Agricultural Chemical Pollutants

Chemical characteristics and their potential risks

Introduction

According to calculations with the publicly available data of the Food and Agriculture Organization of the United Nations (FAO; 2013), there were 1563 billion hectare (ha) of both arable land and land with permanent crops available worldwide in 2012. Of this, about 75% is located in low- and middle-income countries.

In agriculture, the most environmentally hazardous and controversial substances with the highest bioactivity are pesticides. Large volumes of these are applied annually (Wesseling et al., 1997). According to the US EPA (United States Environmental Protection Agency, 2015a), a pesticide is defined as a single substance or a mixture of substances used for preventing, destroying, repelling or mitigating any pest (e.g. insects, mice, and other animals, unwanted plants, fungi, and microorganisms).

Along these lines, the EPA estimated that worldwide about 2.4 million tonne of active pesticide ingredients are used each year. This means that given the global area of arable land and permanent crops, the average annual use of pesticides is about 1.53 kg/ha (United States Environmental Protection Agency, 2011; Food and Agriculture Organization, 2013). Hence, chemical substances are used intensively for the removal of unwanted pests and plants on crops and in fields since mechanical removal is considered too time, labor, and cost intensive. In line with population growth and increased intensification of agriculture, the application of pesticides has also increased and intensified in low- and middle-income countries (Henriques et al., 1997; Ecobichon, 2001). Other substances of environmental concern, like phosphorous, nitrogen, and other fertilizers, which are causing eutrophication, do not fall within the scope of this study. However that is not to say that they are not of environmental concern.

Currently, about 1300 active pesticide substances are known (European Commission, 2015). They vary markedly in their chemical characteristics, modes of action, effectiveness, and impacts. According to their use, toxicity, chemical structure, and persistence, the most hazardous insecticides (I) and herbicides (H) are (Fishel, 2014a, b, 2015; International Agency for Research on Cancer, 2015; European Commission, 2015):

- Bipyridylium (H)
- Carbamates (I,H)
- Organochlorines (I)
- Organophosphates (I)
- Pyrethroids (I)
- Triazines (H)

In general, in low- and middle-income countries more investigation about the fate, occurrence, and the human and environmental health risks of pesticides is required.

Application of pesticides has increased and intensified in low- and middle-income countries.

Toxicological potential

Most of the pesticides used are not highly specific to one target organism. They are not easily degradable as shown by their half-lives, which range from several days to years. Also, they are applied in large quantities all over the world (~1.5 kg/ha; Deer, 2004). Adding to this, especially in low- and middle-income countries, pesticides that are banned already in high-income countries, such as Europe or the USA, are still used or stockpiled in low- and middle-income countries where regulations, environmental controls, infrastructure, and the risk awareness of those hazardous pollutants are lacking (Kesavachandran et al., 2009; Carneiro et al., 2012). Several of these pesticides, especially the organochlorines, have a high toxic and bioaccumulation potential (Bedi et al., 2013). In addition, metabolites of degraded pesticides and their effects on environmental and human health are often unknown or unclear (Somasundaram and Coats, 1991; Belfroid et al., 1998). Pesticides used in low- and middle-income countries, their environmental relevance, their physicochemical properties, and the trends in their use are summarized in Table 1. The human toxicological potential of substances is indicated by their lethal dose for 50% of the organisms tested – the (LD_{50})[3] values for rats – and their eco-toxicological potential as indicated by the environmental quality standards (Ecotox Centre, 2015). The environmental quality standards, MAC-EQS (maximum allowable concentrations) and AA-EQS (annual average concentrations), represent the acute and chronic environmental concentrations of chemical agents that, if exceeded, indicate a risk to aquatic organisms in surface water bodies.

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Pesticides that already are banned in high-income countries are still used or stockpiled in low- and middle-income countries.

[3] LD_{50} is a standardized measure for expressing and comparing the toxicity of chemicals.

