Modes of Action of Different Classes of Herbicides

Shariq I. Sherwani, Ibrahim A. Arif and Haseeb A. Khan

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/61779

Abstract

The mode of action of herbicides is important for understanding the management, classification, organization, and hierarchy of the herbicides. It also provides an insight into herbicide resistance, which continues to be a problem in sustainable agricultural management. The overuse of herbicides, just like other pesticides such as insecticides, has led to increased development of resistance among weeds, causing injury and destruction of useful plants in agriculture, land management, and other related industries. This chapter focuses on the main theme while providing in-depth analysis of the different modes of action of various classes of herbicides. The modes of action of herbicides are as variable as their chemical compositions as they focus on controlling susceptible plants through various biochemical means. Depending upon the specific mode of action at work, it may involve a plant enzyme or a biological system that the herbicide may interrupt, thus injuring or disrupting the regular plant growth and development and causing eventual plant death. Having an in-depth knowledge of the mode of action of herbicides is important in choosing a specific herbicide for a specific crop, understanding the injury symptoms, and devising an appropriate crop-management strategy.

Keywords: Herbicides, mode of action, resistance, translocation, regulator

1. Introduction

Herbicides or weedkillers belong to a class of pesticides that are used in the management of undesired plants in the areas of agriculture, landscaping, forestry, gardening, and industry [1, 2]. Weeds cost billions of dollars’ worth of damage each year to crops, particularly corn and soybean in the United States and Canada, to which the maximum quantity of herbicides are applied [3-5]. Similar economic and environmental losses have been associated with nonindigenous plant species in Southeast Asia [6,7]. The control of weeds and other unwanted plants in a cost-effective manner is very important to agriculture and other related industries. Herbicide use, though essential for limiting and eliminating the weed populations, poses its
own set of problems and risks; its use must be minimized to account for the desired economic and environmental effects [8-10]. The problem associated with weed control is amplified due to herbicide resistance that some of the weed species have developed over the course of time due to the overuse of herbicides or their evolution (process of natural selection) toward favorable conditions [11]. Weeds may be resistant to specific herbicides (selective) or may be resistant to a broad spectrum of herbicides (nonselective) [11-13]. These inherent features have evolved based upon the various mechanisms such as absorption, metabolism, translocation, detoxification, and site of action, which confer resistance to the weeds [14-16].

In order for a successful weed elimination and control strategy to be effective, all of the above conditions must be met. Most of the herbicides, as described in this chapter, interact and interfere with the metabolic machinery and other biochemical pathways of weeds and cause irreversible damage, tissue injury, leading to the eventual death and elimination of the weeds [17]. Herbicides may vary based upon their complex chemical structures, characteristics, and properties with other members of their family, and are grouped according to their mode of action and target specificity [18-20]. The mode of action of herbicides includes inhibition, interruption, disruption, or mitigation of the regular plant growth [21-23].

Herbicides are classified based upon different aspects, such as mode of action, site of action, chemical families, time of application, selectivity, translocation, etc. [24-26]. It is important to note here that even a particular herbicide-resistant weed could be susceptible to a specific herbicide provided the amount and the rate of application are appropriate. On the other hand, excessive use of herbicides could damage the crop and also impart resistance to the same weeds which were intended for control or elimination. Therefore, it is important to strike a balance between these strategies and find the optimum medium for the best and maximum effect.

Based upon the time of application, herbicides are classified as preemergence or postemergence [27] as shown in Figure 1. When applied preemergent, they may be effective against grassy weeds or broad-leaf weeds [28,29]. On the other hand, when applied postemergent, they may be selective (specific target) or nonselective (broad target) [28]. At the preemergent stage, the herbicide may be applied to the soil or even the seeds may be treated with them. With postemergent applications, the seedlings are sprayed with specific herbicides so as to eliminate weeds. Selectivity is defined as the capacity of a herbicide to kill a target plant without harming or killing the nontarget plants [30]. Selective herbicides are highly specific and are best suited for the control of a specific weed associated with a specific crop; most of the herbicides used in agriculture and related industries are highly selective. Upon contact, they act by getting absorbed and translocated into the xylem or the phloem of the weeds, by inhibiting or disrupting the metabolic machinery or other biosynthetic pathways, and by injuring or killing the weeds [31]. Nonselective herbicides, on the other hand, have a limited use in agriculture and other related industries, but they are effective in land-reclamation projects where the land needs to be cleared of all vegetation or where the weeds may be localized, away from the plants of interest. Glyphosate, however, has been used worldwide as a nonselective herbicide, but it acts more selectively when used in association with genetically engineered crops, which have been developed for resistance against glyphosate [21,32,33]. The selectivity or nonselectivity of herbicides depends upon various factors, such as plant physi-
ology, soil topography, environment, timing of application, rate of application, and application technique [26]. The classification of herbicides is equally important for managing and understanding herbicide resistance, which continues to be a problem in sustainable agricultural management [24,25]. The overuse of herbicides, just like other pesticides such as insecticides, may lead to increased development of resistance among plants, causing injury and destruction of useful plants in both agriculture and land management [6]. Understanding the reasons for classifying the herbicides based upon their modes of action, instead of the chemical family or the site of action, will help to understand the reasons behind the development of resistance due to their overuse.

Plants interact differently with different herbicides based upon their absorption, translocation, metabolism, and physiological response. The mode of action may be prevalent at the tissue or cellular levels and the tissue-injury symptoms are similar for a specific group. Herbicides are also selective in their mode of action, crop/weed favorability, and soil topology. Herbicides may either be applied directly to the foliage or be added to the soil during plowing/tilling [34]. Herbicides may have a vertical or horizontal translocation movement of the chemicals representing different groups [35-37]. There are other herbicides that kill upon contact on the foliage and are potent enough such that they do not require translocation either way. Plants are intact systems that consist of organs, tissues, cells, and molecules, which are reservoirs of organized biochemical processes that take place uninterrupted. Herbicides may be absorbed by the plants via the roots (soil-based herbicides) or the shoots (spray-based herbicides) [38]. The metabolic activity requires the movement of sap through the xylem (translocation of water and nutrients) and phloem (translocation of sugars) [39,40]. When the herbicides penetrate the cell walls of the weeds, they cause tissue injury and permeate the sap, in the process, interrupting various biochemical pathways. Upon interaction with the herbicides, weeds are killed by the dysfunction of their biochemical processes.

Traditionally, herbicides were mixed with the soils, but at present, the trend is leaning toward spraying herbicides and also developing herbicide-resistant crop varieties [6,41]. Given the environmental concerns associated with aerosols, soil pollution, and water-system contamination, developing environment-friendly herbicides has become a priority [42,43]. The United States Environmental Protection Agency (US EPA) has many regulations and guidelines in place for the proper manufacturing, sale, and use of herbicides (www.epa.com). The rate of application of herbicides and their strategic placement are of prime importance and depend upon the kind of weeds that need to be killed. Herbicides with higher rates of absorption and retention (during spraying) require a less volume and a less potency as compared to their counterparts. The weather/temperature conditions (mild, temperate, or tropical) determine the effectiveness of herbicides on a specific crop. Along with the temperature, the humidity and the plant vigor also play important roles in designing the herbicide application strategy [44,45]. An understanding of the leaf-surface coverage area, leaf-surface properties, and the chemical properties of the herbicide is essential for maximum success [46-48].

