

Review

Advances in the Agro-Environment Migration of Organic Chemical Pollutants and Their Biotransformation in Crops

Yifei Hua ^{1,†}, Yi Yuan ^{2,†}, Yi Qin ¹, Chenyi Zhang ¹, Xiaodong Wang ¹, Shengjun Feng ^{3,*} and Yichen Lu ^{1,*} ¹ College of Food Science and Light Industry, Nanjing Tech University, Nanjing 211816, China² Horticultural Research Institute, Yunnan Academy of Agricultural Sciences, Kunming 650205, China³ College of Horticulture Science, Zhejiang Agriculture and Forestry University, Hangzhou 311300, China

* Correspondence: 20170039@zafu.edu.cn (S.F.); yichenlu@njtech.edu.cn (Y.L.)

† These authors contributed equally to this work.

Abstract: Global production, consumption and emission of various chemicals continue to rise, despite growing evidence of their harmful effects on environmental quality, food safety and human health. Agronomy, a nature-dependent industry, is considered to be extremely sensitive to chemical pollution. Hence, it is of great importance for food safety and human health to study the migration and biotransformation of chemical pollutants among agricultural elements, such as soil, water and crops. Thus, this review focused on typical organic pollutants (TOPs) in the agro-environment, such as pesticides, antibiotics and persistent organic pollutants (POPs), firstly describing their sources and the current state. Then, we further elucidated the mechanism and influence factors of the TOP-based uptake, translocation and biotransformation of TOPs in crops, including the apoplastic and symplastic pathway, enzyme-assisted nontarget resistance and the physicochemical properties of different TOPs. In addition, future insight into the identification of detoxified genes and lower-toxic metabolism of TOPs was presented in this review, which provides valuable information for breeding agro-products with lower chemical contaminants. In a nutshell, our review discussed comprehensive research progress on TOPs' fates and offered theoretical guidance for pollution control and ecological risk assessment in agroecosystems.

Keywords: agrochemicals; antibiotics; environmental fate; plant metabolism; biotransportation



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1. Introduction

Agricultural products, including cereals, fruits and vegetables, are an indispensable part of daily life [1]. China is a great agricultural country that accounts for 7% of the farmland, yields 5.5% of the food resource, and feeds 20% of the population around the globe [2]. Hence, the security of agriculture in China is the top priority. However, the contradiction between the pursuit of more industrial benefits and environmental pollution is a critical threat to agricultural production. In particular, the increasing appearances of chemical contaminants, such as pesticides, antibiotics and persistent organic pollutants (POPs), have an adverse effect on crop growth. Subsequently, the residues accumulating in the edible parts of crops could be harmful to organisms in the food chain [1].

Agrochemicals are the most widely used chemicals in the world, and their consecutive input into farmland caused many environmental problems [3]. For instance, the detection profiles of Shandong province showed that the maximum residue of omethoate in wheat grain reached 2.1028 mg kg⁻¹, nearly 10 times than the maximum residue limit (MRL = 0.02 mg kg⁻¹) of national standards in China (GB/T 2763-2021), causing serious crop contamination [4]. The issue of excessive residues of pesticides in exported vegetables has frequently happened because of different standards for MRL around the globe. For example, the MRL of pesticide malathion in beans is 2 mg kg⁻¹ in China, which is stricter than in the United States of America (8 mg kg⁻¹). Furthermore, the MRLs of fungicide

thiamethoxam in mushrooms are 5 mg kg^{-1} in China, 40 mg kg^{-1} in the United States, 10 mg kg^{-1} in Europe and 60 mg kg^{-1} in Japan, respectively [5]. Thus, the most effective way to avoid the pesticide-based trade boundary is the decrease pesticide residue in agriculture products as much as possible. Except for pesticide residues, other contaminants from surrounding media could be taken up by crops and accumulated in vivo. Recently, POPs are a matter of concern due to their high toxicity and tendency to accumulate in food chains [6]. More seriously, POPs are organic chemicals that can persist in the environment for a longer period due to their nonbiodegradability [6]. In Nanjing, 16 polycyclic aromatic hydrocarbons (PAHs) belonging to the POP family were detected in nine common vegetables. In particular, the accumulation contents of benzo(a)anthracene (BaA), chrysene (CHR), benzo(b)fluoranthene (BbF) and benzo(a)pyrene (BaP) at $60.5\text{--}312 \text{ ng g}^{-1}$ significantly exceeded the MRL of 12 ng g^{-1} based on the standard (Commission Regulation (EC) number 1881/2006 amended by Commission Regulation (EU) number 835/2011) [7–9]. In addition, the residue concentrations of these PAHs in different species were ranked as leafy vegetables > fruit vegetables > root vegetables [7]. Li et al. [10] found that phenanthrene (PHE) residues ($44.3 \text{ } \mu\text{g kg}^{-1}$) were observed at the highest level in vegetables and Benzo(g, hi)perylene (Bghip) residues were at the highest level in the edible part of maize ($35.7 \text{ } \mu\text{g kg}^{-1}$) and wheat ($157.7 \text{ } \mu\text{g kg}^{-1}$), such as corn and grain, which indicated that different PAHs have their individual or unique pathways in different crop species or tissues [11]. More recently, veterinary antibiotics are intensively and widely used in animal farming as a result of their high residues in animal manure, which, as an important agricultural fertilizer, becomes a predominant reservoir of veterinary antibiotics in agroecosystems [12]. According to the profiles from Guangdong Provincial Key Laboratory of Food Quality and Safety [13], $30.5 \text{ } \mu\text{g kg}^{-1}$ of enrofloxacin, $120.0 \text{ } \mu\text{g kg}^{-1}$ of ciprofloxacin and $33.9 \text{ } \mu\text{g kg}^{-1}$ of norfloxacin were detected in bean sprouts. Moreover, the adsorption of veterinary antibiotics in crops could have a toxic effect on growth and cause oxidative stress [14–16].

The above-mentioned evidence has clarified an urgent fact that TOP residues are widespread in agriculture and food environments and have been undergoing various biotransportation and biotransformation in organisms to produce plenty of derivatives and metabolites, which pose a serious threat to human health and environmental safety [17–19]. Hence, the analysis of the migration, transformation, and degradation mechanisms of chemical contaminants from agricultural sources is critical to the risk assessment and prevention of chemical contaminants [3,20–22].

