally cross-pollinate with wild plant species, resulting in herbicide-resistant progeny (Nalia et al., 2019). Genes for herbicide resistance can spread from biotech crops to wild plants, including weeds, through pollen transfer. This can happen between plants of the same species, different species, or even different genera. In Argentina, this has led to seven weed species, including *Sorghum halepense* (Johnsongrass), developing resistance to glyphosate, allowing them to infest glyphosate-resistant soybean fields (Heap, 2014). Critics of genetically engineered (GE) crops often hold them largely responsible for the increasing prevalence of superweeds. While they acknowledge that farmers overused glyphosate and share some responsibility, they also point out that farmers had limited choices. The structure of the agricultural system, especially in large-scale commodity farming, leaves few affordable alternatives to using herbicides. Many critics argue that the heavy reliance on glyphosate is not just a farmer's decision but a built-in feature of an unsustainable farming system (Bain et al., 2017).

## 7. SOME MAJOR HERBICIDE RESISTANT WEEDS

### 7.1 *Amaranthus*

A study aimed to find out how widespread herbicide-resistant waterhemp (*Amaranthus tuberculatus*) is in Minnesota. Researchers tested 90 populations from 47 counties using eight herbicides. All were resistant to imazamox, 89% to glyphosate, 47% to atrazine, 31% to fomesafen, 22% to mesotrione, 10% to 2,4-D, and 2 populations to dicamba. While none were fully resistant to glufosinate, 22% showed reduced sensitivity. Most populations were resistant to multiple herbicides, with some resistant to up to seven, showing the need for better weed control methods (Singh et al., 2024). Two *Amaranthus tuberculatus* populations from Illinois showed resistance to imazethapyr (an imidazolinone herbicide) but remained sensitive to chlorimuron (Patzoldt and Tranel, 2007). A waterhemp population in North Carolina showed resistance to five herbicides and had mutations in the ALS and PPX2 genes. It remained sensitive to 2,4-D, dicamba, and glufosinate. More research is needed to clarify resistance to atrazine, glyphosate, and mesotrione (Jones et al., 2023).

### 7.2 Blackgrass (*Alopecurus myosuroides*)

Blackgrass resists herbicides by using ABC transporters (AmABC1 and AmABC2) to move detoxified herbicide metabolites into vacuoles. These transporters, working with a glutathione transferase, help detoxify herbicides and increase resistance, confirmed by tests in yeast (Goldberg-Cavalleri et al., 2023). Repeated herbicide use drives rapid adaptation in blackgrass. Research shows that target-site resistance mainly comes from existing genetic variation, while non-target-site resistance is more complex, involving multiple genes (Kersten et al., 2021). Blackgrass in Northern Europe shows multiple-herbicide resistance (MHR), which threatens cereal crops. Studies found eight key proteins linked to MHR, some similar to human multidrug resistance (MDR) proteins. MHR has three types and differs from usual plant stress responses, indicating it's a unique, evolving resistance trait (Tétard-Jones et al., 2018).

### 7.3 Junglerice

In Kirtipur, central Nepal, *Echinochloa colona* was identified as a dominant weed affecting rice (*Oryza sativa* L. var. Taiching-127) fields (Manandhar et al., 1970). *E. colona* is a challenging weed in crops, and certain populations in Greece have developed resistance to glyphosate. Although some herbicides are effective against specific populations, others show limited control (Travlos et al., 2020). A junglerice biotype in Mississippi shows resistance to four herbicides. Key genes were found more active in resistant plants, and malathion increased their herbicide sensitivity

(Wright et al., 2018).

### 7.4 Rigid ryegrass

A survey in northern Tunisia showed widespread resistance of rigid ryegrass to ACCase (Acetyl-CoA Carboxylase) and ALS (Acetolactate Synthase) herbicides, with 58% and 52% of populations resistant, respectively. Resistance varied by region and is well established (Khammassi et al., 2019). A population of *Lolium perenne* subsp. *multiflorum* (Italian ryegrass) was found with individuals showing high levels of non-target-site resistance (NTSR) to FOP (aryloxyphenoxypropionate) herbicides, partial resistance to pinoxaden and cycloxydim, but remained sensitive to tepraloxym and clethodim (Kaundun, 2021).

