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Review

Pesticides Toxicity, Removal and Detoxification in Plants: A Review

Boyu Zhang [1,†], Fang Lv [2,†] and Jing Yang [1,*]

[1] Key Laboratory of Quality and Safety Control for Subtropical Fruit and Vegetable, Ministry of Agriculture and Rural Affairs, Collaborative Innovation Center for Efficient and Green Production of Agriculture in Mountainous Areas of Zhejiang Province, College of Horticulture Science, Zhejiang A&F University, Hangzhou 311300, China; mycr0416@stu.zafu.edu.cn
[2] Jixian Honors College, Zhejiang A&F University, Hangzhou 311300, China; 202124060105@stu.zafu.edu.cn
* Correspondence: yangjing@zafu.edu.cn
† These authors contributed equally to this work.

Abstract: Pesticides play a crucial role in agricultural production by preventing diseases and pests and ensuring food yield. However, the irrational use of pesticides can lead to numerous issues that compromise crop quality and counteract the original intentions of their application. Therefore, it is necessary to identify more effective methods to counteract pesticide stress. Here we review the impacts of herbicides, insecticides, and fungicides on plants and the measures taken to reduce pesticide residues on plants. We have found that despite the substantial differences in the mechanisms of action of the aforementioned three types of pesticides, the adverse effects they inflict on plants are similar, and at certain dosages, they can severely constrain plant growth and disrupt physiological functions. Also, most current research on using exogenous growth regulators to alleviate pesticide stress still focuses on photosynthesis, the antioxidant system, three-stage detoxification, and secondary metabolites, neglecting the search for genes that respond to pesticide stress. We believe that by combining biological protection with post-harvest treatment techniques and exploring potential genes that are responsive to pesticide stress, a better strategy for dealing with pesticide stress can be found, thereby promoting sustainable agricultural development.

Keywords: pesticide stress; pesticide degradation; ROS; detoxification; plant growth regulators

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1. Introduction

Pesticides refer to chemical agents used in agriculture for the prevention and treatment of plant diseases, pests and weeds, and for the regulation of plant growth [1]. The European Union considers plant-protection products and biocides as pesticides. In the latest regulations on pesticides in China, they are defined as a substance or a mixture of several substances and their formulations used to prevent and control diseases, insects, grass, mice and other harmful organisms that harm agriculture and forestry, as well as to purposefully regulate the growth of plants and insects. At present, the use of pesticides remains a crucial strategy to avoid crop losses and for maintaining food security, but it can cause damage to plants.

With the development of human society, the types of pesticides used in production have increased, including insecticides, fungicides, herbicides, rodenticides, molluscicides, acaricides repellents, nematicides and growth regulators. According to data provided by the Food and Agriculture Organization of the United Nations [2], the most used pesticides are herbicides, insecticides and fungicides. We selected a few typical developed and developing countries from the FAO database to illustrate the usage of these three types of pesticides in recent years. As shown in Figure 1, countries classified as developed countries, such as the United States, Germany and Australia, have long implemented policies restricting the use of pesticides, and the amount of pesticides applied in agriculture has remained stable, with a slight increase in recent years. Meanwhile, some developing countries started late in pesticide management, and their consumption of pesticide is still increasing annually. Statistical data show a staggering increase of 1169% in pesticide consumption in Pakistan over the past twenty years [3]. From 1990 to 2019, China's annual usage was about 1.42 million tons [4]. Despite the Chinese Ministry of Agriculture's implementation of a "zero growth action in the use of pesticides and fertilizers" by 2020, leading to a significant reduction in pesticide consumption since 2015, the overall efficiency of pesticide usage is still far from some major developed countries. Moreover, there is a noticeable discrepancy in pesticide usage among different provinces in China [5]. These phenomena indicate that the issue of irrational pesticide use will persist.

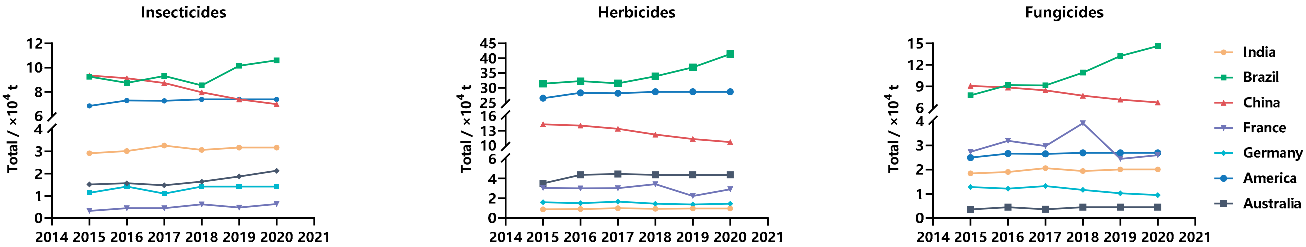

Figure 1. Usage of insecticides, herbicides and fungicides from 2015 to 2020 [2]. (Note: the data filtering was performed by entering the keyword "pesticide" in FAO, combining and selecting countries (e.g., China) + elements (Agricultural) + items (e.g., Insecticides + (Total)) + years (e.g., 2015)).

Another problem is farmers' lack of specialized knowledge, which leads to unscientific spraying of pesticides, further exacerbating the hazards associated with pesticide residue [3]. Most countries have established corresponding legal systems for the use of pesticides to reduce their potential negative impacts on human health and the environment. The FAO and the WHO laid down key principles for pesticide management and gave guidance on forming a legal national framework, which is a prerequisite for the reduction of the potential negative impact of pesticides on human health and the environment [6]. However, residual chemical pesticides may pose risks to human health [7], including increased incidences of cancer, chronic kidney disease, immune system suppression, infertility [8], endocrine disruption and neurobehavioral disorders [9].

During the application of pesticides, they do not merely remain on the surface of the plants but are also absorbed into the plant through the root system or stomata. ROS production is a general defense mechanism, and the destruction of plant antioxidant and detoxification systems only by pesticides has been systematically organized in previous studies (Tables 1 and 2), such as leading to an increase in reactive oxygen species (ROS) within the cells and affecting the photosynthetic rate of the plants. Due to the scavenging abilities of substances such as phenols, flavonoids and vitamins, fluctuations in the levels of many nutrients within the plants may occur simultaneously. These issues are not in line with the Sustainable Development Goals proposed by the United Nations in 2015. Therefore, the problem of pesticide residues has greatly aroused the interest of scholars, prompting them to seek effective solutions.

In order to minimize the residual of pesticides on the exterior of plants, researchers have employed various means including physical, chemical and biological methods. Moreover, the study of alleviating the stress and accelerating the degradation of pesticides by the plants themselves has become a prominent field. At the present time, the more commonly used method is to pre-treat with growth regulators. Compared to the research and reviews on the effects of herbicides and fungicides on plants, there are far fewer articles related to insecticides. Here, we hope to provide a theoretical foundation and valuable insights for alleviating the stress imposed by insecticides, herbicides and fungicides.

Table 1. A list of studies on the impacts of insecticides on plants.