Herbicides are grouped based upon their chemical structures, which consist of a base-specific molecule surrounded by a side chain or a group(s) [49]. A modification of a functional group leads to a modification in the activity, selectivity, and persistence of herbicide and also
determines its mode of action. The overuse of herbicides has increased the chances of damage and injury to the non-target weeds/plants while also causing groundwater contamination [6,10,50]. This chapter describes the different modes of action of herbicides based upon whether they are inhibitors, regulators, or disruptors of various biosynthetic pathways and hence classified accordingly. Slight variations have been observed in the group-classification system in scientific publications but those are of minor concern. The mechanism of the action of herbicides for killing a weed is well understood and requires that, in order for it to be effective, the herbicide must undergo the following processes, in the sequential order, listed below [51] and also as illustrated in Figure 2:
1. Contact – Must come in contact with the weed
2. Absorption – Must be absorbed by the weed
3. Movement – Must move to the site of action in the weed
4. Toxicity – Must possess or acquire sufficient level of toxicity or potency to kill the weed
5. Death – Must cause injury to the weed leading to eventual death

2. Herbicide resistance

Herbicide resistance is a widespread problem in agriculture and related industries [11,21]. The resulting loss of crops can be significant for farmers and other growers. Instead of using a passive approach to herbicide-resistance management, the use of proactive strategies based upon the latest advancements and knowledge will deliver the best results [52-54]. The results of a successful herbicide-resistance management strategy can be quantified in terms of both the cost-effectiveness and the total output of the harvest [55]. The maximum loss occurs during the initial stage of the crop’s planting, particularly when the soil and/or the seeds are not treated with herbicides [56,57]. It is at this stage that the seeds are the most vulnerable and the weeds are the most robust and must be treated accordingly [34,58]. If left untreated or not appropriately treated, the weeds can get out of control, take over the crop/plants, and also become resistant leading to long-term and devastating economic consequences for farmers and growers [59,60]. Therefore, it is important to select a weed-resistant variety of crop instead of attempting to deal with the populations of weeds, which may be resistant to such herbicides, thus increasing the overall cost of cultivation [61,62].

Weeds have been shown to have acquired unprecedented resistance to several herbicides due to their indiscriminate use over the years [21,63]. This may be due to the result of mutation or substitution of a single base, thus changing the reading frame of the amino acid and the amino acid itself [64-68]. This modification, usually in the quinone-binding region of the peptide, decreases the binding capacity of the herbicide and renders it to be vulnerable and less effective [49,69,70]. If the mutation is at the gene level, it may be a single-gene mutation or a multigene mutation and would impart the weed a higher or lower level of resistance, respectively [71-74]. Recent advances have shown that slight alterations in the binding affinity of the herbicides to the crops, via different pathways, particularly the photosynthetic pathway, have led to the development of various effective herbicide strategies [69,75,76]. Despite the concerns of genetically modified (GM) crops, the recombinant DNA technology is one such tool that allows for the development of crop-safe and effective herbicides, which kill only the weeds when applied to the entire crop [77,78]. However, the processes of natural selection and gene transfer may allow the weeds to acquire herbicide resistance quickly [21,79]. On the other hand, identifying resistance among weeds is an extremely challenging task, which requires different tools at one’s disposal [12]. Some of the observational tools, necessary for controlling the weed and other undesirable plants during cultivation, include:

1. Loss of consistent control of the weed population
2. Effect of environment/weather conditions on the weed population
3. Rate of application of herbicides on the weed population
4. Soil topography (effect of overuse or crop rotation on the weed population)
5. Use of herbicides with a similar mode of action
6. Use of herbicides with related chemical families

Herbicide resistance, like antibiotic resistance, is a common occurrence among weeds and is a result of overuse of a specific herbicide and soil conditions [21,80]. In order to avoid and overcome the development of herbicide resistance, different herbicides must be used at different points in time on the same crop [81]. Crop rotation is also recommended to maintain soil integrity and soil vigor [29]. The genotype of different plants lends them to interact differently due to conformational variations and compatibility with various chemical groups [82]. For example, Kochia and pigweed are resistant to triazine and ALS-inhibiting herbicides [83]. Certain genetically modified (GM) crop plants, which may inadvertently come in the path of the herbicides (carry-over) may able to overcome the harmful effects of these herbicides [11,84,85]. Cross-resistance is another concerning issue in agriculture and related industries as some weeds and pests have acquired resistance to several herbicides, which are related by their mode of action [86-88]. For example, herbicides belonging to separate chemical families but within the same mode of action [e.g., acetolactate synthase (ALS) inhibitors] may acquire herbicide resistance against both the chemical families. Crop rotation on the same piece of land is highly influential and beneficial in minimizing the development of herbicide resistance as the soil comes in contact with various microorganisms and interacts differently with different chemicals in the surrounding micro-ecosystem [21,29]. The crop rotation allows for different herbicides to be used, which reduces the selection for resistance. The weed-control effect is the maximum at the emergence stage and the minimum at the maturity stage, as the plant goes through the stages of emergence, seedling, vegetative, flowering, and maturity, respectively [89].

3. Mode of action

The modes of action of herbicides are as variable as their chemical compositions and focus on controlling susceptible plants through various biochemical means. The weed-control effect is the maximum at the emergence stage and the minimum at the maturity stage, as the plant goes through the stages of emergence, seedling, vegetative, flowering, and maturity, respectively [89]. Depending upon the specific mode of action at work, it may involve a plant enzyme or a biological system that the herbicide may interrupt, thus injuring or disrupting the regular plant growth and development and causing eventual plant death. Extensive research in the area of herbicides has led to their classification based upon their modes of action into various groups, which are discussed in detail in this chapter. It is important to note that the modes of action discussed in this chapter, though comprehensive, are not exhaustive by any measure. Newly discovered groups and unexplained (unknown) groups continue to be added to the list, reflecting slight variations of classification, as new research knowledge continues to emerge. Also, some scientists may have a slightly different method of classification as well as different
groups, but those are only slight variations. What is important, however, is that having an in-
depth knowledge of the mode of action of herbicides is necessary in choosing a specific
herbicide for a specific crop, understanding the injury symptoms, and devising an appropriate
crop-management strategy and using an appropriate herbicide. Even though this chapter
focuses on the herbicide’s mode of action, it also introduces the reader to a vast array of topics
such as herbicides, herbicide resistance, group-numbering system for designating various
herbicides based upon their mode of action, etc. Herbicides belonging to a specific group have
the same mode of action even though they may belong to a different chemical family. Finally,
the environmental fate of herbicides (persistence, degradation, mobility) with specific refer‐
cence to the groundwater, water sterilization, soil contamination, and environmental and public
health concerns will enlighten the reader on the importance of using the herbicides diligently
and according to the regulations, guidelines, and labeling. The modes of action, as discussed
in this chapter, are listed below:

1. Lipid biosynthesis inhibitors
2. Amino acid biosynthesis inhibitors
3. Plant growth regulators
4. Photosynthesis inhibitors
5. Nitrogen-metabolism inhibitors
6. Pigment inhibitors
7. Cell-membrane disruptors
8. Seedling-growth inhibitors

3.1. Group 1: Acetyl Coenzyme A Carboxylase (ACCase) inhibitors

Also known as lipid biosynthesis inhibitors, these herbicides inhibit the ACCase enzyme
activity and are used typically for controlling grass during the cultivation of broadleaf crop
varieties or crop rotation. The ACCase enzyme catalyzes the primary step in the fatty-acid
synthesis, thus blocking the production of phospholipids necessary for synthesizing the lipid
bilayer, which is indispensable for cell structure and function [90-92]. The chemical family of
aryloxyphenoxypropionate, cyclohexanedione, and phenylpyrazolin operates by inhibiting
the ACCase enzyme. These herbicides are also known by their chemical family nicknames –
FOPs, DIMs, and DENs [93]. Many broadleaf crop varieties, including grasses, have a natural
resistance to these herbicides due to a strong and less-sensitive ACCase system [94].