2. The Main TOPs Existing in Agroecosystems

2.1. Types of TOPs

Agro-environmental pollutants are currently categorized into agrochemicals, antibiotics and POPs (Figure 1) [23]. Agrochemicals are classified into organic and inorganic pesticides [24,25]. Organic pesticides are well-known to be used as insecticides, fungicides, herbicides, rodenticides, molluscicides and nematocides [26]. The updated additions are pyrethrins and neonicotinoids. Inorganic pesticides include copper sulfate, ferrous sulfate, copper, lime and sulfur. Since dealers misuse pesticides out of standards with backward techniques, only nearly 30% of pesticides applied can be attached to crops, and the remaining 70% losses in the surrounding area, such as soil, water or atmosphere, lead to an unexpected bioavailability [27]. Furthermore, the ongoing need for pesticides contributes to the serious environmental risk regarding pesticide residues [28]. The profiles of each class of pesticide show that herbicides dominate the biggest market (more than 26%) in China [29]. Not surprisingly, herbicide residues have become the largest source of organic pollution in the agricultural environment. According to the mode of action (MOA), herbicides are classified into two types: systemic conductive and thixotropic compounds [30,31]. Systemic conductive herbicides (SCH) could be absorbed and conducted to all plant tissues for harmful microbes, pests or weed control; however, the adsorbed and accumulated SCHs are more potential to damage nontarget plants, such as crops. Thixotropic herbicides usually

have high toxicity, and their overuse usually causes adverse effects on nontarget organisms, including crops and human beings [32]. For instance, atrazine, a broad-spectrum triazine herbicide, could be taken up by crops and distributed quickly to shoots and leaves, which leads to high accumulation in the water environment, soil, fruits and vegetables [33,34]. Its environmental residues have aroused the concern of the Food Safety Committee in many countries [35]. Paraquat is a widely used thixotropic herbicide with high hydrophilicity and poor translocation in plants, which has been demonstrated in the role of fatal toxicity in the human lung [36]. With respect to antibiotics, the loss of large amounts of antibiotics and their degradation products into the soil environment, such as through animal excreta, livestock wastes, human-derived biosolids and irrigation water, is due to insufficient absorption by humans or animals [37]. The types and abundance of antibiotics in agricultural soils vary considerably depending on the land-use management regime and soil type [38]. For example, antibiotic contamination in vegetable, paddy and upland soils varies greatly depending on the fertilization regime [39]. High residue concentrations of several antibiotics were found in agricultural soils, such as beta-lactam (5.89 mg kg^{-1}), fluoroquinolones (2.09 mg kg^{-1}), sulfonamides (6.92 mg kg^{-1}) and tetracyclines (10.00 mg kg^{-1}) [38,40]. Recently, POPs have been discovered across the globe, including regions where they have never been used. The 1998 Aarhus protocol on persistent organic pollutants (POPs) listed 16 different substances, including 11 pesticides, 2 industrial chemicals and 3 by-products (Figure 1) [41–43].

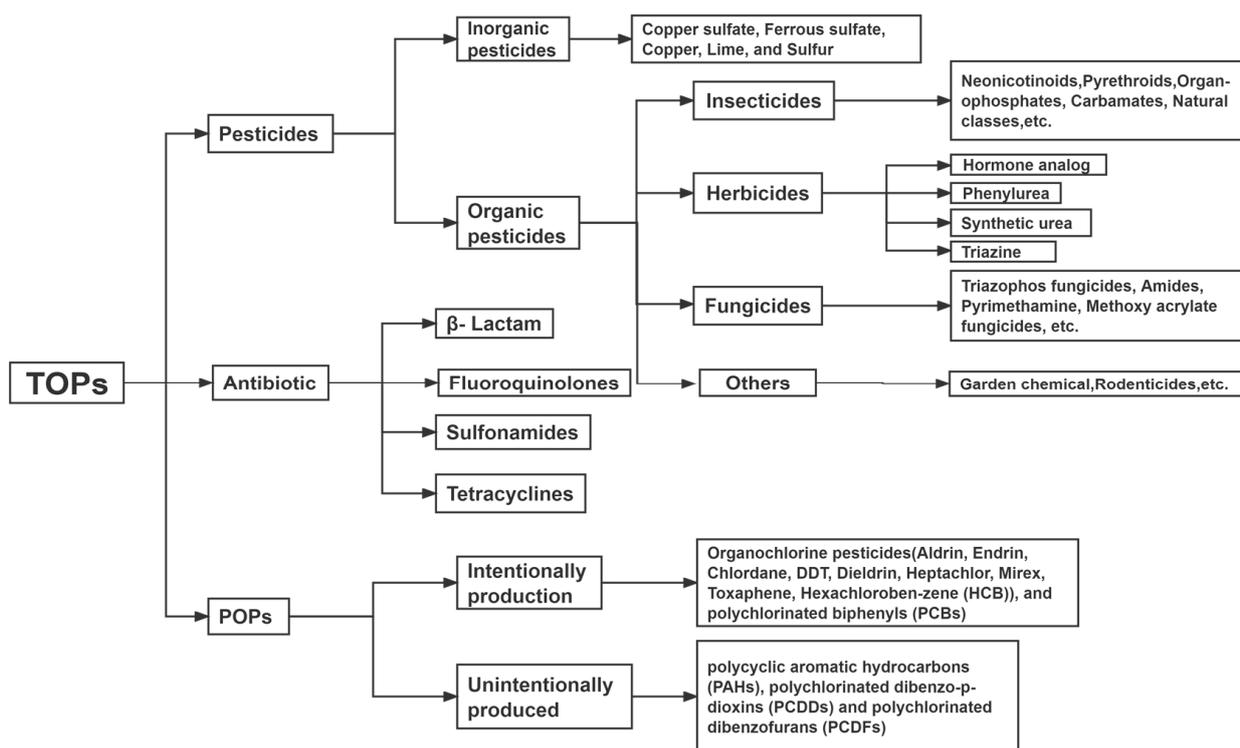


Figure 1. The classification of typical organic pollutants in the agricultural environment.

2.2. Environmental Sources

The TOPs in the agro-environment are mainly from illegal abuse and factory emissions (Figure 2). Chemical pesticides can ensure the efficiency of modern agriculture. According to the Food and Agricultural Organization of the United Nations (FAO), the global consumption of agrochemicals in 2019 was 4.2 million tons, of which herbicides account for the major share. However, there are differences in the proportion of applications of different agrochemicals across countries, because of their characterization of the cropping pattern, climate, and technology diffusion. For example, herbicides are the major group

of agrochemicals consumed in the United States of America, whereas insecticides are the major group in countries such as India, which lead to a difference in major residues in the agro-environment of different regions. Unfortunately, it is known that 3 billion kilograms of pesticides are used annually worldwide, while only 1% are effectively used to control pests and weed damage in target crops [24]. Furthermore, especially in developing economies, unscientific practices in the selection and use of agrochemicals are common (Figure 2) [44,45]. Moreover, the end users mainly rely on guidance from pesticide retailers who are not aware of the suitable dose and desire to increase the volume of pesticide sales. These law-violated actions promote stress and risks to the soil environment [46].