Plants	Pesticides Types	Concentration	Main Results	Reference
Onion (*Allium cepa* L.)	Imidacloprid	1.75 μg/mL, 17.5 μg/mL, 175 μg/mL, 1750 μg/mL	Root length↓	[10]
Pok choy (*Brassica rapa* L.)	Imidacloprid	10 mg/L	Proline↑, Sucrose↑, Raffinose↑, Disaccharides↑, Glutathione oxidized↑	[11]
Wheat (*Triticum aestivum* L.)	Imidacloprid	100 mg/kg, 200 mg/kg	Jasmonic acid in root and leaf↓, Indole acetic acid in root and leaf↓, Abscisic acid in root and leaf↑, Ferulic acid↓	[12]
Cucumber (*Cucumis sativus* L.)	Imidacloprid	2.75 mM	Fv/Fm↓, Ascorbic acid↓, Glutathione↓, Glutathione oxidized↑	[13]
Lettuce (*Lactuca sativa* L.)	Imidacloprid, Fenvalerate	10mg/L	Under IMI treatment, Iron↓, Arginine↓, Cysteine↓, Homoserine↓, 4-hydroxyisoleucine↓, Proline↓, Amino acid↓, Under FEN treatment, Iron↑, Flavonoid↓, Vitamin C↓	[14]
Rice (*Oryza sativa* L.)	Chlorpyrifos	5.0 mg/L	Peroxidase↑, Superoxide dismutase↑, Malondialdehyde↑, Protein↓, Chlorophyll↑	[15]
Cucumber (*Cucumis sativus* L.)	Chlorpyrifos	0.6 kg/ha	H^+ efflux↑, K^+ efflux↑, H_2O_2↑, O_2^-↑, Superoxide dismutase↑, Chlorophyll a↓, Chlorophyll b↓, Carotene↓	[16]
Canadian waterweed (*Elodea canadensis* Michx.), needle spikerush (*Eleocharis acicularis* L.), water mint (*Mentha aquatica* L.)	Chlorpyrifos	50 μg/dm^3, 100 μg/dm^3, 150 μg/dm^3	Glutathione peroxidase↑, Glutathione s-transferase↓, Chlorophyll a↓, Chlorophyll b↓, Carotene↓	[17,18]

Note: The up arrow "↑" indicates an increase, the down arrow " ↓ " indicates a decrease.

Table 2. A list of studies on the impacts of fungicides and herbicides on plants.

Plants	Pesticides Types	Concentration	Main Results	Reference
Maize (*Zea mays* L.)	Metolachlor	0.5 mg/L, 1.0 mg/L, 2.0 mg/L, 4.0 mg/L, 8.0 mg/L	Malondialdehyde↑, Ascorbic acid peroxidase↑, Glutathione peroxidase↑, Catalase↑, Germination↓, Biomass production↓, Vigor index↓, Ethyl carbamate$_{50}$↓	[19]
Trifolium pratense L. *Lotus corniculatus* L. *Trifolium repens* L. *Cichorium intybus* L.	Glyphosate	1440 g a.i./ha	cumulative number of *Trifolium pratense* L. flowers↓, cumulative number of *Lotus corniculatus* L. flowers↓, cumulative number of *Trifolium repens* L. flowers↑,	[20]
Cency (*Centaurea cyanus* L.), Silno (*Silene noctiflora* L.), Vioar (*Viola arvensis* Murray), Cerar (*Cerastium arvense* L.), Cirar (*Cirsium arvense* L.), Epimo (*Epilobium montanum* L.), Knaar (*Knautia arvensis* L.), Tarof (*Taraxacum officinale* F.H. Wigg.), Trfpr (*Trifolium pratense* L.)	bromoxynil, ioxynil Bromoxynil, Metsulfuron-Methyl, Clopyralid, Glyphosate	280 g/ha 240 g a.i./ha 6 g a.i./ha 80 g/ha 1440 g/ha	Cumulative number of flowers↓, Flowering time↓	[21]
Reed (*Phragmites australis*)	Metolachlor	245 µg/L	Malondialdehyde↑, Reactive oxygen species↑, Chlorophyll↓then↑, Superoxide dismutase↑, Peroxidase↑, Catalase↑	[22]
Rice (*Oryza sativa* L.)	Diuron	0.125 mg/L, 0.25 mg/L, 0.5 mg/L, 1.0 mg/L, 2.0 mg/L	Elongation↓, Biomass↓, Chlorophyll↓, Malondialdehyde↑, Superoxide dismutase↑, Peroxidase↑, Glutathione reductase↑, Polyphenol oxidase↑, Ascorbic acid peroxidase↑, Catalase↑, Glutathione↑then↓, Jasmonic acid↑	[23]

Table 2. *Cont.*

Plants	Pesticides Types	Concentration	Main Results	Reference
Arabidopsis (*Arabidopsis thaliana*)	Dichlorprop	0.1 μM, 0.2 μM, 0.3 μM	Plant growth↓, H_2O_2↑, Jasmonic acid↑, Salicylic acid↑, Abscisic acid↓then↑	[24]
Tomato (*Solanum lycopersicum* L.)	Carbendazim	1 mM	Malondialdehyde↑, Fv/Fm↓, Superoxide dismutase↑, Catalase↑, Ascorbic acid peroxidase↑, Glutathione peroxidase↓, Ascorbic acid↓	[25]
Rice (*Oryza sativa* L.)	Bismerthiazol	10 mg/L, 20 mg/L, 50 mg/L	Jasmonic acid↑, OsAOS1↑, OsAOS2↑, H_2O_2↑, Volatile chemicals↑,	[26]
Tomato (*Solanum lycopersicum* L.)	Triazoles	3.52×10^{-6} mol	Weight of thick stems↓, Weight of thin stems↓, Weight of leaves↓, Fruit weight↓, Quercetin↓, Naringin↓, Salicylic acid↓, Chlorogenic acid↑, Hesperidin↑	[27]

Note: The up arrow "↑" indicates an increase, the down arrow " ↓ " indicates a decrease.

2. The Physiological and Biochemical Effects of Pesticides on Plants

Pesticides play an important role in agricultural production, as they can protect cultivated plants from diseases, weeds and pests to increase crop yield, especially for monoculture crops. However, the enhancement of pesticide toxicity has been shown to trigger oxidative stress in plants, significantly increasing the levels of ROS, for example O_2^- and H_2O_2 [11]. Excessive amounts of H_2O_2 can subsequently damage the plant's DNA [28], proteins [29], lipids [30] and other substances. Such damage to the plant's physiological and biochemical responses severely hinders growth and development, ultimately reducing crop yield.

Meanwhile, pesticides are transformed, metabolized and decomposed by plants via their detoxification systems, which include non-enzymatic and enzymatic antioxidant defense mechanisms [31]. Normally, a steady-state balance exists between ROS and the antioxidant system [32]. After the pesticide application, a series of substances, particularly antioxidants, exhibit regular fluctuations within the plant [17]. However, the molecular mechanisms by which pesticides affect plants are not yet fully understood [29]. Several physiological and biochemical changes that happen in plants after pesticide application are discussed in this section.

2.1. Pesticides Affect Plant Photosynthesis

Plants are equipped with specific sensors that enable them to recognize and perceive abiotic stresses, thus allowing them to make appropriate adjustments to their growth, metabolism and development [33]. Pesticide stress has been found to adversely affect the photosynthesis of plants, an essential energy conversion process during their growth and development that directly impacts their yield. The rate of photosynthesis is influenced by many factors, such as the stomatal conductance, concentration of Ca^{2+} and chlorophyll content.