3.2. Group 2: Acetolactate Synthase (ALS) inhibitors

Also known as amino acid synthesis inhibitors, these herbicides inhibit the action of the
acetolactate synthase (ALS) enzyme. Also known as acetohydroxy acid synthase (AHAS), ALS
catalyzes the first step in the synthesis of the branched-chain amino acids, such as leucine,
iso leucine, and valine [95]. These are also referred to as the AHAS inhibitors or branched-chain
amino acid inhibitors. Comprising the imidazolinones, pyrimidinylthiobenzoates, sulfonyla-
minocarbonyltriazolinones, sulfonylureas, and triazolopyrimidines chemical family, the ALS inhibitors are a part of the largest group of herbicides, which function with the amino acid synthesis inhibitor mode of action [96]. They may show cross-resistance to other herbicides and act by reducing the production of the branched amino acids in the presence of the ALS enzyme, causing plant wilting and, ultimately, plant death.

3.3. Group 3: Root growth inhibitors

Also known as the seedling root growth inhibitors, these herbicides inhibit cell division as part of their mode of action, which, ultimately, blocks root extension and growth. They are applied preemergent or preplant in vegetables and ornamentals. Their site of action is the microtubule and is marked by the assembly of the herbicide–tubulin complex inside the microtubules. This complex inhibits the polymerization of microtubules during assembly but remains unaffected during depolymerization [97]. A loss in the structure and function of the microtubule causes cell death by compromising the cell-wall formation due to the nonalignment of the spindle fibers and nonseparation of the chromosomes during mitotic cell division. This group is represented by the benzamide, benzoic acid (dimethyl-2,3,5,6-tetrachloroterephthalate (DCPA), dinitroaniline, phosphoramidate, and pyridine chemical family, which act by causing the loss of microtubule formation leading to the obstruction of cell division and elongation as evidenced by the swelling of the root tips.

3.4. Group 4: Plant growth regulators

Also known as synthetic auxins, this group includes hormone-based herbicides and is used to keep broadleaf weeds out during the cultivation of corn, wheat, and sorghum. The mode of action of the endogenous indole acetic acid (IAA) is mimicked by the herbicides belonging to the chemical family represented by benzoic acid, phenoxyacetic acid, pyridine carboxylic acid, and quinoline carboxylic acid [98]. The specific molecular binding site responsible for the IAA activation is yet to be established and remains unknown. All of these chemicals disrupt the nucleic acid metabolism and the cell-wall integrity by activating the adenosine triphosphate (ATP)ase proton pump, which increases the enzyme activity in the cell wall [99]. These regulators mimic the IAA activity, thus increasing the transcription, translation, and the protein biosynthesis activities within the cell leading to uninhibited vascular growth, causing cell bursts and ultimate cell and plant death.

3.5. Groups 5, 6, and 7: Photosynthesis inhibitors – Photosystem II (PSII) inhibitors

The mode of action of these herbicides is the inhibition of the photosynthetic pathway, specifically the Photosystem II (PSII). Due to their excessive use, some weeds have become resistant to these herbicides developed on this metabolic principle. Group 5 is represented by the chemical family of triazine, triazinone, phenylcarbamates, pyridazinones, and uracils. Group 6 is exemplified by nitriles, benzothiadiazinones, and phenylpyridazines. Group 7 comprises phenyl urea and amides. All of these groups represent different binding schemes as compared to each other with several similarities. All of these PSII herbicides inhibit the photosynthetic pathway by binding the Q$_{B}$-binding site of the D1 protein complex present in
the chloroplast thylakoid membrane. The binding disrupts the electron transport system (ETS) from Q$_A$ to Q$_B$ and also blocks the CO$_2$ fixation, ATP generation, and nicotinamide adenine dinucleotide hydrogen phosphate (NADPH$_2$) production required for various biochemical pathways as part of the plant growth and development [70,100]. As a result of the blockage at the level of the electron transport chain (ETC), the plant is unable to reoxidize Q$_A$, which generates the triplet-chlorophyll (3Chl), which forms singlet-oxygen (1O$_2$) upon reacting with molecular oxygen (O$_2$). The unsaturated fatty acids and lipids release hydrogen in the presence of triplet-chlorophyll (3Chl) and singlet-oxygen (1O$_2$) while forming a lipid radical, thus causing lipid peroxidation. Lipid peroxidation causes the lipids in the bilayer and other proteins to be oxidized, producing reactive oxygen species (ROS) [70,100]. Some of these herbicides also cause the disruption of the carotenoid, anthocyanin, and protein biosynthetic pathways and affect the transcription machinery as well. The oxidation, ultimately, causes the loss of chlorophyll and other pigments like the carotenoids from the cell membranes exposing the cells and cell organelles to harsh conditions leading to their collapse, disintegration, and eventual plant death [101,102]. Due to their overuse, some weeds have acquired resistance to these PSII inhibitor herbicides, such as atrazine and metribuzin [103].

3.6. Groups 8 and 15: Shoot-growth inhibitors

Also known as seedling shoot growth inhibitors, the herbicides designed with this mode of action are applied as part of the soil preparation and act effectively before the grass and broadleaf weeds emerge. The site of action of the Group 8 herbicides is at the location of the lipid synthesis machinery in the cell membrane. These Group 8 herbicides are represented by the chemical family of phosphorodithioates and thiocarbamates and inhibit the biosynthesis of lipids, fatty acids, proteins, isoprenoids, flavonoids, and gibberellins [104]. The site of action of the Group 15 is at the very-long-chain fatty acid (VLCFA) location in the cell membrane [105,106]. Group 15 herbicides are represented by the chemical family of chloroacetamide, acetamide, oxyacetamide, and tetrazolinone. These herbicides conjugate with acetyl COA and certain sulphhydroxy-containing molecules via thiocarbamate sulfoxides, which inhibit the long-chain fatty acids during the seedling shoot growth stage of the plant and affect the weeds’ preemergence.

3.7. Group 9: Aromatic amino acid inhibitors

The mode of action of these herbicides is as an amino acid synthesis inhibitor. This mode of action is specific to glyphosate (glycines), which are nonspecific herbicides that act by inhibiting the amino acid synthesis. These herbicides kill or cause injury to any plant that they come in contact with and hence are approved only for use in glyphosate-resistant crops, such as corn, cotton, canola, and soybean. Glyphosates inhibit the 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase enzyme necessary in the generation of the EPSP from shikimate-3-phosphate and phosphoenolpyruvate as part of the shikimic acid pathway [107]. As a result, the necessary levels of the aromatic amino acids (tryptophan, tyrosine, and phenylalanine) are depleted, thus compromising the biosynthetic metabolic pathways leading to eventual plant death [108]. As a herbicide, glyphosate use is the most prevalent in the world due to its broad-spectrum
properties and for being environmentally- and user-friendly. Glyphosates are available as ammonium salts, diammonium salts, dimethylammonium salts, isopropylamine salts, as well as potassium salts. The ease of access to the target (broad-spectrum), and the ease of translocation (via the xylem and the phloem), and the failure of the weeds to overcome their effect make the Group 9 herbicides as ideal candidates for killing weeds associated with the glyphosate-resistant crops.