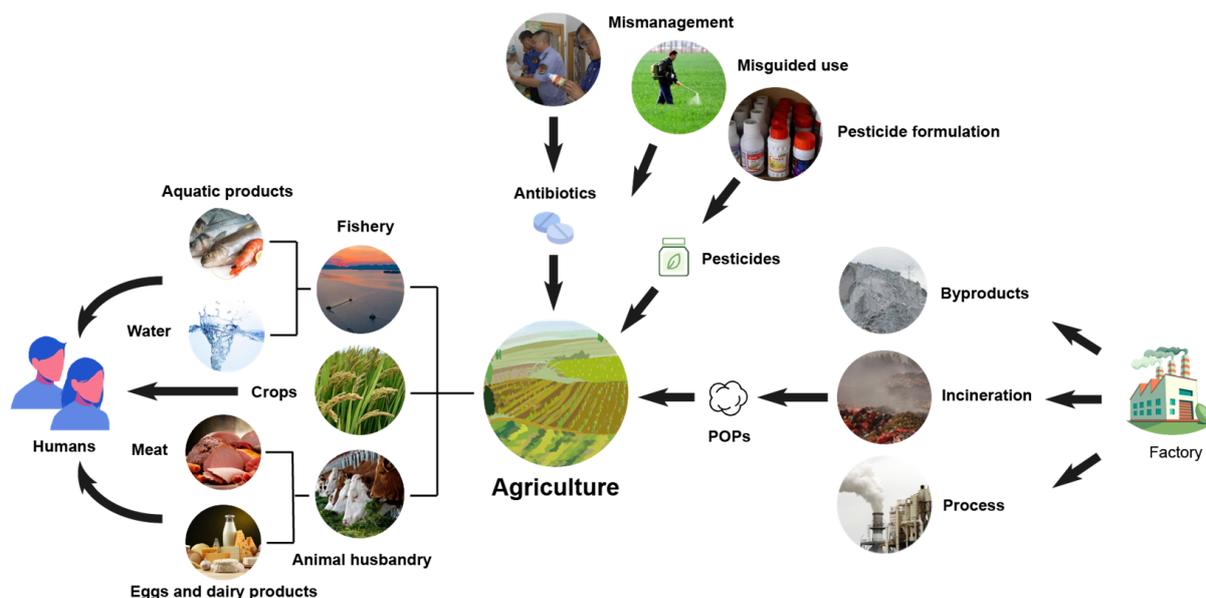


Figure 2. The sources and spread of typical organic pollutants in the agricultural environment.

Like pesticides, the large consumption of antibiotics around the globe was estimated to be 225,000 tons in 2020 [47]. Antibiotics are largely associated with anthropogenic activities (e.g., municipal sewage discharge, livestock farming, aquaculture) and inevitably enter the environment after use and excretion (Figure 2). The release of untreated wastewater or the constant input also increases the environmental residue and subsequently exerts ecotoxic effects on aquatic organisms [48]. China is the largest producer and user of antibiotics in the world, with its annual usage accounting for approximately 45% of global consumption, 30–90% of which (about 162,000 tons per year) cannot be metabolized and then enters the soil and water environment [49,50].

POPs are present in the ecosystem for a longer period and can move through the environment over long distances when released from various sources. The major sources of POPs are attributed to anthropogenic activities, such as effluent disposal, agricultural runoff, drainage leakages, urban runoff, landfilling leachate mixing and huge atmospheric deposition (Figure 2). Usage of household insecticides, vector control agents and pest management devices are a few of the various sources of POP contamination, such as chlorine-containing pesticides. The residual % of most organic insecticides present in water sources or land sediments is diagnosed to be much higher in particle concentration in agriculture-based sectors compared to other regions that do not initiate farming activities [51]. Moreover, industrial production, such as metal smelting and waste incineration, is also owing to POP emissions [6]. Such categories of POPs can enter into atmospheric air and extend their availability all around the universe, even in the Arctic/ Antarctic continent. Due to their long distance to the atmospheric region of boundary deposition/migration and persistence in the natural environment, the risks of POPs have been highly noticed by the public [51].

2.3. Hazards of Organic Chemical Pollutants on the Agricultural Environment

Global consumption and production of TOPs continue to rise, leading to growing adverse effects on environmental quality and human health. However, the toxicity and severity of the detrimental impacts vary by type of chemical compound [52]. The specific hazards caused by the presence of TOPs in different environments are depicted in Table 1. Concerning pesticide pollution, significant environmental incidents were reported in more than 20% of countries in a global survey on pesticide management in agriculture. Herbicides such as trifluralin and triazines, as well as nicotine insecticides, are said to be detrimental to biodiversity in soil and water, particularly to soil organisms and soil enzyme activity. Recent studies demonstrated that most copper-based fungicides and several herbicides, such as triazines, alachlor, atrazine, paraquat and glyphosate, could significantly alter the symbiotic association of soil microbes with plants, impacting their nutrient-fixing and solubilizing abilities [53]. More seriously, environmental toxicology experiments have shown that some agrochemicals exhibit strong inhibitory effects on the growth of nontarget plants and affect the survival of other animals [48]. Herbicides such as atrazine and isoproturon were found to be accumulated in crops and inhibit seed germination and elongation of the coleoptile [54–56]. Residual triazole fungicides in the aquatic environment are highly toxic to both vertebrates and invertebrates [57]. Popular neonicotinoid pesticides not only pollute the water environment but also prevent bees from pollinating [58]. Epidemiological data show that there are approximately 3 million cases of acute poisoning caused by organophosphorus pesticides (OCPs) in the world each year.

Antibiotics used in this agriculture have been associated with a high frequency of resistant bacteria in the soil and livestock tissues such as the gut flora of chickens, swine and other food-producing animals (Table 1). Without appropriate regulation, a huge diverse reservoir of resistant bacteria and resistance genes could facilitate the emergence and spread of resistant pathogens to humans, and even the ongoing transmission of such resistant organisms within the human population. Thus, the use of antibiotics in agriculture is routinely described as a major contributor to the clinical problem of resistant disease in human medicine [59]. In addition, the residue of antibiotics in the farmland has toxic effects on crop growth and development. Tomato was demonstrated to be ultrasensitive to doxycycline [60]. Sulfadimethoxine affects negatively photosynthesis in plants and ofloxacin decreases the protein of plants [61]. Clarithromycin and sulfadiazine can be absorbed by vegetables and remain in the tissue for a long time and can be directly taken in by humans and cause potential risks [62].