Guard cells are capable of sensing a variety of abiotic and biotic stimuli from the internal and external environments and can rapidly respond to unfavorable conditions by closing the stomata [34]. Ca^{2+} plays a crucial role in the response of stomata to external stimuli [35]. An increase in cytosolic free Ca^{2+} concentration within guard cells has been observed as a response to stimuli that induce stomatal closure [36]. When plants are subjected to pesticide stress, an increase in H_2O_2 triggers an influx of Ca^{2+}, leading to elevated free Ca^{2+} and resulting in stomatal closure [37]. Meanwhile, K^+ levels decrease, which on the one hand promotes stomatal closure and on the other hand inhibits stomatal opening [38].

Moreover, the chlorophyll content influences the rate of photosynthesis. Under pesticide stress, there is a corresponding decrease in chlorophyll content within plants. For instance, under the stress of a low dosage of toxaphene (0.60 kg/ha), the levels of chlorophyll a, chlorophyll b and carotenoids were found to be 23.63%, 30.61% and 17.27% lower, respectively, compared to control plants. A higher dosage of toxaphene (1.20 kg/ha) led to an even greater reduction in the levels of chlorophyll a, chlorophyll b and carotenoids, by 45.252%, 52.14% and 37.27%, respectively [16]. When cucumber leaves are exposed to imidacloprid (IMD, 2.75 mM), the Fv/Fm decreased by 25.3% [39]. These impacts on photosynthesis lead to the inhibition of plant growth and development, thereby possibly reducing crop yield.

2.2. Pesticides Affect the Plant Active Oxygen Scavenging System

In the normal life of plants, a balance is maintained between the production and elimination of ROS within plant cells to prevent cellular damage. However, this oxidative balance can be disrupted when plants are subject to stress, including pesticide stress, leading to a significant increase in ROS [40]. Following treatment with IMD (10 mg/L), the production of H_2O_2 in lettuce roots increased by 50.0%, while treatment with fenvalerate (10 mg/L) resulted in a 93.8% increase [14]. Notably, proline, serving as an organic osmolyte, accumulates in plant tissues under oxidative stress to provide protection against the induced oxidative damage. Elevated concentrations of pesticides significantly increase the proline content in *Stevia rebaudiana* roots [41]. Compared to the control, the level of proline in sprouts treated with IMD (10 mg/L) increased 1.50-fold [11]. Concurrently, the content of malondialdehyde (MDA), a product of peroxidation, also increased [39]. When maize was treated with metolachlor at concentrations of 1.0 and 2.0 mg/L, the MDA content increased by 26.0% and 48.9% [19]. To counteract the negative effects of ROS, plants' long-term adaptation to biotic and abiotic stresses has promoted the development of enzymatic systems [42]. The primary enzymatic antioxidants in plants include superoxide dismutase (SOD), ascorbate peroxidase (APX), glutathione peroxidase (GPX), and catalase (CAT), with SOD playing a central role in the ROS scavenging [40]. For example, in Arabidopsis, the activity of CAT in leaves treated with 0.2 μM dichlorprop (DCPP) was higher than in the control; specifically, CAT activity in leaves treated with (R)-DCPP increased 2.46-fold, and in leaves treated with (S)-DCPP, 0.62-fold [24]. Therefore, at relatively lower concentrations of pesticides, the detoxification systems in plants enhance the activity of antioxidative enzymes, thereby adapting to the increased ROS [43]. Notably, within certain limits, the activity of antioxidative enzymes is directly proportional to the concentration of pesticides, ensuring plant protection. High concentrations of pesticides may inhibit the function of antioxidative enzymes and the biosynthesis of glutathione (GSH) [44], causing irreversible damage.

A balanced redox homeostasis and an appropriate content of vitamin C (VC, also known as AsA) are essential for the normal development of plants and their defensive responses to adverse environmental stimuli [45]. VC has a role in scavenging ROS within a certain physiological range, thereby enhancing plant stress resistance. In addition to directly neutralizing ROS through reactions with superoxide and hydroxyl radicals, VC can also alleviate plant oxidative stress through various pathways. For instance, VC may act as a chain-breaking antioxidant, disrupting peroxidation processes and reducing lipid peroxidation caused by pesticides, and can also participate in a redox cycle with vitamin E (VE), reducing lipid peroxidation radicals and alleviating oxidative stress through the plant cell's key antioxidant system, the glutathione–ascorbate (GSH-AsA) cycle [46]. The levels of VC, acting as an antioxidant, might decrease after pesticide application.

2.3. Pesticides Affect Plant Growth and Metabolites

Pesticide stress has been shown to be detrimental to plant growth and development. It was observed that when rice plants were treated with 0.125 mg/L of butachlor, their elongation rate, biomass and chlorophyll content decreased significantly, to only 58.3%, 46.3% and 50.5% of the untreated control [23]. The growth of onion roots was significantly reduced ($p < 0.01$) by 37.94% and 56.03% following treatment with 175 µg/mL and 1750 µg/mL of IMD [10]. The shoot length of maize decreased by 30.7%, 37.0%, 38.2% and 55.1% under the treatments of 1.0, 2.0, 4.0 and 8.0 mg/L of alachlor, respectively [19]. These inhibitory effects on plant growth are unacceptable for agricultural production.

The growth of plants is related to various metabolites, and unfavorable stress conditions can lead to a decrease in the activity of several synthetic enzymes, including those responsible for synthesizing proteins, nucleic acids, lipids and carbohydrates. The activity of hydrolytic enzymes for proteins, nucleic acids, sugars and lipids increases with the intensification of stress. Long-term or severe stress can cause irreversible damage to plants [47]. To avoid such outcomes, plants resort to osmotic adjustment under stress conditions. The main osmoregulatory substances include soluble proteins, soluble sugars, proline, etc. The soluble protein content in rice tissues was significantly downregulated by 8.06% and 14.7% under the stress of 5.0 mg/L and 20 mg/L of endosulfan [15]. In lettuce exposed to 10 mg/L of IMD and fenvelarate, the levels of most amino acids in the roots were significantly reduced, and the content of flavonoid, an important active metabolite, in lettuce decreased by 25% after treatment with 10 mg/L of fenvalerate [14]. The effects of pesticides on plant metabolic substances are extensive and complex (Figure 2). During the defense process in plants, substances with osmoregulatory functions (such as sugars and proteins), secondary metabolites involved in scavenging ROS (flavonoids and phenolics), as well as the precursor amino acids required for their synthesis, are all affected to varying degrees.