3.8. Group 10: Glutamine-synthesis inhibitors

The mode of action is nitrogen metabolism-based and is specific to glufosinate, which is nonspecific in nature. These herbicides can be used in glufosinate-resistant crop cultivation during postemergence of the resistant seedlings. Glufosinate and bialophos (phosphinic acids) inhibit the activity of the enzyme, glutamine synthetase (GS), which converts glutamate and ammonia to glutamine [109,110]. GS plays a key role in nitrogen metabolism (nitrogen fixation and nitrate/ammonia nutrition) by re-assimilating the ammonia generated during respiration. These herbicides disintegrate the proteins by disrupting the optimum activity of GS leading to an accumulation of ammonia, which lowers the pH gradient on either sides of the cell membrane. This causes the disruption of various cell functions, particularly shutting down the PSI and PSII systems leading to the uncoupling of the photophosphorylation [100,111]. Since GS is located in important organelles like the chloroplast and cytoplasm, these herbicides are highly effective in controlling weeds and other undesired plants.

3.9. Groups 12, 13, and 27: Pigment synthesis inhibitors

Also known as carotenoid biosynthesis inhibitors, these herbicides destroy the green pigment, chlorophyll, which is necessary for photosynthesis in the plants. These herbicides are also known as bleachers as they impart a white color to the plant tissues after coming in contact with the plant foliage leading to cell and tissue injury and ultimately killing the weeds. As part of their mode of action, these herbicides inhibit the pigment synthesis, specifically the catalysis of the 4-hydroxyphenyl pyruvate dioxygenase (HPPD) enzyme and are also referred to as the HPPD-inhibitors. Group 12 is represented by the chemical family of amides, anilidex, furanones, phenoxybutan-amides, pyridiazinones, and pyridines. These herbicides containing these chemicals disrupt the carotenoid biosynthetic pathway by inhibiting the function of the phytoene desaturase enzyme [112]. Group 13 is represented by the chemical family, Isoxazolidinone, and the site of action is at the location of the diterpene synthesis. Group 27 is represented by the chemical family, Isoxazole, and they are also HPPD inhibitors. Carotenoids play a key role in quenching the oxidative control of singlet O_2 (\(\cdot O_2\)) among healthy plants. Upon being treated with these herbicides containing the pigment synthesis inhibitors (Groups 12, 13, and 27), the level of carotenoids is highly reduced leading to the presence of unbound lipid radicals. These lipid radicals compromise the uptake of the membrane lipids and fatty acids, causing lipid peroxidation, which renders the chlorophyll, other cell membrane lipids, and some proteins dysfunctional. As a result of membrane leakage, the cell contents are exposed and destroyed rather rapidly causing wilting and eventual plant death.
3.10. Group 14: PPO inhibitors

The PPO inhibitors act by disrupting the cell membranes and hence their mode of action is categorized as cell membrane disrupters and their site of action is the cell membrane. Most of these herbicides are applied at the postemergence stage while some are used at the preemergence stage of the seedling. The mode of action of these herbicides depends upon the inhibition of protoporphyrinogen oxidase (PPO) enzyme (also known as PPG oxidase or Protox inhibitors), which catalyzes the chlorophyll and heme biosynthesis [protoporphyrinogen IX (PPGIX) to protoporphyrin IX (PPIX) oxidation catalysis]. These herbicides are represented by the chemical family, diphenylether, aryl triazolinone, N-phenylphthalimides, oxadiazoles, oxazolidinediones, phenylpyrazoles, pyrimidindiones, and thiadiazoles. As the PPO is inhibited, it causes the over-accumulation of the PPIX, which interacts with the light in the chlorophyll and produces the triplet-PPIX. Upon reacting with $O_2$, triplet-PPIX forms $^3O_2$ causing the hydrogen-bond disruption in the unsaturated fatty acids and lipids in the membrane, which causes lipid peroxidation [113]. As a result of the cell membrane disruption, the lipids and proteins become oxidized causing the chlorophyll and other pigments to leak and causing cell disintegration, wilting, and eventual plant death.

3.11. Group 22: Photosynthesis inhibitors – Photosystem I (PSI) inhibitors

Upon contact with the plant foliage, these herbicides act by penetrating and destroying the cell lipid bilayer leading to the breakdown of the cell membranes and hence their mode of action is categorized as cell membrane disrupters. These herbicides are nonselective in nature and are applied usually prior to harvesting the crop. These herbicides are represented by the bipyridilium chemical family and are also known as PSI electron diverters as they accept electrons from PSI and, in the process, generate herbicide radicals. Upon interacting with $O_2$, the herbicide radicals form superoxide radicals, which, in the presence of the superoxide dismutase enzyme, form hydrogen peroxide ($H_2O_2$) and hydroxyl radicals [114]. These radicals disrupt the unsaturated fatty acids, chlorophyll, lipids, and proteins in the cell membrane. As a result, the cell membrane is disrupted beyond repair causing leakage of the cell cytoplasm, which leads to wilting and eventual plant death.

4. Conclusion

Due to the overuse of herbicides, agricultural weeds and other undesirable plants develop resistance, which must be contained or eliminated in order for the maximum output of the harvest. Herbicide resistance occurs due to the overuse of herbicides over the years. It is important to follow the lead in developing a proactive and robust herbicide resistance management strategy for minimizing the agricultural loss. Similar techniques can be extrapolated to the land management, ornamental, and other related industries to minimize the evolution of the herbicide-resistant varieties of weeds and other pests. Based upon the available body of knowledge, recent advances in agricultural research, and latest techniques, it is advisable to use different herbicides (different modes of action) at different times of the year.
and with different crops so that the weeds do not develop resistance to the herbicides as quickly as that have been reported. Deciding which herbicide is the most effective and the most environmental friendly option for a specific crop can be a daunting task particularly with so many products competing for attention in the multibillion dollar herbicides market. Most of these herbicides are developed based upon similar weed control and pest management strategies and are designed based upon their mode of action. Rearranging various chemical groups within the chemical family, which most of the companies tend to do while developing their key products, may not be the best strategy as the weeds tend to develop a quick resistance to such chemicals or groups of chemicals. Therefore, it is imperative that the herbicides be designed to obtain the maximum effect with regard to their mode of action so as to control or eliminate weeds and destroy their capacity to acquire the herbicide resistance.