The persisting nature of POPs enables them to persist in the biota over a longer duration of time, hence symbolizing a longer-duration exposure hazard and enhancing the risk effect. POPs, such as dichlorodiphenyltrichloroethane (DDT) and poly-fluoro chloro compounds (PFCs), are found not only in living organisms such as animals and plants but also in humans, causing endocrine disruption, cardiovascular disease, obesity and diabetes via the alteration of endocrine functions and reproductive systems in humans and wildlife [51]. More recently, some POPs have also been implicated in reduced immunity in infants and children, and the concomitant increase in infection, as well as developmental abnormalities, neurobehavioral impairment and cancer and tumor induction or promotion. For instance, based on the pieces of evidence that polychlorinated biphenyls (PCBs) can formulate oxygen reactive molecules, lipid peroxidation, alkylating and oxidative DNA components, PCBs are categorized as carcinogenic by the International Cancer Research Agency (IARC) for human beings. Crops, as the first link in human food, are susceptible to the residues of soil POPs, which are carriers of POPs into the human body via the consumption of contaminated rice or meat from livestock raised on contaminated straw (Figure 2) [63]. It was found that high levels of POPs accumulated in edible parts of Cucurbitaceae such as squash, zucchini and cucumber [64]. Edible meat and meat products from China [65], the United States of America [66], Russia [67], Britain [68] and Germany [69] are contaminated by polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs), polycyclic aromatic hydrocarbons (PAHs) and OCPs.

Table 1. Environmental hazards are caused by typical organic chemical pollutants.

TOPs	Sources	Environmental Hazards	Reference
Pesticide	<ul style="list-style-type: none"> Direct use, misuse and abuse in agriculture, animal husbandry and fisheries, etc. 	<ul style="list-style-type: none"> Water and soil contamination Poisoning of terrestrial vegetation and aquatic plants Nontarget organisms taking various degrees of damage 	[57,70–78]
Antibiotic	<ul style="list-style-type: none"> Misuse and abuse in agriculture and aquaculture Urban, medical and industrial waste pollution, etc. 	<ul style="list-style-type: none"> Soil flora dysbiosis Drinking water contamination Poisoning of mammals and aquatic animals and health risks to humans and livestock 	[79–84]
POPs	<ul style="list-style-type: none"> Contaminated water Contaminated animal products, such as milk and meat Forest and grassland fires, volcanic eruptions Combustion processes such as automobile exhaust and industrial production, etc. 	<ul style="list-style-type: none"> Persisting in the environment and polluting the water environment Cause of animal deaths and human diseases Contaminated soil that prevents the growth of crop vegetation 	[85–93]

3. Transport Behavior of Organic Chemical Pollutants in the Agricultural Environment

Different TOPs, due to their different sources and application methods, will inevitably lead to differences in their transport behavior and influencing factors in agroecosystems. In this review, the environmental-to-crop transport behavior of different organic pollutants and their influencing factors are presented according to their sources and application scenarios (Figure 3A). In general, the dissipation or migration of TOPs is affected by processes such as photolysis, volatilization, plant uptake and runoff/leaching as a result of prevailing soil and environmental conditions.

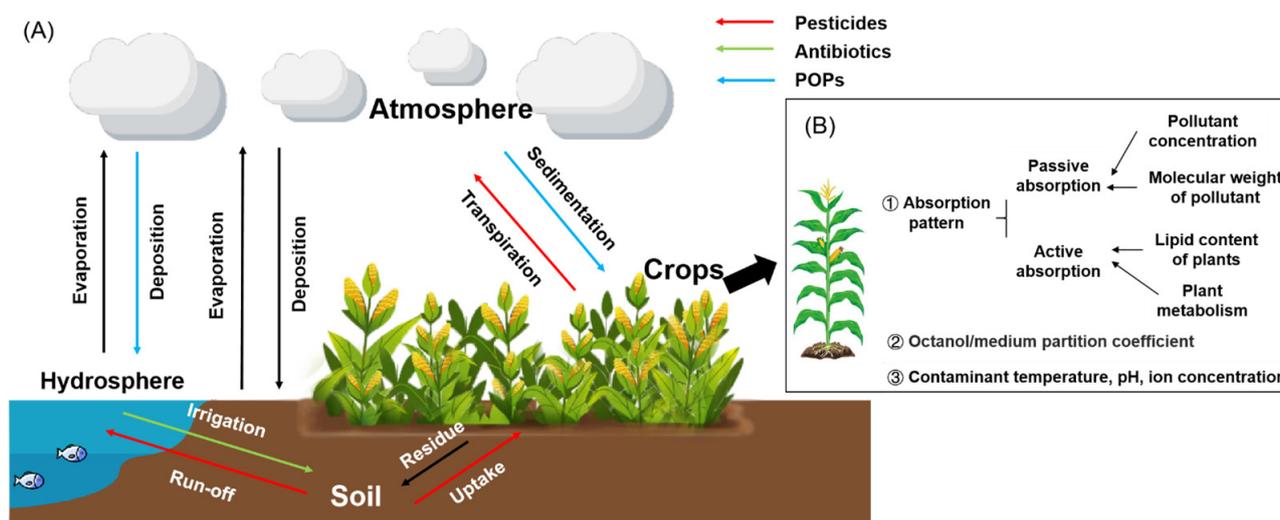


Figure 3. Transport behavior of organic chemical pollutants in the environment. (A) Transport of organic pollutants in the atmospheric, aqueous and agricultural environments; (B) factors influencing the migration of organic chemical contaminants in crops.

For agrochemicals, the predominant application habits are foliar spraying and soil mixing. Except for the part absorbed by plants, a majority of pesticides remain in the pedosphere. Hence, agrochemical dissipation in soils is critical to understanding their potential movement offsite. It has long been recognized that a pesticide that will sorb to soils is governed by plenty of complex interactions relating to the chemical properties and the composition of the soil, including particle size, cation-exchange capacity, soil organic carbon (composition and concentration), clay mineralogy, temperature and moisture content [94].

The faster dissipation rates are usually in soil environments with higher temperature, moisture and organic carbon contents, possibly due to stronger microbial activity in such soils [95,96]. Moreover, biopores (negative relationship with soil particle size) can lead to preferential flow and facilitate the leaching of pesticides into groundwater, which is an important loss pathway of relatively polar pesticides such as diuron, metribuzin, simazine, atrazine, tebuthiuron and hexazinone [97]. The current study reported that the levels of pesticides in soil pore water and plant uptake are in positive correlation with the uptake of plants. The pH of soil pore water affects the dissociation of pesticides, especially ionizable pesticides, and subsequently alters their accumulation in plants [64].

The slow degradation of antibiotics in organisms and the constant input of untreated sewage wastewater and animal manure fertilization into aquatic environments result in persistent behavior and subject organisms to long-term exposure [98–100]. Sediments, serving as habitats for plants and animals, are the natural repositories for various chemical residues in the waters. Meanwhile, they can act as a source to release the sorbed contaminants into the water when their hydraulic conditions and aquatic physicochemical properties such as pH, organic carbon, and metal ions are changed [101]. The released antibiotics from water are absorbed by crop plants through irrigation. A recent report found that the concentration of antibiotics in farm water is 1–6 mg L⁻¹, which is much higher than that in the aquatic environment [102]. In sediments, important factors controlling antibiotics' behavior might include logK_{OW}. Chen et al. reported that the distribution coefficient (K_d) is an important factor controlling antibiotics' behavior instead of K_{OW}. Ternes et al. found that antibiotics with log K_d of 2.7 or lower, such as fluoroquinolones, were demonstrated to have a low sorption potential on the solid phase [103]. In soil environments, the ionic strength of antibiotic contaminations affects their migration ability. Generally speaking, weakly acidic, weakly alkaline and lipophilic classes of antibiotics showed an easy binding with the soil particles and are tougher to transport to other environments.