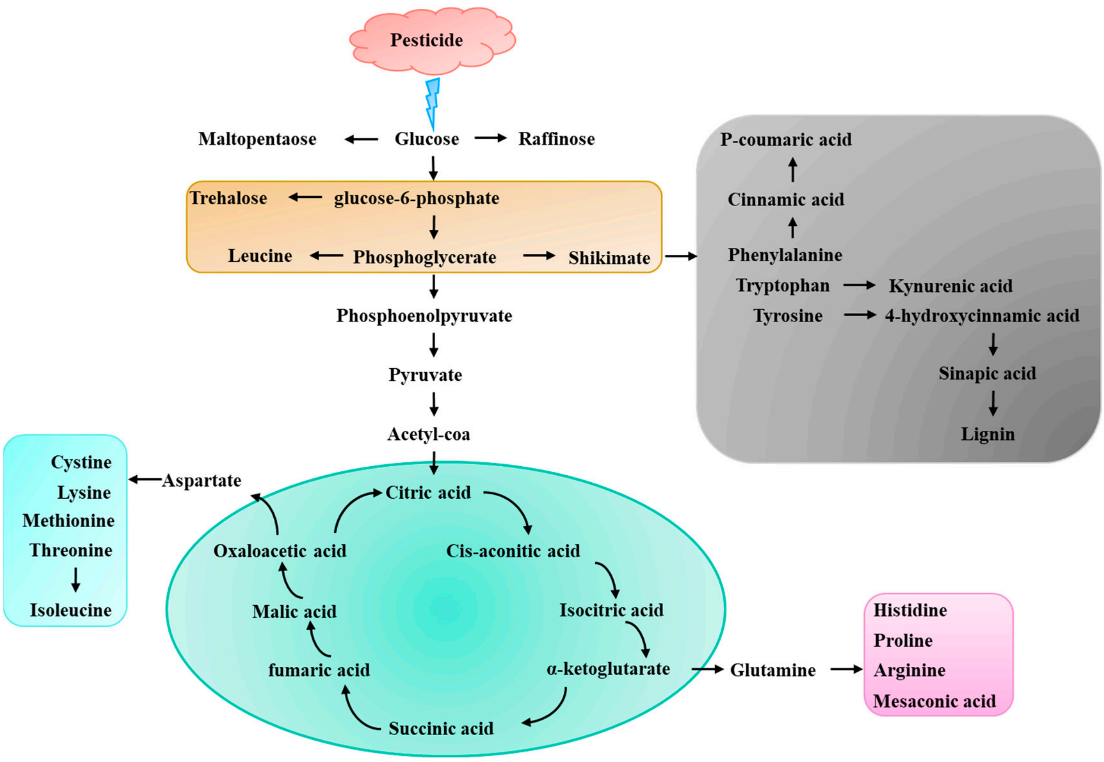

Figure 2. The corresponding nodes of metabolites affected by pesticides in biosynthesis [11,14,48].

3. The Degradation of Pesticides Outside of the Plant

For pesticides that remain on plants, the optimal approach is to remove or degrade them as much as possible through various means, prior to their absorption by the plant or ingestion by animals. The degradation of pesticides outside of the plant can be divided into non-biological degradation and biological degradation [49]. Non-biological degradation is further divided into physical degradation and chemical degradation [42].

3.1. Non-Biological Degradation

Physical degradation refers to the elimination of pesticides through physical means, based on the physical properties of the pesticides. Among various physical degradation methods, washing is the most commonly used [1]. As early as the last century, studies showed that washing could remove the majority of pesticide residues. Immersing peaches in a hot alkali solution and rolling them can remove 99.7% of the Gardona on the surface of the fruit [50]. In recent years, more effective methods have been developed, such as the ultrasonic method, which is characterized by its speed and short duration. Ultrasonic radiation can effectively and quickly degrade dichlorvos and dithianon, with the degradation effect influenced by the ultrasonic power, temperature and pH value. Among these, ultrasonic power is one of the most critical factors. Studies have shown that increasing power has a beneficial effect on the degradation of both dichlorvos and dithianon. When samples are treated for 60 min, the concentration of dichlorvos at 300 W is 1.2 and 1.9 times higher than at 600 and 900 W [51]. Similarly, with the increase in ultrasonic power, the degradation of another organochlorine pesticide, trichlorfon, also improves. Upon reaching a power of 375 W, the degradation rate constant was recorded as 0.022 min^{-1}. However, beyond this value, a decline in the degradation rate was observed [52]. Ionizing radiation, because of its simplicity, wide applicability, and no need for additives, is a promising technology suitable for an industrial scale. In a solution saturated with air at a dose of 1 kGy (kilogray, 1 kg of irradiated material absorbs 1000 joules of energy), chemical oxygen demand (COD) and total organic carbon (TOC) are reduced by 30% and 7%, respectively. At this dose, approximately 95% of paraquat is exhausted [53]. Adsorption refers to the use of adsorbent materials, such as activated carbon and quartz sand, to adsorb and remove pesticide residues. The degree of adsorption is mainly related to the presence of ions, ligand exchange, charge transfer, dipole interactions, hydrogen bonding and covalent bonding [54,55]. However, the use of traditional adsorbent materials still has limitations. For example, it is difficult to recover these adsorbents from mixed solutions, and the reuse of adsorbent materials [56] and improper handling may lead to secondary pollution [57]. Magnetic nanocomposites of coated ferrites (MOF), as newly developed pesticide adsorbent materials, can effectively degrade 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) [58]. Current advancements in nanomaterials such as graphene provide efficient, low-cost and eco-friendly prospects [59]. The use of new, low-pollution and small-molecule materials to remove residual pesticides seems to have become a trend.

Chemical degradation refers to the process of promoting pesticide degradation through the interaction with appropriate chemical reagents. Typical chemical degradation methods include hydrolysis [60], oxidation [61] and photolysis [62]. The rate of photocatalytic degradation of pesticides in aqueous solutions by nanocomposite materials is influenced by the pH value: under alkaline conditions, the higher the pH of the solution, the more hydroxyl radicals responsible for the photocatalytic degradation of pesticides are produced, and the faster the degradation rate [56]. In recent years, advanced oxidation processes (AOPs) based on peroxymonosulfate (PMS) have attracted considerable interest due to their potential efficiency in pesticide degradation [63]. The $ZnO@SiO_2@Fe_3O_4$/PMS/UV hybrid system, as a promising and efficient AOP for pesticide degradation, can achieve a degradation rate of 73.8% for dichlorophen (DZ) after a 60 min reaction [64]. Photolysis can decompose pesticides into non-toxic substances such as water and carbon dioxide. Studies on the photocatalytic treatment of glyphosate wastewater with TiO_2 showed that when the amount of TiO_2 increased from 1.0 g/L to 6.0 g/L under the same other conditions, the degradation rate of glyphosate increased by nearly 40% [65]. Otherwise, physical and chemical degradation methods are often used in combination [66].

3.2. Biological Degradation

Biological degradation (biodegradation) refers to the process of breaking down residual pesticides into smaller molecules using the biological activity of organisms [42]. The most commonly used methods include enzymatic, engineering-bacterial, bacterial-strain and plant degradation [67]. The use of the bacterial strain streptomyces toxytricini (D2) has presented a new pathway for the degradation of cypermethrin (CYP). The study results indicate that this strain actively participates in the pesticide degradation process, converting D2 into five main intermediates: 3-phenoxybenzaldehyde, 3-phenoxybenzoic acid, methyl salicylate, phenol and phthalic acid [68]. Notably, microorganisms secrete hydrolytic enzymes to participate in pesticide degradation. For example, the Est804 enzyme achieved degradation rates of 77.35%, 84.73% and 74.16% for CYP, fenpropathrin (FE) and lambda-cyhalothrin (LCT), respectively, within 30 min [69]. IMD, as an important insecticide, has become a new pollutant. Thus far, Pseudomonas has been found to have an extremely high degradation effect on IMD, being capable of degrading 46.5% of 0.5 mmol/L IMD within 40 h [70]. Carbamate pesticides, as a key detection variety of pesticide residues, have been found to be degraded by the E. coli strain R-SYB082 via the hydrolysis enzyme, with an enzyme activity of 2883 U/L and a degradation rate of EC up to 90.7% [71]. Plants have also been found to enhance the bioactivity of root microorganisms through the secretion of substances or enzymes, thereby promoting the biodegradation of pollutants [72]. Due to the diversity of pesticide varieties, finding strains with specific degradation functions has become a complex and long-term task.