### 7.5 Wild Oat (*Avena fatua* L.)

In Bajío, Mexico, 70% of wheat and barley fields had herbicide-resistant wild oats (*Avena fatua*) with common mutations like Trp-1999-Cys and Asp-2078-Gly. These mutations cause cross-resistance to ACCase herbicides. Four distinct metabolic patterns were also found, showing different resistance mechanisms across farms (Tafoya-Razo et al., 2022). The study found that resistance to three herbicides in wild oat populations from Manitoba is controlled by single dominant genes. Different resistant populations carry distinct resistance genes, which appear to be genetically linked. This linkage may explain how these wild oats developed resistance to multiple herbicides, even without being exposed to all of them (Karlowsky et al., 2006).

### 7.6 Horseweed

In Michigan, 20 horseweed populations revealed that 60% were resistant to glyphosate, 35% to 2,4-D, and 20% to dicamba. Resistance to these herbicides showed some correlation. The main factors influencing resistance were how often crops were rotated (44%), previous occurrences of resistance (33%), and the location where samples were collected (22%). These findings emphasize the importance of diverse weed management practices to help slow the spread of resistance (Sulzback et al., 2025). Horseweed in Montana is increasingly resistant to glyphosate, showing 2.5 to 8 times more resistance than susceptible plants. Resistant plants had lower shikimate buildup. Other herbicides remain effective, causing over 90% damage (Kumar et al., 2017).

## 8. TRACKING THE GROWTH OF HERBICIDE RESISTANCE ACROSS DECADES

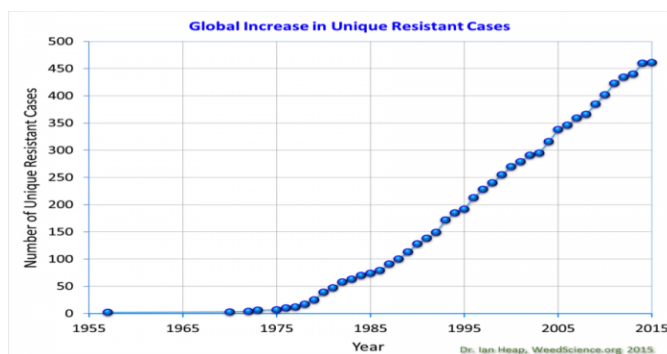


Figure 2: Global increase in herbicide-resistant weed species from 1950 to 2015 (Heap, 2023).

There a notable increase in the number of distinct herbicide-resistant weed species reported globally between 1950 and 2015. While resistance was uncommon in the earlier years, there has been a sharp rise since the 1980s, highlighting increasing difficulties in managing weeds and maintaining herbicide efficacy. This pattern demonstrates the intensifying selection pressure on weed populations caused by extensive and repeated herbicide applications (figure 2).

## 9. STRATEGIES FOR MANAGING HERBICIDE RESISTANCE IN WEEDS

### 9.1 Learn the biological characteristics of the weeds that are present

By understanding when weeds sprout, how long they grow, how many seeds they produce, how those seeds spread, and how long seeds survive in the soil, people can create plans that target the weed's weakest points in its life cycle. Knowing how weeds grow and behave in farming systems helps us design strategies that take advantage of their weaknesses, shifting the competitive edge towards the crop (Neve et al., 2003a; Neve et al., 2003b). Managing herbicide resistance effectively for the long term

involves more than just controlling weeds to save crops in one season. It's essential to reduce the exposure of weeds to herbicides. This helps stop the spread of herbicide-resistant weeds and lowers the number of weed seeds in the soil for future planting. By understanding a weed's key biological characteristics, we can specifically target certain stages of its life cycle. This not only helps control weed populations and seed levels but also allows for a more accurate assessment of how likely resistance is to develop (Ward et al., 2014b).

## 9.2 Herbicide Mixing

Using mixtures of herbicides with different modes of action was significantly more successful in lowering glyphosate resistance in *Amaranthus tuberculatus* compared to rotating herbicides over time. Fields applying more complex herbicide combinations were up to 83 times less likely to develop resistant weeds. On the other hand, frequent use of glyphosate and high herbicide turnover without mixing led to increased resistance. These findings highlight that effective resistance management relies more on herbicide mixing than on rotation alone (Evans et al., 2016).