Unlike agrochemicals and antibiotics, and besides in water, sediments and soils, more evaporative POPs can exist in the atmosphere for more than weeks before reaching land and plant surfaces. The possible reason for the long-distance migration of POPs is the reduction in component volatility at mild temperatures, but pollutants that volatilize at high-temperature latitudes are transported by winds to icy polar regions where they concentrate and condensate [104]. Some POPs such as PAHs that landed on foliage slowly diffused into the tissues of leaves and were immobilized by lipid-like substances in the leaf cuticle. Higher lipid content in leaves leads to higher uptake of PAHs, which causes toxic accumulation of POPs in plants [105,106]. Interestingly, a novel global transportation mechanism of PFCs was elucidated. Specifically, owing to the lower vapor pressure of their ions, polyfluorinated POPs can be moderately abundant in water or bound to particulates or sediments and might be transferred via oceanic currents or sea spray [51].

4. Transport and Transformation of Organic Chemical Pollutants in Crops

A large amount of evidence that the existence of TOPs in agricultural circles can be transferred into crop tissues towards uptake indicates that a key point in protecting food chain safety is the elimination of risks in crops [107–109]. Metabolic tolerance as an important strategy of nontarget resistance in higher plants is potentially important for resisting TOPs stresses. In general, the metabolism of xenobiotics *in vivo* is classified as two processes, namely transportation and biotransformation.

4.1. Biotransportation Processes in Soil–Plant

The transferred pathway of TOPs from the surroundings to crops is illustrated in Figure 3B. The modes of TOPs in plant cells from environments have two types: passive and active absorption models, respectively [110]. Plants' adsorptive types of xenobiotics are largely dependent on their physicochemical properties, such as molecular weight, concentration, solubility, etc. The molecular weight of pollutants is an important influence factor for determining the adsorption model. Xenobiotics with molecular weights less than

500 Da are readily absorbed by crop roots and leaves through passive diffusion, whereas those with molecular weights more than 500 Da usually require ATPs to facilitate active uptake by root [3]. Thus, most pesticides (<300 Da) enter plants by passive transport, while some large molecules such as POPs or endocrine disruptors (EDCs) (e.g., phenoxyacid herbicides) rely on active transport [111,112]. Furthermore, chemical solubility, which is calculated by the octanol/media partition coefficient, plays an essential role in the uptake of TOPs from the environment to crops (Figure 3B) [113–116]. The octanol/medium partition coefficient is defined as the ratio of the concentration of organic chemicals between the n-octanol and medium phases. The values of the octanol–water partition coefficient (K_{OW}) and octanol–air partition coefficient (K_{OA}), which are usually expressed in logarithmic form, are commonly used to characterize the lipophilicity or hydrophilicity of chemical contaminants and study the distribution or absorption of TOPs in various mediums. When the log K_{OW} values of organic chemical contaminants are in the range of -1 to 5 , they easily enter the plant roots by passive adsorption [117]. For instance, quinolone antibiotics metformin (log $K_{OW} = 3.3$), ciprofloxacin (log $K_{OW} = 1.5$) and narasin (log $K_{OW} = 5.9$) were easily absorbed by roots of carrots and barley [115]. However, tetracycline antibiotics (log $K_{OW} = -1.37$) entered alfalfa via active transportation [113].

Similarly to antibiotics, most of the POPs with log $K_{OW} < 4$ are more likely to accumulate via roots and then translocate to other plant tissues, whilst highly hydrophobic PAHs with log $K_{OW} > 4$ may strongly adsorb on the root epidermis and are unlikely to be penetrated the inner roots and translocated within the plant [118]. In addition, POPs were found to be transported for long distances through atmospheric circulation, due to their high log K_{OA} value (>8). These POPs with high log K_{OA} values usually exist in the gas phase, are easily captured by plant leaves and have the potential to biomagnify in food chains [119,120]. In addition, the temperature, pH and ionic strength of the pollutants have an impact on their transition behavior from the environment to crop (Figure 3B). Especially in the aquatic environment, the migration rates of chlortetracycline, hygromycin and tetracycline increased with increasing temperature [121]. Chen et al. [122] found that the migration rate of sulfamethoxazole in groundwater (pH = 5.6) was higher than that of ciprofloxacin because sulfamethoxazole presents a non-ionic form in a weakly acidic solution.

After entering into crop roots, the distribution of TOPs in plant tissues is dependent on two main driving forces, including the transpiration stream and water migration (Figure 4A). The transpiration stream, as an important internal driver of plant transport, is characterized by the transpiration stream concentration factor (TSCF), which is the ratio of the concentration of chemicals in the transpiration stream to the concentration in the external solution [123]. It is an important indicator to determine the upward transfer capability of TOPs. By contrast, the absorbed TOPs could rely on water migration to directly run back from the above-ground part to root or fruit tissues via bidirectional translocation (so-called assimilate transportation; Figure 4A) [123,124]. The flow of assimilates is accomplished by active transport and is one of the characteristics of higher plants [125]. Some pesticides can be excreted by root via assimilating transportation. For example, the foliar application of alachlor can enhance its content in the nutrition solution, because the flow of assimilates moves the contaminants from phloem to root for excretion.