Although biodegradation is a slower process compared to physical and chemical degradation [73], and there are many challenges to overcome for its widespread application [74], such as the degradation process of microorganisms being affected by numerous factors including biological (metabolic activity, acid release, enzyme activity), non-biological (surface morphology, terrain, surface hydrophobicity, charge distribution) and environmental (temperature, pH, salinity, oxygen level) [75] factors, its advantages of low cost, safety, and almost no secondary pollution make it a prominent research field, and significant progress has been achieved in the experimental stage. Given its enormous potential in cost reduction, biodegradation could potentially be suitable for large-scale applications in the future [76].

4. Pesticides Degradation in Plants

Pesticides have been observed to initiate the defense system of plants. The detoxification process employed by plants is elaborated upon, and is divided into three primary steps (Figure 3). Initially, plants leverage enzymes to hydrolyze or oxidize the toxic components in pesticides into intermediate products. These intermediate products are further metabolized by conjugation to an endogenous substance to form low-toxicity substances. Lastly, these conjugates are transported into vacuoles or apoplast for further degradation [77–80].

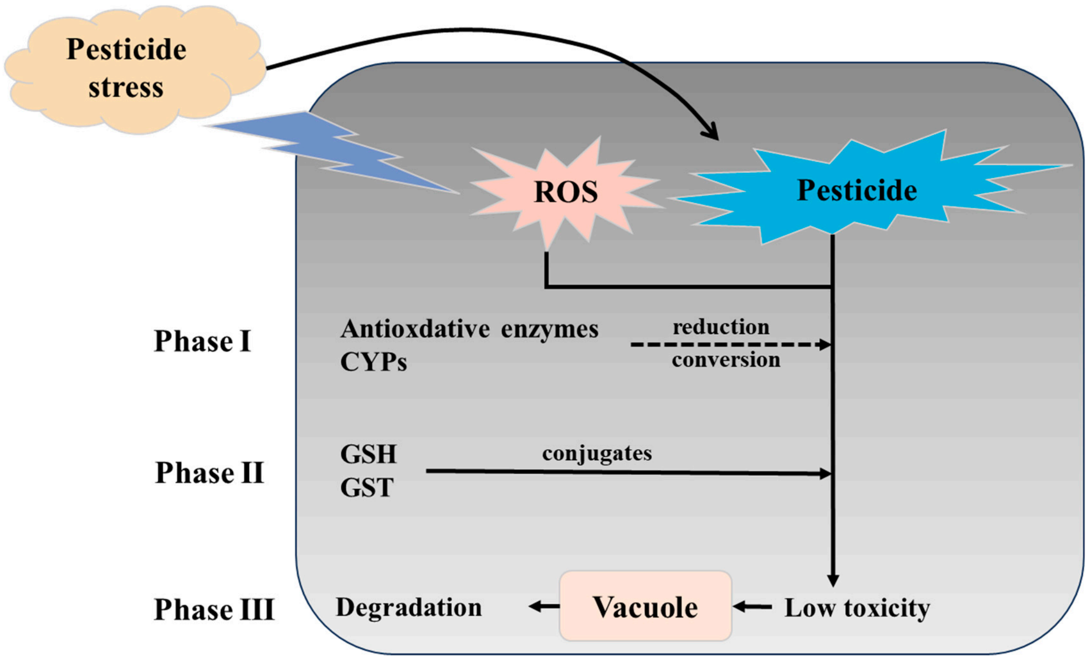

Figure 3. Simplified diagram of three-step detoxification [79–82].

4.1. A Brief Description of Pesticides Detoxification

The activation of the plant defense system is intricately tied to the generation of ROS, which encompasses singlet oxygen ($^1O_2$), hydrogen peroxide (H_2O_2), superoxide (O_2^-) and hydroxyl radical (-OH) [79]. After being exposure to pesticide stress, the cellulose and the lipid bilayer of plant membranes can efficiently bind hydrophobic organic pollutants [77], and the hydrophobic components of these molecules, such as aromatic or alkyl groups, are more susceptible to oxidation [83]. The enzyme RUBP (ribulose-1,5-bisphosphate) carboxylase/oxygenase utilizes oxygen to produce glycolate, which is further transformed into H_2O_2 by peroxidases [79]. Oxygen can also be oxidized into superoxide O_2^- in the presence of NADPH. The content of ROS is reduced and oxidative damage to plants is eliminated by the action of enzymatic systems, including CAT, SOD, POD, GPX and members of the cytochrome P450 family [79,84]. Pesticide toxins are subsequently directly or indirectly conjugated via glutathione-S-transferase (GST) through the potent reducing capacity of GSH [85]. Additionally, other substances such as AsA, glucose and amino acids [78] could also bind with these toxins to generate low-activity and low-toxicity products [86]. Overall, enzymes and secondary metabolites are responsible for clearing ROS caused by pesticides, while P450, GST and GSH are responsible for the degradation and transport of toxic substances.

4.2. Main Factors in the Three-Step Detoxification Process

Herbicides are recognized for their ability to selectively exterminate weeds with a mild inhibitory effect on crop growth. Crucial to the initial step of herbicide metabolism is the cytochrome P450 family [87], particularly monooxygenases, which catalyze oxidation reactions by adding a hydroxyl group to organic molecules. An array of CYP450 family members participate in the metabolism and degradation of herbicides. *CYP81A6* enhances plant tolerance to bentazon (a PSII inhibitor) and multiple sulfonylurea ALS inhibitors, such as ethametsulfuron-methyl, pyrazosulfuron-ethyl, sulfosulfuron, metsulfuron-methyl, flazasulfuron and chlorimuron-ethyl [88]. *CYP81A9* has also shown the ability to metabolize sulfonylurea herbicides like flupyrsulfuron-methyl [89]. *CYP72A31*, moreover, amplifies rice's tolerance to the inhibitor bispyribac-sodium [90]. The overexpression of both *CYP81A12* and *CYP81A21* in Echinochloa phyllopogon resulted in an increased tolerance to the ALS inhibitor bentazone [91]. Despite numerous studies investigating the detoxification effect of CYP450s on herbicides, the enzyme's detoxification role regarding insecticides remains undefined. Nevertheless, considering the extensive variety of CYP450 family members, their potential contribution to the detoxification process of other pesticides should not be overlooked.

In the subsequent phase of pesticide detoxification, the primary members are GSH, GST and GR. GSTs facilitate the attachment of GSH to electrophilic centers of external or internal compounds, thereby detoxifying hazardous substances [39,92]. In wheat, GST is capable of mediate the binding between GSH and fenoxaprop-ethyl [93]. In circumstances where GSH content diminishes, GR, an NADPH-dependent enzyme, facilitates the conversion of oxidized glutathione (GSSG) back to GSH [94]. The gene *GR1*, which is responsible for encoding the cytosolic GSH reductase, may be influenced by ROS in chloroplasts of Arabidopsis, and the GSH reductase gene *GR2* is also associated with fluctuations in the active oxygen content within the photosynthetic electron transport chain [94]. In the tertiary phase, the metabolites that are introduced into the vacuole can undergo further metabolism and degradation by gamma-glutamyl transpeptidase (GGT) and certain carboxypeptidases [85].