| Group | Mode of Action | Site of Action | Chemical Family |
|-------|----------------|----------------|-----------------|
| 1     | Lipid-Synthesis Inhibitors | ACCase Inhibitor | Aryloxyphenoxypropionate (FOPs), Cyclohexanedione (DIMs), Phenylpyrazolin (DENs) |
| 2     | Amino-Acid Synthesis Inhibitors | ALS Inhibitors | Imidazolinones, pyrimidinylthiobenzoates, sulfonylaminocarbonyltryiazolinones, sulfonylureas, triazolopyrimidines |
| 3     | Root-Growth Inhibitors | Microtubule Inhibitors | Benzamide, benzoic acid (DCPA), dinitroaniline, phosphoramidate, pyridine |
| 4     | Plant-Growth Inhibitors | Site of Action Unknown | Benzoic acid, phenoxy carboxylic acid, pyridine carboxylic acid, and quinoline carboxylic acid |
| 5     | Photosynthesis Inhibitors | Photosystem II Inhibitors | Triazine, triazinone, phenylcarbamates, pyridazinones, and uracils. |
| 6     | Photosynthesis Inhibitors | Photosystem II Inhibitors | Nitriles, benzothiadiazinones, and phenylpyridazines |
| 7     | Photosynthesis Inhibitors | Photosystem II Inhibitors | Phenyl, urea, and amides |
| 8     | Shoot-Growth Inhibitors | Lipid-Synthesis Inhibitors | Phosphorodithioates and thiocarbamates |
| 9     | Amino-Acid Synthesis Inhibitors | EPSP Synthase Inhibitors | Not designated by any specific chemical family |
| 10    | Nitrogen-Metabolism Inhibitors | Glutamine-Synthesis Inhibitors | Not designated by any specific chemical family |
| 12    | Pigment-Synthesis Inhibitors | HPPD Inhibitors | Amides, anilide, furanones, phenoxybutan-amides, pyridazinones, and pyridines |
| 13    | Pigment-Synthesis Inhibitors | Diterpene-Synthesis Inhibitors | Isoxazolidinone |
| 14    | Cell-Membrane Disrupters | PPO Inhibitors | Diphenylether, ari triazolinone, N-phenylphthalimides, oxadiazoles, |
**Modes of Action of Different Classes of Herbicides**

| Group  | Mode of Action                     | Site of Action                     | Chemical Family                                                                 |
|--------|-----------------------------------|-----------------------------------|---------------------------------------------------------------------------------|
| 15     | Shoot-Growth Inhibitors           | Very-Long-Chain Fatty Acid (VLCFA) Inhibitors | Chloroacetamide, acetamide, oxyacetamide, and tetrazolinone.                     |
| 22     | Cell-Membrane Disrupters          | PSI Inhibitor                      | Bipyridilium                                                                     |
| 27     | Pigment-Synthesis Inhibitors      | HPPD Inhibitors                   | Isoxazole                                                                        |

*Table 1. Modes of action of different classes of herbicides*

**Acknowledgements**

This work was supported by Prince Sultan Research Chair for Environment and Wildlife, King Saud University, Riyadh, Saudi Arabia.

**Author details**

Shariq I. Sherwani¹, Ibrahim A. Arif² and Haseeb A. Khan³*

*Address all correspondence to: khan_haseeb@yahoo.com*

1 Department of Internal Medicine, Dorothy M. Davis Heart and Lung Research Institute, The Ohio State University College of Medicine, Columbus, Ohio, USA

2 Prince Sultan Research Chair for Environment and Wildlife, Department of Botany and Microbiology, College of Science, King Saud University, Riyadh, Saudi Arabia

3 Department of Biochemistry, College of Science, King Saud University, Riyadh, Saudi Arabia

**References**

[1] Pretty J. Agricultural sustainability: concepts, principles and evidence. Philosophical Transactions of the Royal Society B: Biological Sciences. 2008;363:447–465. DOI: 10.1098/rstb.2007.2163.

[2] Thrall PH, Oakeshott JG, Fitt G, et al. Evolution in agriculture: the application of evolutionary approaches to the management of biotic interactions in agro-ecosystems. Evolutionary Applications. 2011;4:200–215. DOI:10.1111/j.1752-4571.2010.00179.x.
[3] Adkins S, Shabbir A. Biology, ecology and management of the invasive parthenium weed (Parthenium hysterophorus L.). Pest Management Science. 2014;70:1023–1029. DOI:10.1002/ps.3708.

[4] Chandler JM, Hamill AS, Thomas AG. Crop Losses due to Weeds in Canada and the United States. Champaign, IL: Weed Science Society of America; 1984.

[5] Hussain S, Khaliq A, Matloob A, Fahad S, Tanveer A. Interference and economic threshold level of little seed canary grass in wheat under different sowing times. Environmental Science and Pollution Research International. 2015;22:441–449. DOI: 10.1007/s11356-014-3304-y.

[6] Aktar MW, Sengupta D, Chowdhury A. Impact of pesticides use in agriculture: their benefits and hazards. Interdisciplinary Toxicology. 2009;2:1–12. DOI:10.2478/v10102-009-0001-7.

[7] Nghiem LTP, Soliman T, Yeo DCJ, et al. Economic and environmental impacts of harmful non-indigenous species in Southeast Asia. PLoS One. 2013;8:e71255. DOI: 10.1371/journal.pone.0071255.

[8] Pimentel D, McLaughlin L, Zepp A, et al. Environmental and economic effects of reducing pesticide use - a substantial reduction in pesticides might increase food costs only slightly. Bioscience. 1991;41:402–409.

[9] Pimentel D. Silent spring, the 50th anniversary of Rachel Carson’s book. BMC Ecology. 2012;12:20. DOI:10.1186/1472-6785-12-20.

[10] Ronald P. Plant genetics, sustainable agriculture and global food security. Genetics. 2011;188:11–20. DOI:10.1534/genetics.111.128553.

[11] Owen MD, Zelaya IA. Herbicide-resistant crops and weed resistance to herbicides. Pest Management Science. 2005;61:301–311.

[12] Busi R, Vila-Aiub MM, Beckie H J, et al. Herbicide-resistant weeds: from research and knowledge to future needs. Evolutionary Applications. 2013;6:1218–1221. DOI: 10.1111/eva.12098.

[13] Gressel J. Evolution of herbicide-resistant weeds. Ciba Foundation Symposium. 198;102:73–93.

[14] Ma R, Kaundun SS, Tranel PJ, et al. Distinct detoxification mechanisms confer resistance to mesotrione and atrazine in a population of waterhemp. Plant Physiology. 2013;163:363–377. DOI:10.1104/pp.113.223156.

[15] Sammons RD, Gaines TA. Glyphosate resistance: state of knowledge. Pest Management Science. 2014;70:1367–1377. DOI:10.1002/ps.3743.

[16] Van Eerd LL, Stephenson GR, Kwiatkowski J, Grossmann K, Hall JC. Physiological and biochemical characterization of quinclorac resistance in a false cleavers (Galium spurium L.) biotype. Journal of Agricultural and Food Chemistry. 2005;53:1144–1151.
[17] Hove-Jensen B, Zechel DL, Jochimsen B. Utilization of glyphosate as phosphate source: biochemistry and genetics of bacterial carbon-phosphorus lyase. Microbiology and Molecular Biology Reviews. 2014;78:176–197. DOI:10.1128/MMBR.00040-13.

[18] Fonnet-Pfister R, Chemla P, Ward E, et al. The mode of action and the structure of a herbicide in complex with its target: binding of activated hydantocidin to the feedback regulation site of adenylosuccinate synthetase. Proceedings of the National Academy of Sciences USA. 1996;93:9431–9436.

[19] Grossmann K. What it takes to get a herbicide’s mode of action. Physionomics, a classical approach in a new complexion. Pest Management Science. 2005;61:423–431.

[20] Tresch S, Niggeweg R, Grossmann K. The herbicide flamprop-M-methyl has a new antimicrotubule mechanism of action. Pest Management Science. 2008;64:1195–1203. DOI:10.1002/ps.1618.

[21] Green JM, Owen MDK. Herbicide-resistant crops: utilities and limitations for herbicide-resistant weed management. Journal of Agricultural and Food Chemistry. 2011;59:5819–5829. DOI:10.1021/jf101286h.