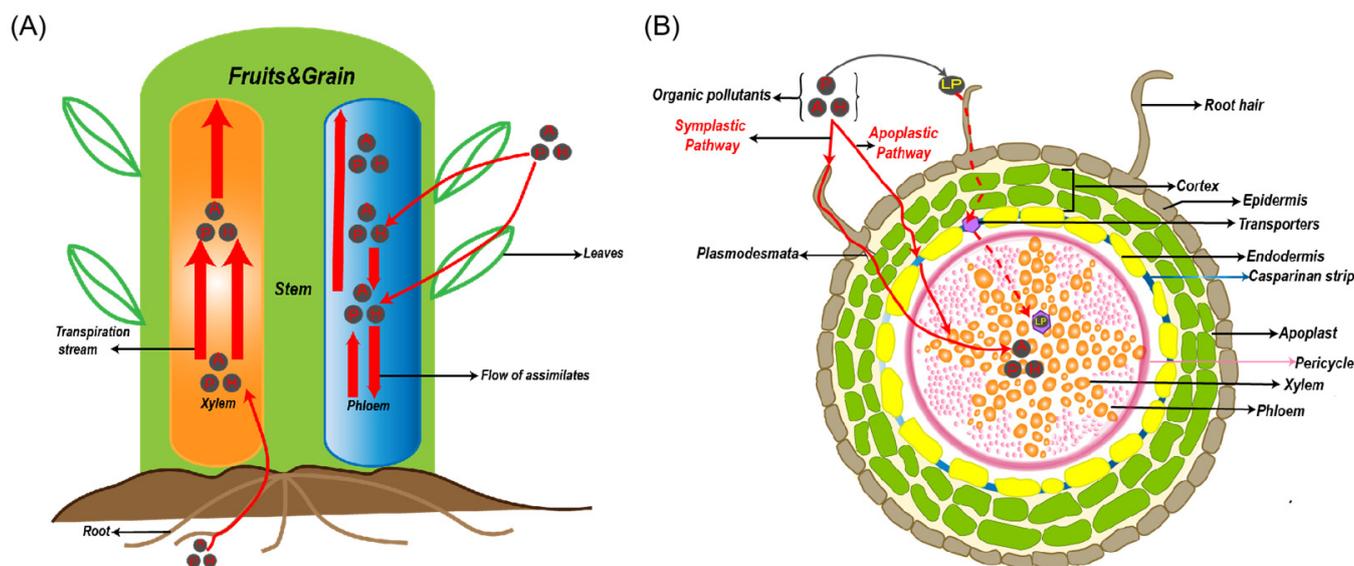


Figure 4. Transport of organic chemical pollutants. (A) Pathways of organic pollutant translocation in vascular tissues of crops; (B) root transport of organic pollutants in crops (abbreviations: H, herbicide; LP, lipophilic pesticides; A, antibiotics; P, POPs).

In the distribution process, TOPs have to penetrate biofilms of various cells or tissues, such as the epidermis, cortex, endodermis, etc. [117]. The penetration of organic chemical contaminants in the root system can take place through both the apoplastic pathway and the symplastic pathway. Which distribution pathway chosen by TOPs in plant tissues is determined by molecular weight, lipophilicity or hydrophilicity, dissociation constant pK_a , and pH (Figure 4B). For example, 1,3-dinitrobenzene ($S_W = 533 \text{ mg L}^{-1}$; $\log K_{OW} = 1.49$) and 2,4-dinitrobenzene ($S_W = 300 \text{ mg L}^{-1}$; $\log K_{OW} = 1.98$), which have relatively high water solubility, are mainly transported in plants via the symplastic pathway, whereas phenanthrene ($S_W = 1.29 \text{ mg L}^{-1}$; $\log K_{OW} = 4.46$) and pyrene ($S_W = 7.87 \text{ mg L}^{-1}$; $\log K_{OW} = 3.72$) are transported via the apoplastic pathway [126]. Notably, some of the highly lipophilic pesticides enter the root cortex by the apoplastic or symplastic route, but they are also blocked from further transport in the Casparian strip. Therefore, transporter proteins are needed as carriers to aid in the transport of these pesticides [3,124,127]. The Arabidopsis PDR1 protein is a paraquat transporter protein that promotes paraquat accumulation in plants [128]. Because of the species specificity of transporter proteins, differences in crop species also significantly affect the distribution of contaminants in the crop. For instance, sulfamethoxazole and norfloxacin have a higher translocation capacity in radishes than in cabbage when exposed to the same dose [129]. These chemical parameters are usually associated with bioconcentration factors (BCFs, a ratio of TOC content in plant tissues and environments), including the root concentration factor (RCF), stem concentration factor (SCF), leaf concentration factor (LCF) and translocation factor (TF, a ratio of TOP content in one tissue and the other tissue), which are used to calculate the transfer capability of pesticides from roots to stems or stems to leaves. Of note, a significant positive correlation between the root enrichment factor ($\log RCF$) and $\log K_{OW}$ of TOPs was found in recent studies [130,131]. Wang et al. simultaneously applied imidacloprid, acetamiprid, tricyclazole, azoxystrobin, tebuconazole and difenoconazole in maize and found that pesticides with higher $\log K_{OW}$ and lower S_W are more easily accumulated in roots, while pesticides with lower $\log K_{OW}$ and higher S_W are more liable to be translocated from roots to shoots [132]. This indicates that pesticide accumulation is positively correlated with $\log K_{OW}$ value and negatively with water solubility (S_W). In general, chemicals with $\log K_{OW}$ at the range of 1 to 3 are easily translocated from roots to the phloem [133]. For ionic organic pollutants, their transport distribution in plant tissues depends on the acid ionization constant (pK_a), which has been identified as a fundamental parameter for predicting the uptake, bioaccumulation,

metabolism and elimination in animals; absorption and translocation in plants; and sorption to—and consequently, mobility in—soil. The dissociation constant (pK_a) is associated with the lipophilicity, solubility, protein binding and permeability of organic contaminants, which directly affect the absorption, distribution, metabolism and excretion processes of TOPs [134]. It was found that acid pollutants with $pK_a < 7$ and $\log K_{OW} < 3$ are more easily translocated through the xylem to the fruit; alkaline contaminants with $pK_a > 7$ and $\log K_{OW} < 0$ can be transported simultaneously in the vascular tissue parts [135]. For example, thiamethoxam and its metabolite clothianidin ($\log K_{OW} = -0.13-0.905$, $pK_a = 9.0-11.1$) have lower $\log K_{OW}$ and higher pK_a values than difenoconazole ($\log K_{OW} = 4.4$, $pK_a = 1.07$), resulting in them being less likely to dissociate. Consequently, thiamethoxam and its metabolite clothianidin are more likely to penetrate biofilms and undergo translocation and accumulation in rice than difenoconazole [136].

4.2. Biotransformation Process in Plant

Biotransformation, also known as metabolism, is an important mechanism by which organisms metabolize and detoxify organic chemical pollutants. Since plants do not have specific excretory organs, biotransformation becomes an important way for plants to defend themselves against xenobiotics. Recent studies have found that metabolic detoxification is the most important mechanism of nontarget resistance in plants, and its process is complex and requires the involvement of specific enzymes [112]. In general, the metabolic detoxification mechanism of TOPs is divided into three main phases in crops (Figure 5) [137]: phase I metabolism—the formation of hydrophilic functional groups through redox or hydrolysis reactions; phase II metabolism—these functional groups undergo secondary enzymatic reactions to affix endogenous molecules such as sugars, amino acids, and glutathione; and phase III metabolism—transporters recognize metabolic conjugates and transport them into the vesicle or fix them in the cell wall [138].