In addition to the detoxification factors previously discussed, nitric oxide (NO) regulates the stomatal opening and plant defense. This is achieved by controlling the overproduction of ROS via a modification in the activity of various ROS scavenging enzymes [95]. Furthermore, NO regulates mitogen-activated protein kinases (MAPKs) in response to ROS and hormones [96]. Moreover, assorted hormones including indole-3-acetic acid (IAA), salicylic acid (SA), jasmonic acid (JA), ethylene (ET) and abscisic acid (ABA) can stimulate the activation of the aforementioned factors [97]. The role of hormone-mediated defense pathways is significant and cannot be ignored, which has prompted scholars to study the resistance mechanism of hormones to pesticides.

5. Exogenous Plant Growth Regulators Alleviate Pesticide Stress and Promote the Degradation of Pesticides by Plants

Plant growth regulators have been studied by many researchers for their role in helping plants resist various stresses, such as high temperatures, cold, drought, salinity and heavy metals. Interestingly, despite the vast differences in the mechanisms of action of insecticides, herbicides and fungicides, they have been found to exert similar adverse effects on plant physiology and biochemistry. Similarly, plant growth regulators are also known to mitigate the stress caused by pesticides (Figure 4).

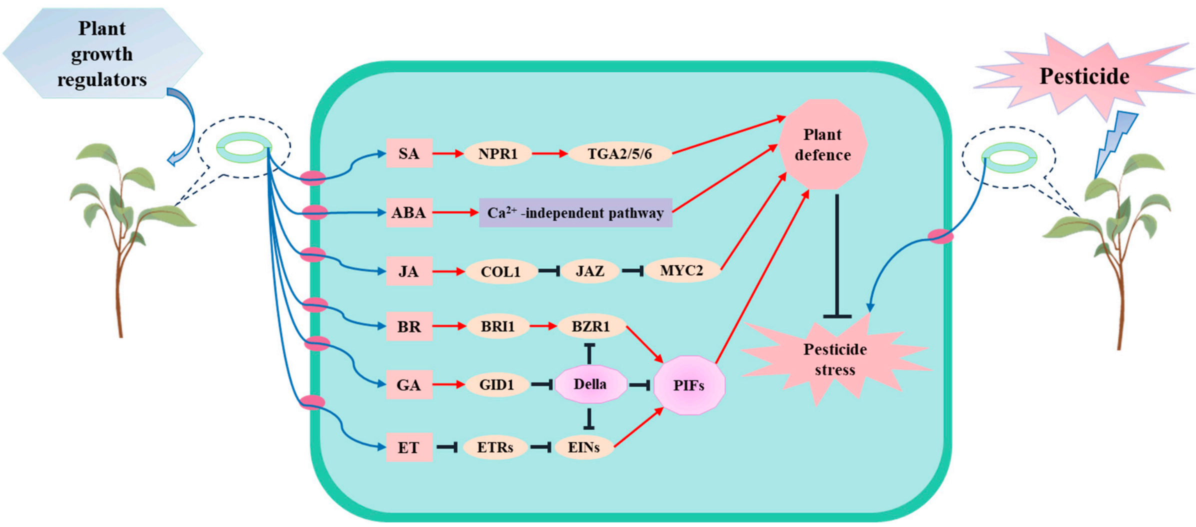

Figure 4. Plant growth regulators alleviate pesticide stress [98–100].

5.1. Pesticides Influence the Synthesis and Metabolism of Plant Signaling Molecules by Affecting Genes, Thereby Altering Hormone Levels

Pesticides are known to affect the synthesis and metabolic genes of plant growth regulators, thereby impacting hormone content. The most commonly studied plant growth regulators used to counteract pesticide stress include SA, JA, brassinolide (BR) and melatonin (MT). SA, widely recognized for its defense against viruses, and JA, which primarily counters insect stress and is antagonistic to SA, both show a significant increase in their levels within plants following pesticide treatment. After treatment with (R)-DCPP in Arabidopsis, the content of JA was positively correlated with the (R)-DCPP concentration, and the variations in SA followed a similar pattern to those of JA [24]. Conversely, after treatment with norflurazon (NF), the expression of *ICS2* involved in SA synthesis was significantly downregulated, as was the transcription level of AOS, a key enzyme in JA biosynthesis [101]. In rice, *OsbHLH6* has been found to regulate both SA and JA signaling, with JA signaling being activated early and SA signaling later. *OsCOI1a*, which is located in the nucleus, is strongly induced by atrazine (ATZ) and enhances the degradation of ATZ in rice, possibly through DNA demethylation promoting its expression [102]. Single treatment with isoproturon (IPU) in Arabidopsis led to a fourfold increase in SA content compared to the control [103], and pesticide treatment also enriched JA-related genes. After Chlorothalonil (CHT) treatment, the expression of genes related to JA synthesis (*ACX3*, *ACX4* and *KAT2*) was upregulated [104]. When wheat plants were exposed to 0.25 to 2 mg/L IPU, the concentration of endogenous methyl jasmonate (MeJA) gradually increased. At 1 mg/L IPU, the MeJA concentration in roots and shoots was twice than that of the control [105]. BRs, as efficient defense hormones, are also affected by pesticides. *OsBR6ox*, which is located in the chloroplasts of rice, has its expression upregulated under ATZ and acetochlor (ACT) stress [106]. MT, which was discovered later than the aforementioned hormones, also has the function of enhancing plant stress resistance. Overexpression of the MT biosynthesis gene *caffeic acid O-methyltransferase 1* (*COMT1*) increased the ability of tomatoes to reduce carbendazim (MBC) phytotoxicity and residues [25]. Exogenous MT and CHT treatment increased the content of endogenous MT in tomato leaves, with the MT + CHT treatment resulting in the highest MT content, a 230% increase compared to the control [107]. Since plant MT is synthesized from tryptophan sequentially by four enzymes, these genes are all significantly upregulated when induced by MV stress. However, during methyl viologen (MV) treatment, 1 mM MT pretreatment significantly inhibited the expression of *MdTDC1*, *MdT5H4*, *MdAANAT2* and *MdASMT1* in apples [108]. These studies indicate that pesticides upregulate plant growth-regulator synthesis genes, thereby activating downstream defense systems.

5.2. Exogenous Plant Growth Regulators Have Been Found to Alleviate the Damage That Pesticides Cause to the Photosystem

In mitigating the damage caused by pesticides to the photosystem, exogenous plant growth regulators demonstrated significant efficacy. Taking SA as an example, at a concentration of 0.01 mM, it significantly improved the decline in chlorophyll a, chlorophyll b and carotenoid levels in tomato leaves caused by thiram. By the fifth day, these levels increased by approximately 24%, 23% and 14%, respectively, and this effect peaked on the eleventh day with increases of 60%, 57% and 43%, respectively [109]. Moreover, the reduction in chlorophyll content in Arabidopsis caused by norflurazon (NF) could be restored with SA treatment. However, the restorative effect of SA was not achieved by involving photosynthesis-related genes such as *GUN1* or by increasing the levels of photosynthesis-related proteins, but likely through other post-transcriptional regulation mechanisms [101]. Under preconditioning with another hormone, MeJA, the chlorophyll concentration in rice increased by 33% compared to treatment with IPU alone, and in strains overexpressing *OsCOI1a* (without the additional application of MeJA), there was a significant increase in chlorophyll concentration compared to the IPU treatment [105]. BR and MT have also been used in research to alleviate pesticide toxicity. Compared to corn treated only with Dizineon (DZ), the photosynthetic rate (Pn) increased by 106% and stomatal conductance (Gs) by 165% in the brassinolide (EBL) preconditioning group [110]. CHT, MV and IMD treatments individually lowered the Fv/Fm levels in tomato [25,107] and cucumber leaves [13], and MT preconditioning significantly mitigated the reduction in the maximum quantum yield of PSII caused by pesticides. Plant growth regulators ensure the normal growth of crops, which may provide a new approach to the rational application of pesticides.