[22] Grossmann K, Kwiatkowski J, Tresch S. Auxin herbicides induce H₂O₂ overproduction and tissue damage in cleavers (Galium aparine L.). Journal of Experimental Botany. 2001;52:1811–1816. DOI:10.1093/jexbot/52.362.1811.

[23] Varanasi VK, Godar AS, Currie RS, Dille JA, Thompson CR, Stahlman PW, Mithila J. Field evolved resistance to four modes of action of herbicides in a single kochia (Kochia scoparia L Schrad.) population. Pest Management Science. 2015;71:1207–1212. DOI:10.1002/ps.4034.

[24] Duke SO. Overview of herbicide mechanisms of action. Environmental Health Perspectives. 1990;87:263–271.

[25] Torrens F, Castellano G. Molecular classification of pesticides including persistent organic pollutants, phenylurea and sulphonylurea herbicides. Molecules. 2014;19:7388–7414. DOI:10.3390/molecules19067388.

[26] Varshney S, Hayat S, Alyemeni MN, Ahmad A. Effects of herbicide applications in wheat fields: is phytohormones application a remedy? Plant Signaling and Behavior. 2012;7:570–575. DOI:10.4161/psb.19689.

[27] Wagner G, Nadas E. Effect of pre-emergence herbicides on growth parameters of green pea. Communications in Agricultural and Applied Biological Science. 2006;71:809–813.

[28] Grossmann K, Ehrhardt T. On the mechanism of action and selectivity of the corn herbicide topramezone: a new inhibitor of 4-hydroxyphenylpyruvate dioxygenase. Pest Management Science. 2007;63:429–439.
[29] Wright TR, Shan G, Walsh TA, et al. Robust crop resistance to broadleaf and grass herbicides provided by aryloxyalkanoate dioxygenase transgenes. Proceedings of the National Academy of Sciences USA. 2010;107:20240–20245.

[30] Crafts AS. Selectivity of herbicides. Plant Physiology. 1946;21:345–361.

[31] Fernandez V, Brown PH. From plant surface to plant metabolism: the uncertain fate of foliar-applied nutrients. Frontiers in Plant Science. 2013;4:289. DOI:10.3389/fpls.2013.00289.

[32] Devos Y, Cougnon M, Vergucht S, Bulcke R, Haesaert G, Steurbaut W, Reheul D. Environmental impact of herbicide regimes used with genetically modified herbicide-resistant maize. Transgenic Research. 2008;17:1059–1077. DOI:10.1007/s11248-008-9181-8.

[33] Gustafson DI. Sustainable use of glyphosate in North American cropping systems. Pest Management Science. 2008;64:409–416. DOI:10.1002/ps.1543.

[34] Anwar MP, Juraimi AS, Mohamed MTM, Uddin MK, Samedani B, Puteh A, Man A. Integration of agronomic practices with herbicides for sustainable weed management in aerobic rice. The Scientific World Journal. 2013;2013:916408. DOI: 10.1155/2013/916408.

[35] Anderson DM, Carolan VA, Crosland S, Sharples KR, Clench MR. Examination of the translocation of sulfonylurea herbicides in sunflower plants by matrix-assisted laser desorption/ionisation mass spectrometry imaging. Rapid Communications in Mass Spectrometry. 2010;24:3309–3319. DOI:10.1002/rcm.4767.

[36] DeBoer GJ, Thornburgh S, Ehr RJ. Uptake, translocation and metabolism of the herbicide florasulam in wheat and broadleaf weeds. Pest Management Science. 2006;62:316–324.

[37] Martini LF, Burgos NR, Noldin JA, de Avila LA, Salas RA. Absorption, translocation and metabolism of bispyribac-sodium on rice seedlings under cold stress. Pest Management Science. 2015;71:1021–1029. DOI:10.1002/ps.3882.

[38] Turgut C. Uptake and modeling of pesticides by roots and shoots of parrot feather (Myriophyllum aquaticum). Environmental Science and Pollution Research International. 2005;12:342–346.

[39] Lemoine R, Camera SL, Atanassova R, et al. Source-to-sink transport of sugar and regulation by environmental factors. Frontiers in Plant Science. 2013;4:272. DOI: 10.3389/fpls.2013.00272.

[40] Pate JS, Atkins CA, Hamel K, McNeil DL, Layzell DB. Transport of organic solutes in phloem and xylem of a nodulated legume. Plant Physiology. 1979;63:1082–1088.

[41] Dzantor EK, Felsot AS, Beck MJ. Bioremediating herbicide-contaminated soils. Applied Biochemistry and Biotechnology. 1993;39–40:621–630.
[42] Duke SO, Powles SB. Glyphosate: a once-in-a-century herbicide. Pest Management Science. 2008;64:319–325. DOI:10.1002/ps.1518.

[43] Williams GM, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide roundup and its active ingredient, glyphosate, for humans. Regulatory Toxicology and Pharmacology. 2000;31:117–165.

[44] Hunsche M, Noga G. Effects of relative humidity and substrate on the spatial association between glyphosate and ethoxylated seed oil adjuvants in the dried deposits of sessile droplets. Pest Management Science. 2012;68:231–239. DOI:10.1002/ps.2250.

[45] Long P, Huang H, Liao X, Fu Z, Zheng H, Chen A, Chen C. Mechanism and capacities of reducing ecological cost through rice–duck cultivation. Journal of the Science of Food and Agriculture. 2013;93:2881–2891. DOI:10.1002/jsfa.6223.

[46] Basu S, Luthra J, Nigam KD. The effects of surfactants on adhesion, spreading, and retention of herbicide droplet on the surface of the leaves and seeds. Journal of Environmental Science and Health Part B. 2002;37:331–344.

[47] Liu Z. Effects of surfactants on foliar uptake of herbicides - a complex scenario. Colloids and Surfaces B: Biointerfaces. 2004;35:149–153.

[48] Menendez J, Bastida F. The correlation of the spraying volume with herbicide adherence and herbicide penetration in glyphosate treatments. Communications in Agricultural and Applied Biological Sciences. 2004;69:815–820.

[49] McCourt JA, Pang SS, King-Scott J, Guddat LW, Duggleby RG. Herbicide-binding sites revealed in the structure of plant acetohydroxy acid synthase. Proceedings of the National Academy of Sciences USA. 2006;103:569–573. DOI:10.1073/pnas.0508701103.

[50] Piver WT. Contamination and restoration of groundwater aquifers. Environmental Health Perspectives. 1993;100:237–247.

[51] DeBoer GJ, Thornburgh S, Gilbert J, Gast RE. The impact of uptake, translocation and metabolism on the differential selectivity between blackgrass and wheat for the herbicide pyroxsulam. Pest Management Science. 2011;67:279–286. DOI:10.1002/ps.2062.

[52] Hassanali A, Herren H, Khan ZR, Pickett JA, Woodcock CM. Integrated pest management: the push–pull approach for controlling insect pests and weeds of cereals, and its potential for other agricultural systems including animal husbandry. Philosophical Transactions of the Royal Society B: Biological Sciences. 2008;363:611–621. DOI:10.1098/rstb.2007.2173.

[53] Hobbs PR, Sayre K, Gupta R. The role of conservation agriculture in sustainable agriculture. Philosophical Transactions of the Royal Society B: Biological Sciences. 2008;363:543–555. DOI:10.1098/rstb.2007.2169.
[54] Walsh MJ, Powles SB. Management of herbicide resistance in wheat cropping systems: learning from the Australian experience. Pest Management Science. 2014;70:1324–1328. DOI:10.1002/ps.3704.