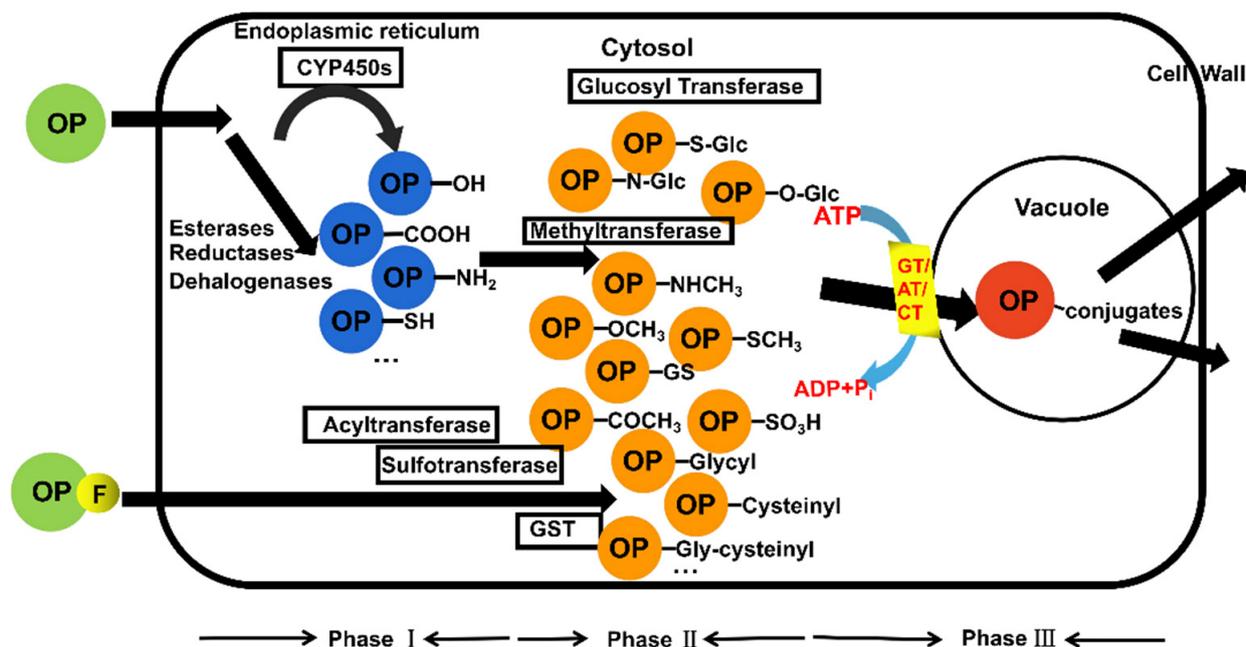


Figure 5. Schematic diagram of organic pollutant transformation in crop cells. (Abbreviations: OP, organic pollutants; F, functional group; CT, glutathione-conjugate transporter; AT, ATP-dependent transporter; GT, ATP-dependent glucoside-conjugate transporter).

The most important part of phase I metabolism is the oxidation reaction [139], which generally occurs in the endoplasmic reticulum, and the main catalyzed enzymes include cytochrome P450 monooxygenase (CYP450), peroxidase, phenoloxidase and laccase (Figure 5).

In the action of phase I metabolizing enzymes, organic pollutants undergo hydroxylation, dealkylation, epoxidation, desulfurization and ester hydrolysis to produce more hydrophilic oxidative metabolites, which play a functional role in introducing active reaction sites for subsequent phase II reactions [140]. Xiang et al. discovered that a wheat P450 gene *CYP71C6V1*, which encodes a 5-phenylcyclic hydroxylase, could metabolize chlorsulfuron and triasulfuron to form 5-hydroxy-chlorsulfuron and 5-hydroxy-trisulfuron, respectively [141]. Chu et al. also demonstrated that CYP450s catalyzes the hydroxylation of PCBs in reeds and rice [142]. The hydroxylation reaction is an important intermediate reaction step in the biodegradation of TOPs, as the products are more hydrophilic than the precursors and can easily undergo subsequent metabolic reactions. Dealkylation is also an important reaction process of phase I metabolism. It is generally believed that the first step of this reaction is also the hydroxylation of alkyl groups. Studies have shown that pesticides with different chemical structures, such as diquat, simazine and chlordane, can undergo dealkylation reactions to reduce the toxicity of pesticides to crops [143]. However, some of the phase I metabolic reactions can also lead to increased toxicity of the products, such as epoxidation. It has been reported that human CYP1A1 metabolizes benzo[a]pyrene to form epoxidized benzo[a]pyrene, which further binds to DNA and causes base mutations [144].

Most phase II conjugation reactions are based on phase I-based metabolism (Figure 5). Phase II metabolism catalyzes the reaction of hydrophilic groups introduced by phase I metabolism, such as hydroxyl, amino, carboxy or thiol groups, with endogenous molecules to form conjugates. Obviously, if the organic chemical pollutant itself has reactive functional groups, the phase II reaction can also occur directly. The main enzymes in this process comprise of methyltransferases, glycosyltransferases, acetyl-transferases, glutathione-S-transferases (GST), etc. Methylation plays an important role in the process of crop detoxification. The reaction occurs through the binding of functional groups of phase I metabolites, such as amino, phenol groups and thiol groups, by methyltransferases, resulting in $-NHCH_3$ and $-OCH_3$ and $-SCH_3$ groups [145]. Liscombe et al. found that the C-methylation of ethyl groups on atrazine in alfalfa and other plants was characterized accordingly [146]. Rezek et al. also found that there are specialized methyltransferases for the induction of hydroxylated-PCB methylation, and the hydroxylated PCBs enter the hydroxyl-substituted aromatic ring as alternative substrates for subsequent methylation of the biosynthesis pathway [147]. By contrast, the demethylation reaction of clarithromycin in lettuce generates metabolites that are more toxic than the parent. Interestingly, glycosylated metabolites of clarithromycin manifest less toxicity [62]. Recently, various glycosylation reactions have been found in plants and animals, which are catalyzed by glycosyltransferases (UGTs). UGTs catalyze the replacement of deprotonated nucleophilic sites in xenobiotics (acceptors) by UDP-glucose moiety and form β -glycosidic bond products. According to the nucleophilic sites (hydroxyl, carboxyl and thiol groups) binding with the C1 carbon of UDP-glucose, glucosylated reactions are divided into *O*-, *N*- and *S*-glucosylation, respectively. Current experiments have demonstrated that *O*-glucosylation is the most predominant metabolic mode of TOP detoxification [148]. The *O*-glucosylation products of sulfadimethoxine and sulfamethoxazole were found to be most abundant in crop tissues, accounting for 80–90% of the total metabolites [149]. Furthermore, hydroxylated TOPs are more susceptible to glycosylation reactions in plants. For instance, many glycosylated PCB adducts were yielded by the addition of glucose moiety to monohydroxylated PCBs in carrots [150]. Moreover, several *S*-glucosinolates and *N*-glucosinolates were identified in chemicals in the amino group or thiol group, such as isoproturon and atrazine [151,152]. Acetylation is usually a subsequent detoxification reaction after glycosylation in xenobiotics metabolism. Malonyltransferase as a catalyst helps glycosylated TOPs react with malonyl-CoA to form malonylglucoside [153]. The ionic malonylglucoside in plant cytoplasm (pH = 7.0–7.5) benefits from being transported into vacuoles by anionic transporters, which facilitates the decay of toxic compounds and lower cell toxicity [154].