5.3. Exogenous Plant Growth Regulators Are Known to Enhance Enzymatic Activity, Thereby Reducing Cellular Damage Caused by Pesticides

As we know, the application of pesticides may have some toxic side effects, including the excessive production of reactive oxygen species and the inhibition of plant growth (Tables 1 and 2). Previous studies have shown that the exogenous application of these four different substances (SA, JA, BR and MT) can all produce a similar mitigating effect on pesticide stress.

On the one hand, these substances could effectively activate antioxidant systems and alleviate the burst of ROS caused by pesticides and reduce damage to plant cells. For example, SA can concurrently weaken the toxicity caused by clothianidin (CLO), dinotefuran (DFN) and difenoconazole (DFZ) to cucumber, where just 1 mg/L of SA significantly reduced the H_2O_2 content in cucumber roots by 74%, 62% and 52%, respectively, and the MDA content by 56%, 57% and 37%, while proline content significantly increased by 35%, 29% and 35%, respectively [13]. Similarly, EBL reduced lipid peroxidation induced in seeds by 35% in plants treated with EBL (0.01 μM) + DZ [110]. Relative electrolyte leakage reflects the extent of leaf membrane damage. MeJA spray treatments alleviated the stress induced by IPU in stems and roots by 27.80% and 22.34%, respectively [105]. The activities of four critical antioxidants—SOD, CAT, POD—which play a significant role in the ROS scavenging system, are notably increased to combat the burst of ROS caused by pesticides to plant cells, whether under the stress of herbicides or fungicides. SOD has the function of reducing O_2^- and simultaneously generating H_2O_2. After being treated with ametryn (AME) and DZ in corn, SOD activity increased by 34.8% (roots) and 33.4% (seeds) [110,111], and with additional pretreatment with SA and EBL, SOD activity further increased by 21.8% and 174%. MT pretreatment not only further increased SOD activity caused by MV, but also significantly enhanced the activities of CAT, POD and APX [108].

Furthermore, the enzymes within the plant's own detoxification systems are positively regulated by these substances. GST not only plays a role in scavenging ROS during stress but also binds the metabolic products of pesticides with glutathione. Compared to treatment with IPU alone, MeJA reduced the GST activity in wheat roots by 22.7% [105]. However, the activities of *GST1*, *GST2* and *GST3* in tomatoes exposed to thiram were significantly higher than the control group on the fifth day, and with a 1 mM SA pretreatment, their activities further increased by 5 times, 50%, and 3 times, respectively [111]. These two opposing conclusions may be attributed to the differences in the pesticides used or the defense pathways activated by different hormones not being entirely overlapping. In the past few years, *GRXS25*, induced by EBR and CHT in a ROS-dependent manner, has been identified, which in turn regulates the activity of GSTs [78]. Another study by Yu et al. found that JA treatment could partially restore the inhibition of GSH by buthionine sulfoximine (BSO) [104]. These conclusions may reflect that hormone signaling can operate independently of or upstream of the plant GST signal, thereby affecting the third phase of detoxification transport. Some of the plant growth regulators may have the ability to directly bind to the promoters of detoxifying enzymes, thus directly affecting the detoxification system. In a study on the degradation of CHT in tomatoes, the *TGA2* factor could directly bind to the *GST3* promoter, which is regulated by BR [78]. Identification efforts for these transcription factors are now focused on the CYP and GST families. Unfortunately, although genes from the CYP family that specifically affect herbicide metabolism have been identified, no transcription factor has been found that can be co-regulated by different types of pesticides.

5.4. Exogenous Plant Growth Regulators Reduce Pesticide Residues and Exhibit a Close Correlation with Secondary Metabolites

Although the mechanisms of action of pesticides differ, research on commonly used pesticides reveals that their adverse impacts on plants are often similar. Plant growth regulators can block the accumulation of pesticides within plant tissues. For example, 1 mg/L of SA can inhibit the accumulation of DFZ in cucumber roots. This may be due to the SA inhibiting the absorption of DFZ through cucumber roots [13]. In the analysis of pesticide degradation products, it was found that MeJA promotes the transformation of IPU into many derivatives [105], and IMD residues on MT-pretreated cucumbers were significantly reduced over the subsequent twelve days [39]. Peculiarly, there are also researchers approaching from the perspective of other metabolites. MT slows down the increase in organic acid content caused by thiamethoxam. In mint leaves treated with insecticides, JA showed a significant negative correlation with quercetin (r = −0.85) and ferulic acid (r = −0.85) ($p < 0.05$), while SA showed a highly significant positive correlation with quercetin (r = 0.82) and caffeic acid (r = 0.83) [112]. JA can enhance a plant's defense against stress by producing more secondary metabolites, such as cuticles, proline, lignin, wax and polyphenols [113].

The reduction in pesticide accumulation and the increase in their degradation product content are related to the plant growth regulator's influence on detoxification responses during phases I–III, including cytochromes, glycosyltransferases and ATP-binding enzymes [111]. The damage caused by pesticides to plants is systemic rather than localized, and perhaps not limited to the detoxification metabolism alone. It may be more effective to combine multiple indicators to better understand the stress of pesticides (Figure 5). It also remains to be researched how pesticide stress is similar to other abiotic stresses.

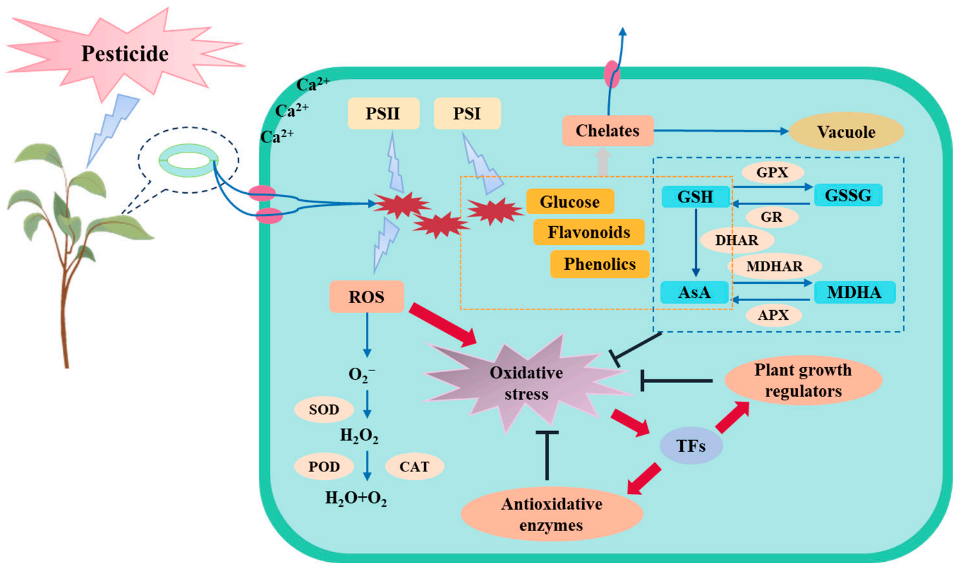

Figure 5. The overall defense of plants against pesticides [84,114,115]. The orange box represents the involvement of secondary metabolites in clearing pesticides, while the blue box represents the involvement of the GSH−AsA cycle in clearing reactive oxygen species.