[55] Chandler D, Bailey AS, Tatchell GM, Davidson G, Greaves J, Grant WP. The development, regulation and use of biopesticides for integrated pest management. Philosophical Transactions of the Royal Society B: Biological Sciences. 2011;366:1987–1998. DOI:10.1098/rstb.2010.0390.

[56] Awan TH, Chauhan BS, Cruz PCS. Influence of environmental factors on the germination of Urena lobata L. and its response to herbicides. PLoS One. 2014;9:e90305. DOI:10.1371/journal.pone.0090305.

[57] Lutman PJ, Berry K, Payne RW, et al. Persistence of seeds from crops of conventional and herbicide tolerant oilseed rape (Brassica napus). Proceedings of the Royal Society B: Biological Sciences. 2005;272:1909–1915. DOI:10.1098/rspb.2005.3166.

[58] Smith K, Evans DA, El-Hiti GA. Role of modern chemistry in sustainable arable crop protection. Philosophical Transactions of the Royal Society B: Biological Sciences. 2008;363:623–637. DOI:10.1098/rstb.2007.2174.

[59] May MJ, Champion GT, Dewar AM, Qi A, Pidgeon JD. Management of genetically modified herbicide-tolerant sugar beet for spring and autumn environmental benefit. Proceedings of the Royal Society B: Biological Sciences. 2005;272:111–119. DOI:10.1098/rspb.2004.2948.

[60] Suckling DM, Sforza RFH. What magnitude are observed non-target impacts from weed biocontrol? PLoS One. 2014;9:e84847. DOI:10.1371/journal.pone.0084847.

[61] Brookes G. Weed control changes and genetically modified herbicide tolerant crops in the USA 1996–2012. GM Crops Food. 2014;5:321–332. DOI: 10.4161/21645698.2014.958930.

[62] Heap I. Global perspective of herbicide-resistant weeds. Pest Management Science. 2014;70:1306–1315. DOI:10.1002/ps.3696.

[63] Duke SO. Taking stock of herbicide-resistant crops ten years after introduction. Pest Management Science. 2005;61:211–218.

[64] Lee KY, Townsend J, Tepperman J, et al. The molecular basis of sulfonylurea herbicide resistance in tobacco. EMBO Journal. 1988;7:1241–1248.

[65] Yadav N, McDevitt RE, Benard S, Falco SC. Single amino acid substitutions in the enzyme acetolactate synthase confer resistance to the herbicide sulfometuron methyl. Proceedings of the National Academy of Sciences USA. 1986;83:4418–4422.

[66] Yu Q, Han H, Powles SB. Mutations of the ALS gene endowing resistance to ALS-inhibiting herbicides in Lolium rigidum populations. Pest Management Science. 2008;64:1229–1236. DOI:10.1002/ps.1624.
[67] Yu Q, Jalaludin A, Han H, Chen M, Sammons RD, Powles SB. Evolution of a double amino acid substitution in the 5-enolpyruvylshikimate-3-phosphate synthase in Eleusine indica conferring high-level glyphosate resistance. Plant Physiology. 2015;167:1440–1447. DOI:10.1104/pp.15.00146.

[68] Zhang XQ, Powles SB. Six amino acid substitutions in the carboxyl-transferase domain of the plastidic acetyl-CoA carboxylase gene are linked with resistance to herbicides in a Lolium rigidum population. New Phytology. 2006;172:636–645.

[69] Dayan FE, Duke SO, Grossmann K. Herbicides as probes in plant biology. Weed Science. 2010;58:340–350. DOI: http://dx.doi.org/10.1614/WS-09-092.1.

[70] Lambreva MD, Russo D, Polticelli F, et al. Structure/function/dynamics of photosystem II plastoquinone binding sites. Current Protein and Peptide Science. 2014;15:285–295. DOI:10.2174/1389203715666140327104802.

[71] Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. Available from: http://www.ncbi.nlm.nih.gov/books/NBK26818/

[72] Birchler JA, Veitia RA. The gene balance hypothesis: from classical genetics to modern genomics. The Plant Cell. 2007;19:395–402. DOI:10.1105/tpc.106.049338.

[73] Griffiths AJF, Miller JH, Suzuki DT, Lewontin RC, Gelbart WM. An Introduction to Genetic Analysis. 7th edition. New York: W. H. Freeman; 2000. Interactions between the alleles of one gene. Available from: http://www.ncbi.nlm.nih.gov/books/NBK21920/

[74] Horvath D. Genomics for weed science. Current Genomics. 2010;11:47–51. DOI: 10.2174/138920210790217972.

[75] Kant S, Seneweera S, Rodin J, Materne M, Burch D, Rothstein SJ, Spangenberg G. Improving yield potential in crops under elevated CO₂: integrating the photosynthetic and nitrogen utilization efficiencies. Frontiers in Plant Science. 2012;3:162. DOI: 10.3389/fpls.2012.00162.

[76] Ort DR, Xinguang Z, Melis A. Optimizing antenna size to maximize photosynthetic efficiency. Plant Physiology. 2011;155:79–85. DOI:10.1104/pp.110.165886.

[77] Bawa AS, Anilakumar KR. Genetically modified foods: safety, risks and public concerns - a review. Journal of Food Science and Technology. 2013;50:1035–1046. DOI: 10.1007/s13197-012-0899-1.

[78] Maghari BM, Ardekani AM. Genetically modified foods and social concerns. Avicenna Journal of Medical Biotechnology. 2011;3:109–117.

[79] Nielsen KM, Bohn T, Townsend JP. Detecting rare gene transfer events in bacterial populations. Frontiers in Microbiology. 2013;4:415. DOI:10.3389/fmicb.2013.00415.
[80] Locke MA, Zablhotowicz RM, Reddy KN. Integrating soil conservation practices and glyphosate-resistant crops: impacts on soil. Pest Management Science. 2008;64:457–469. DOI:10.1002/ps.1549.

[81] Vencill WK, Nichols RL, Webster TM, et al. Herbicide resistance: toward an understanding of resistance development and the impact of herbicide-resistant crops. Weed Science. 2012;60:2–30. DOI: http://dx.doi.org/10.1614/WS-D-11-00206.1.

[82] Delye C, Zhang XQ, Michel S, Matijcek A, Powles SB. Molecular bases for sensitivity to acetyl-coenzyme A carboxylase inhibitors in black-grass. Plant Physiology. 2005;137:794–806. DOI:10.1104/pp.104.046144.

[83] Fitzgerald TL, Kazan K, Li Z, Morell MK, Manners JM. A high-throughput method for the detection of homoeologous gene deletions in hexaploid wheat. BMC Plant Biology. 2010;10:264. DOI:10.1186/1471-2229-10-264.

[84] Firbank LG, Rothery P, May MJ, et al. Effects of genetically modified herbicide-tolerant cropping systems on weed seedbanks in two years of following crops. Biology Letters. 2006;2:140–143.

[85] Green JM. The benefits of herbicide-resistant crops. Pest Management Science. 2012;68:1323–1331. DOI:10.1002/ps.3374.

[86] Whaley CM, Wilson HP, Westwood JM. A new mutation in plant Als confers resistance to five classes of Als-inhibiting herbicides. Weed Science. 2007;55:83–90. DOI: http://dx.doi.org/10.1614/WS-06-082.1.