In higher plants, the methylene or heteroatom (e.g., halogenated elements) of TOPs can be replaced by the thiol of glutathione (GSH) and cysteine (Cys) via an S_N2 nucleophilic

substitution reaction [155]. The interaction between xenobiotic molecules and glutathione is specifically catalyzed by the subfamily of glutathione *S*-transferase (GSTs; E.C. 2.5.1.18). GSH, as an important acceptor of *S*-thiols, is usually composed of glutamic acid, cysteine and glycine. However, two GSH derivatives—homoglutathione (γ -glutamyl-cysteine-glycine; hGSH) and hydroxymethylglutathione (γ -glutamyl-cysteine-serine; hmGSH)—are found in alfalfa and rice, respectively [156]. Several herbicides, such as atrazine and acetochlor, are found to form the conjugation of hGSH and hmGSH in rice [157]. In addition, xenobiotic compounds containing a C=C bond can react with GSH via the Michael reaction [158]. Carbamazepine (CBZ) can be metabolized to cysteinyl CBZ (an amino acid conjugation) via a double-bond addition reaction with cysteine in the root tissues of *Phragmites australis* [131]. Micheal et al. found that the chlortetracycline–glutathione conjugate by the catalysis of GST was found in maize rather than in pinto beans, leading to less phytotoxicity in maize, which indicates that chlortetracycline is detoxified via the induction of GST in maize crops [159]. It is noted that the GSH conjugates can be carried by GSH transporters and are transmitted into the cytosol as a result of detoxification in the cytoplasm [138]. Condensation is another type of amino acid conjugation reaction and plays a detoxified role in xenobiotics. Xenobiotics containing a carboxylic acid group (-COOH) attend to ligands and acyl-CoA by coenzyme A (CoASH) to yield a xenobiotic-CoA thioester intermediate, and then, the acyl group transfers to the amino group of glycine by the catalysis of acyl-CoA: glycine *N*-acyltransferases (E.C. 2.3.1.13) [160]. To date, few studies about TOP condensation in crop plants have been investigated, and its mechanism needs to be further explored.

Phase II metabolic conjugates are usually more hydrophilic than the parent compounds. They can be recognized by the transporter and are excreted out of the cell via the transporter in the phase III process, which is considered another vital detoxification metabolism to eliminate toxic compounds (Figure 5). Phase II metabolic conjugates are usually more hydrophilic than the parent compounds. They can be recognized by the transporter and transported into the large central vacuole or released into the apoplast, which is considered another vital detoxification metabolism to eliminate toxic compounds (Figure 5). Many observations have demonstrated that glutathionated xenobiotic transport is strictly ATP-dependent and is thus likely mediated by ABC-type transporters. The ATP-binding cassette transporters (ABC), a large family of transmembrane proteins, are widely present in organisms and are responsible for transporting xenobiotics. The structure of ABC transporters is highly conserved around most eukaryotic organisms, including plants. A functional ABC transporter is characterized by the presence of a P-type traffic ATPase, which comprises two cytosolic nucleotide-binding domains (NBDs) and two transmembrane domains (TMDs) [161]. In Arabidopsis, based on their domain structure and phylogenetic relationships, the ABC proteins are categorized into eight subfamilies AtABCA–AtABCI, of which ABCA, ABCB, ABCC, ABCD and ABCG have been reported to be associated with resistance to insecticides [162,163]. The specific ABCA and ABCC genes were found to enhance resistance to pyrethroids in *Tribulus Terrestris*. Furthermore, a half-size member of the AtABCG family, AtABCG19, can remove kanamycin from the cytosol and store it in the vacuole, which confers kanamycin resistance under its genetic over-expression in plants [164]. Co-expression of OsSTAR1 and OsSTAR2 in oocytes revealed that their function is a role in the transport of UDP-glucose or its derivatives, including glycosylated xenobiotics [165]. Moreover, DDT enters plants, experiences hydroxylation and glycosylation, and is moved into the vacuole for storage by the ABC transporter [123]. Thus, ABC transporter-based phase III metabolism supplies an alternative strategy for plants to cope with toxic TOPs via excretion from the cell.

5. Perspectives

Over-emissions of artificial compounds into agro-environments cause adverse effects on both agricultural product quality and human health. Hence, the elimination of TOPs from the sources of the food chain is mandatory to reduce their adverse effects on humans,

plants and animals. Phytoremediation or phytodegradation is an effective and eco-friendly method for TOP reduction because it can metabolize organic pollutants into nontoxic or relatively less toxic forms and interrupt the spread of hazards towards the food chain. Recently, a variety of genes encoding detoxifying enzymes or proteins were demonstrated to remove and catabolize TOPs in vivo and in vitro by genetic engineering technologies. For instance, overexpression of two glycosyltransferase genes (ARGT1E and LOC_Os04g40520) could effectively degrade the accumulation of atrazine in the grain of rice and improve rice growth in atrazine-contaminated soil [166]. Moreover, transgenic expression of soybean gene *CYP71A10* in tobacco significantly improved the tolerance of linuron and chlorotoluron [167]. The present advancement in the discovery of valuable genes or enzymes stimulates the breeding of TOP-resistant crops through transgenic technology. Recently, a human P450 gene, *CYP2C9*, was reconstructed into the rice genome, and the obtained transgenic rice showed a rapid degradation for sulfonylurea herbicides [168]. However, the developmental speed of TOP-resistant crops is still slow because enzymes and proteins involved in the detoxification and degradation of TOPs are still rarely discovered in crop plants. It is urgent to continuously explore unknown resistance genes and use them to breed resistant crops. To date, some TOP-resistant rice species, such as glyphosate and glufosinate-resistant species, are mainly obtained through transgenic technology. Given that the safety of genetically modified rice is still controversial in the world, restricting the commercial application of transgenic TOP-resistant rice will last for a long time. Fortunately, CRISPR/Cas9 technology and various gene-editing systems provide an effective way to modify rice endogenous genes and develop new herbicide-resistant rice [169]. Gene-edited transgenic plants can be self-crossed or crossed with nontransgenic plants to separate the CRISPR/Cas9 transgene from the target mutation and obtain progeny without the transgene, which in nature is the same as natural mutants and mutants produced by artificial mutagenesis.

In the near future, the issue of organic chemical pollution in agricultural environments will continue for a long time and has been developing from single pollution to complex pollution. Future research needs to focus on the transport model, metabolic behavior and combined toxicity of TOP metabolites and multipollutant. In addition, more molecular breeding approaches to increase plants' ability to quickly degrade chemical contaminants are still desirable because they cannot only enhance the plant resistance to toxicity but also reduce the pollutants residues for better food safety.

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