6. Conclusions and Prospect

Due to the increasing demand for global food production, pesticide application should be regulated and pesticide residues should be monitored regularly in order protect environmental and human health. The applications of pesticides inevitably leaves residues on or within plants, which may enter the human body via the food chain. Pesticides that have not undergone a comprehensive risk assessment may cause severe acute or chronic effects on humans. Reducing the accumulation of pesticides, enhancing the detoxification capabilities of plants, and increasing their resistance to pesticides are important ways to address the issue of pesticide residues. To date, the use of graphene adsorption, TiO_2 photocatalytic degradation, and bacterial decomposition are all efficient methods for pesticide removal, showing promising prospects for the future. However, these measures are ultimately post-harvest, and pesticides have already caused damage during the growth of plants, which further drives researchers to explore the mechanisms of plant resistance to pesticides and to enhance means for increasing such resistance. Because of the vast array of pesticide types, research on pesticides spans multiple different disciplines, resulting in a still insufficient understanding of pesticide stress. Compared to fungicides and insecticides, the research on herbicides is the most profound, as the target of herbicides is also the plants. Several genes from the *CYPs* have been identified that enhance plant resistance to specific herbicides. These three types of pesticides have been found to disrupt the plant's redox system, enhance the detoxification system, cause disturbances in secondary metabolites, and activate hormonal defense pathways, as shown in Tables 1 and 2, among which hormonal defense has become a means employed by researchers to increase plant resistance to pesticides. The application of plant growth regulators such as SA, JA, BR and MT can mitigate the increase in antioxidant enzyme activity caused by pesticides, enhance the activity of GSTs, accelerate pesticide decomposition and reduce pesticide residues.

It is known that certain molecules in the biological world, possessing specific configurations or conformations, are chiral, meaning that they are not identical to their mirror images and cannot superimpose. A pair of enantiomers often exhibit distinct physiological activities. Consequently, some pesticides with chiral structures may have significantly different toxicities and degradation rates in the environment for their various enantiomers and racemates. In recent years, the selective effects of chiral pesticides have gained widespread attention. Studies have shown that the enantiomers of flufiprole degrade at different rates in Chinese cabbage, spinach, cucumber and tomato. This indicates that when examining the environmental toxicity of chiral pesticides, the stereoselectivity of their enantiomers should be considered [116]. The racemate of the broad-spectrum insecticide fluxametamide has been found to be more toxic to pests such as the diamondback moth [117]. The S-enantiomer of the organophosphate insecticide isofenphos methyl is significantly more toxic to target pests like the southern root-knot nematode, whereas its toxicity to non-target organisms is only twice as high as that of the R-enantiomer on average [118]. Such chiral pesticides may cause toxic effects to non-target organisms, inevitably increasing their potential ecological and health risks. Therefore, studying the stereochemical properties of chiral pesticides is of crucial importance for accurately assessing their risks.

Products extracted from plants, such as saponins and pyrethrum, are considered safer for plants and the environment as pesticides. For saponins, generally, species display the same overall pattern in terms of sensitivity. The most sensitive species are worms, fish and snail embryos, while the tested microbes and arthropods are relatively insensitive [119]. Pyrethrum extracts cause irregular swimming behavior and death in water fleas [120]. In fact, the variety of biopesticides available on the market has been increasing annually, and research on biopesticides has steadily grown over the past twenty years. However, they have sublethal effects on bees, necessitating the proper evaluation of their impact on species (pollinating insects) [121]. In developing countries, further guidance is needed for the effective use and promotion of biopesticides [122].

In modern agriculture, nanotechnology may be a promising field, and the development of new nano-insecticides is currently receiving considerable attention. A. Ipsilon larvae are more sensitive to nano forms of chlorine and sulfur than conventional forms, and their toxicity is higher than conventional forms (about 3.86 times and about 2.06 times, respectively) [123]. Without the use of photoprotectants, up to 82% of EMB (Emamectin benzoate) content in nano-EMB-SP (nano-EMB solid powder) can be protected from UV damage [124]. It can be seen that the nanomaterialization of insecticides can enhance the biological activity of traditional insecticides. There is experimental evidence that the mortality rate of aphids in plants treated with EO-NE (an innovative nano-insecticide containing 4% and 6% EO (orange essential oil) as the active ingredient) is higher than 90% after 48 h. This makes it feasible to use innovative nano-insecticides to combat aphids under practical conditions, with lower toxicity to plants [125]. Compared with traditional insecticides, nano-insecticides reduce environmental pollution, improve crop quality and safety, and are conducive to the sustainable development of the agricultural industry.

Moreover, pesticide stress is a complex process that necessitates a comprehensive study integrating various defense pathways for multi-omic analysis. How pesticides enter the plant system and through what pathways they trigger a series of plant defense responses are questions that remain to be elucidated. It needs to be noted that food safety needs to be guaranteed while maintaining crop yield and quality. This may be a solution by leveraging plant hormones to enhance plant resistance combined with new, cost-effective post-harvest treatment methods and cultivating pesticide-resistant crop varieties, or develop new composite pesticides. In that case, the damage caused by pesticides to plants would be reduced and pesticide residue levels would decline, and finally meet the purpose of healthy crop growth and safe food production.

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Abbreviations

ABA	abscisic acid
APX	ascorbic acid peroxidase
AsA	ascorbic acid
CAT	catalase
DNA	deoxyribo nucleic acid
DZ	dichlorophen
EBL	brassinolide
EC	ethyl carbamate
ET	ethylene
FAO	Food and Agriculture Organization
FE	fenpropathrin
FEN	fenvalerate
Fm	fluorescence maximum
Fv	variable fluorescence
GGT	gamma-glutamyl transpeptidase
GPX	glutathione peroxidase
GR	glutathione reductase
GRXS	glutaredoxin
Gs	stomatal conductance
GSH	glutathione
GSSG	glutathione oxidized

GST	glutathione s-transferase
GUN	genomes uncoupled
H_2O_2	hydrogen peroxide
IAA	indole acetic acid
ICS	isochromatic synthase
IMD	imidacloprid
IMI	imidacloprid
IPU	isoproturon
JA	jasmonic acid
KAT	potassium channel KAT1-like protein
kGy	kilogray
LCT	lambda-cyhalothrin
MAPK	mitogen-activated protein kinases
MBC	carbendazim
Md	malate dehydrogenase
MDA	malondialdehyde
MeJA	methyl jasmonate
MOF	magnetic nanocomposites of coated ferrites
MT	melatonin
MV	methyl viologen
NADPH	triphosphopyridine nucleotide
NF	norflurazon
NO	nitric oxide
O_2	oxygen
O_2^-	superoxide
-OH	hydroxyl radical
Os	oryza sativa
PMS	peroxymonosulfate
Pn	photosynthetic rate
POD	peroxidase
PPO	polyphenol oxidase
Pro	proline
PSII	photosystem II
ROS	reactive oxygen species
RUBP	ribulose-1,5-bisphosphate
SA	salicylic acid
SOD	superoxide dismutase
TDC	tryptophan decarboxylase
TGA	transcription factor
TOC	total organic carbon
VC	vitamin C
VE	vitamin E

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