## 9.3 Pre-Emergence Herbicides in Weed Control

Due to the rise of glyphosate-resistant weeds, growers have recently changed their weed control strategies by using more pre-emergence herbicides and combining overlapping soil residual herbicide treatments (Beckie et al., 2019). Using pre-emergence soil-applied herbicides is a key part of integrated weed management (IWM) because they help control weeds early and can slow the development of resistance to post-emergence herbicides. So far, resistance to pre-emergence herbicides has developed more slowly compared to resistance caused by post-emergence herbicide (Somerville et al., 2017).

## 9.4 Genetically Engineered crops

The widespread use of genetically engineered crops resistant to glyphosate led to a simpler, less varied, and more convenient weed management method, which has unsurprisingly caused many weeds to develop resistance to glyphosate (Powles 2008). According to surveys, reports, and some farmers' experiences, GE crop varieties have led to lower pesticide use and costs, as well as higher profits (Frisvold and Reeves, 2010).

## 10. LIMITATIONS AND CHALLENGES IN MANAGING HERBICIDE RESISTANCE

### 10.1 Evolution of Multiple and Cross Resistance

Effective weed management faces growing obstacles because weed species are evolving to possess resistance against numerous herbicides with distinct modes of action (multiple resistance), alongside resistance to herbicides that share the same mode of action i.e. cross resistance (Beckie and Harker, 2017).

### 10.2 Barriers to Herbicide Mixture Adoption

Farmers face challenges in using herbicide mixtures for resistance management due to higher costs and limited availability of suitable herbicides that meet the required standards. Herbicide mixtures only work well to delay resistance if the chemicals used have similar strength, last about the same time, and don't all encourage resistance in the same way (Beckie, 2006).

### 10.3 Economic and Practical Constraints

Integrated weed management, compared to sole reliance on herbicides, typically requires more financial investment and labor (Renton et al., 2014). Financial constraints frequently compel farmers to opt for short-term, less sustainable approaches (Shaw et al., 2011).

### 10.4 Herbicide Resistance in Minor Crops

Research efforts in herbicide development and resistance management primarily focus on major crops such as maize and soybean, leaving minor crops with fewer resources and less information (Heap, 2023). The absence of localized data and studies on herbicide effectiveness in minor crops hinders the application of integrated weed management practices, which are essential for long-term resistance management (Renton et al., 2014).

## 11. CONCLUSION

Weeds pose a substantial threat to agriculture globally, as they directly compete with crops for crucial resources such as sunlight, nutrients, water, and space. This competition routinely results in decreased crop

yields, compromised quality, and more challenging harvests. Despite this, herbicides have become an indispensable tool in modern agriculture, lauded for their effectiveness and cost-efficiency in enhancing food production and security worldwide. Unfortunately, decades of widespread and continuous herbicide use have led to the evolution of resistant weed populations that can no longer be controlled by these chemicals, thereby endangering the long-term viability of agricultural practices and global food security. Herbicide resistance develops mainly through two mechanisms: target-site resistance (TSR), where the herbicide's target in the plant is altered, and non-target site resistance (NTSR), which involves alternative strategies that reduce herbicide effectiveness. Such resistance has now been documented across nearly all herbicide classes, complicating weed control efforts. As a consequence, farmers often resort to applying higher doses of herbicides, increasing the frequency of application, or using multiple herbicides simultaneously. These practices lead to higher production costs, environmental degradation, and loss of biodiversity. Moreover, while genetically engineered herbicide-tolerant crops were initially introduced to simplify weed management, their extensive use has in some cases exacerbated herbicide resistance by encouraging more frequent herbicide application. Compounding the issue, the discovery and development of new herbicides face numerous challenges, including high research costs, strict regulations, and lengthy approval processes, limiting the availability of novel weed control solutions. Therefore, sustainable agriculture requires integrated weed management approaches that reduce dependence on herbicides and slow the spread of resistance, helping maintain crop productivity and protect the environment in the long term.

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