[87] Deng W, Cao Y, Yang Q, Liu MJ, Mei Y, Zheng MQ. Different cross-resistance patterns to AHAS herbicides of two tribenuron-methyl resistant flixweed (Descurainia sophia L.) biotypes in China. Pesticide Biochemistry and Physiology. 2014;112:26–32. DOI:10.1016/j.pestbp.2014.05.003.

[88] Tehranchian P, Norsworthy JK, Nandula V, McElroy S, Chen S, Scott RC. First report of resistance to acetolactate-synthase-inhibiting herbicides in yellow nutsedge (Cyperus esculentus): confirmation and characterization. Pest Management Science. 2015;71:1274–1280. DOI:10.1002/ps.3922.

[89] Norsworthy JK, Ward SM, Shaw DR, et al. Reducing the risks of herbicide resistance: best management practices and recommendations. Weed Science. 2012;60:31–62. DOI: http://dx.doi.org/10.1614/WS-D-11-00155.1.

[90] Konishi T, Sasaki Y. Compartmentalization of two forms of acetyl-CoA carboxylase in plants and the origin of their tolerance toward herbicides. Proceedings of the National Academy of Sciences USA. 1994;91:3598–3601.

[91] Nikolskaya T, Zagnitko O, Tevzadze G, Haselkorn R, Gornicki P. Herbicide sensitivity determinant of wheat plastid acetyl-CoA carboxylase is located in a 400-amino acid fragment of the carboxyltransferase domain. Proceedings of the National Academy of Sciences USA. 1999;96:14647–14651.
[92] Yang X, Guschina IA, Hurst S, Wood S, Langford M, Hawkes T, Harwood JL. The action of herbicides on fatty acid biosynthesis and elongation in barley and cucumber. Pest Management Science. 2010;66:794–800. DOI:10.1002/ps.1944.

[93] Kaundun SS, Hutchings SJ, Dale RP, McIndoe E. Role of a novel I1781T mutation and other mechanisms in conferring resistance to acetyl-CoA carboxylase inhibiting herbicides in a black-grass population. PLoS One. 2013;8:e69568. DOI:10.1371/journal.pone.0069568.

[94] Zagnitko O, Jelenska J, Tevzadze G, Haselkorn R, Gornicki P. An isoleucineyleucine residue in the carboxyltransferase domain of acetyl-CoA carboxylase is critical for interaction with aryloxyphenoxypropionate and cyclohexanedione inhibitors. Proceedings of the National Academy of Sciences USA. 2001;98:6617–6622.

[95] Whitcomb CE. An introduction to ALS-inhibiting herbicides. Toxicology and Industrial Health. 1999;15:231–239.

[96] Sathasivan K, Haughn GW, Murai N. Molecular basis of imidazolinone herbicide resistance in Arabidopsis thaliana var Columbia. Plant Physiology. 1991;97:1044–1050.

[97] Wloga D, Gaertig J. Post-translational modifications of microtubules. Journal of Cell Science. 2010;123:3447–3455. DOI:10.1242/jcs.063727.

[98] Grossmann K. Auxin herbicides: current status of mechanism and mode of action. Pest Management Science. 2010;66:113–120. DOI:10.1002/ps.1860.

[99] Mira NP, Teixeira MC, Sá-Correia I. Adaptive response and tolerance to weak acids in Saccharomyces cerevisiae: a genome-wide view. OMICS: A Journal of Integrative Biology. 2010;14:525–540. DOI:10.1089/omi.2010.0072.

[100] Roach T, Krieger-Liszkay AK. Regulation of photosynthetic electron transport and photoinhibition. Current Protein and Peptide Science. 2014;15:351–362. DOI:10.2174/1389203714666140327105143.

[101] Mayfield SP, Nelson T, Taylor WC. The fate of chloroplast proteins during photooxidation in carotenoid-deficient maize leaves. Plant Physiology. 1986;82:760–764.

[102] Santabarbara S. Limited sensitivity of pigment photo-oxidation in isolated thylakoids to singlet excited state quenching in photosystem II antenna. Archives of Biochemistry and Biophysics. 2006;455:77–88.

[103] Mechant E, De Mare T, Hermann O, Bulcke R. Resistance of Chenopodium albumto photosystem II-inhibitors. Communications in Agricultural and Applied Biological Sciences. 2008;73:913–917.

[104] Colovic MB, Krstic DZ, Lazarevic-Pasti TD, Bondzic AM, Vasic VM. Acetylcholinesterase inhibitors: pharmacology and toxicology. Current Neuropharmacology. 2013;11:315–335. DOI:10.2174/1570159X11311030006.
[105] Qin YM, Hu CY, Pang Y, Kastaniotis AJ, Hiltunen JK, Zhu YX. Saturated very-long-chain fatty acids promote cotton fiber and Arabidopsis cell elongation by activating ethylene biosynthesis. The Plant Cell. 2007;19:3692–3704. DOI:10.1105/tpc.107.054437.

[106] Trenkamp S, Martin W, Tietjen K. Specific and differential inhibition of very-long-chain fatty acid elongases from Arabidopsis thaliana by different herbicides. Proceedings of the National Academy of Sciences USA. 2004;101:11903–11908.

[107] Herrmann KM, Weaver LM. The shikimate pathway. Annual Review of Plant Physiology and Plant Molecular Biology. 1999;50:473–503.

[108] Maeda H, Dudareva N. The shikimate pathway and aromatic amino acid biosynthesis in plants. Annual Reviews in Plant Biology. 2012;63:73–105. DOI:10.1146/annurev-arplant-042811-105439.

[109] Metcalf WW, van der Donk WA. Biosynthesis of phosphonic and phosphinic acid natural products. Annual Review of Biochemistry. 2009;78:65–94. DOI:10.1146/annurev.biochem.78.091707.100215.

[110] Obojska A, Berlicki L, Kafarski P, Lejczak B, Chicca M, Forlani G. Herbicidal pyridyl derivatives of aminomethylene-bisphosphonic acid inhibit plant glutamine synthetase. Journal of Agricultural and Food Chemistry. 2004;52:3337–3344.

[111] Van Rensen JJS, Vredenberg WJ. Adaptation of photosystem II to high and low light in wild-type and triazine-resistant Canola plants: analysis by a fluorescence induction algorithm. Photosynthesis Research. 2011;108:191–200. DOI:10.1007/s11120-011-9680-y.

[112] Qin G, Gu H, Ma L, Peng Y, Deng XW, Chen Z, Qu L-J. Disruption of phytoene desaturase gene results in albino and dwarf phenotypes in Arabidopsis by impairing chlorophyll, carotenoid, and gibberellin biosynthesis. Cell Research. 2007;17:471–482. DOI: 10.1038/cr.2007.40.

[113] Nwani CD, Lakra WS, Nagpure NS, Kumar R, Kushwaha B, Srivastava SK. Toxicity of the herbicide atrazine: effects on lipid peroxidation and activities of antioxidant enzymes in the freshwater fish Channa punctatus (Bloch). International Journal of Environmental Research and Public Health. 2010;7:3298–3312. DOI:10.3390/ijerph7083298.

[114] Oracz K, El-Maarouf-Bouteau H, Kranzer I, Bogatek R, Corbineau F, Bailly C. The mechanisms involved in seed dormancy alleviation by hydrogen cyanide unravel the role of reactive oxygen species as key factors of cellular signaling during germination. Plant Physiology. 2009;150:494–505.