Main Issues

- It is known that pesticides are highly bioactive even at low concentrations and exposure to pesticides can impair human and environmental health (van der Werf, 1996; Roldán-Tapia et al., 2005; Wesseling et al., 2005; Relyea, 2009; World Health Organization, 2010b; Wu et al., 2011a; Xu et al., 2013)
- The major part of the global arable land and land with permanent crops (about 75%) is located in low- and middle-income countries (Food and Agriculture Organization, 2013) and where the highest amounts of pesticides (around 2.4 million tonne/year) are used globally (United States Environmental Protection Agency, 2011)
- Extremely hazardous pesticides, which are banned in many high-income countries, are still stockpiled in low- and middle-income countries. Additionally, banned pesticides or pesticides that cannot be properly handled in low- and middle-income countries are being used in these countries under inappropriate conditions (Dinham, 2003; Elfvendahl et al., 2004; Wesseling et al., 2005; Pesticide Action Network Asia and the Pacific, 2010)
- Millions of people suffer from pesticide poisoning in low- and middle-income countries (Kesavachandran et al., 2009) mainly because of poor education regarding the handling of pesticides, lower awareness of the toxicity of pesticides, and a lack of regulations governing pesticide use (Kesavachandran et al., 2009; Dawson et al., 2010; Pesticide Action Network Asia and the Pacific, 2010).

3 million people annually are poisoned by pesticides. 99% of these poisoning incidents happened in low- and middle-income countries.

Chronic effects on environmental and human health by exposure to pesticides are often not included in risk assessment studies.

According to the WHO's estimates, about 3 million people around the globe are severely poisoned annually by pesticides. Of these, at least 10% died and 99% of these poisoning incidents happened in low- and middle-income countries. Suicides by ingesting pesticides contributed to about two-thirds of all acute pesticide poisoning cases (Jeyaratnam, 1990; Jeyaratnam and Chia, 1994; Kesavachandran et al., 2009). However this number may be underestimated since in low- and middle-income countries health care centers remain difficult to access and thus many cases of poisoning are not registered and remain unreported. The chronic effects on environmental and human health resulting from exposure to pesticides are often not included in such risk assessment studies (Kesavachandran et al., 2009; Dawson et al., 2010; Pesticide Action Network Asia and the Pacific, 2010). A comprehensive research literature study revealed that the main groups of the most hazardous pesticides used in uncontrolled ways and in high quantities in low- and middle-income countries are organochlorines, organophosphates, bipyridylium herbicides, carbamates, and triazines (Kesavachandran et al., 2009; Pesticide Action Network Asia and the Pacific, 2010). The environmental behavior and toxicity of typical representatives of those pesticide groups considered most harmful in low- and middle-income countries are described in more detail in the following chapter.

Pesticides of environmental concern

A) Organochlorine (OC) insecticides

Organochlorine (OC) insecticides are of particular concern for environmental and human health. Lindane, dichlorodiphenyltrichloroethane (DDT), aldrin, dieldrin, endosulfan, heptachlor, and heptachlor epoxide are OC insecticides (Lewis et al., 2015).

Consumption

The use of most OC insecticides is declining because of international restrictions. For example, the Stockholm Convention 2004 restricted or prohibited the production, import, export, and inappropriate stockpiling of OC insecticides that contain POPs, such as aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, taxophene, chlordecone, α- and β-hexychlorocyclohexane, and lindane (United Nations Environment Programme, 2013d). Nevertheless, OC insecticides still pose risks to environmental and human health. The OC insecticide of most concern for its effects on the environment in several low- and middle-income countries is DDT. DDT was banned in many parts of the world in the 1970s and 1980s because of its environmental persistence and moderate toxicity (National Geographic, 2006). However, DDT has begun to be used again more frequently since 2000, mainly in sub-tropical and tropical low- and middle-income countries in Africa, Latin America, and South Asia. This is because it is an effective and long-lasting insecticide for controlling insects that spread malaria, dengue fever, typhus, and cholera, and because its low cost makes it affordable in poor regions (Loganathan and Kannan, 1994; African Ministerial Conference on Environment and United Nations Environment Programme, 2004; European Commission, 2015). The recommended method for using DDT as a vector control for insects that transmit malaria, dengue fever, typhus, and cholera in low- and middle-income countries is to spray a very low concentration on house walls as an insect repellent. In the past, DDT has also been widely used in agriculture. In low- and middle-income countries, the use of DDT should be strictly controlled and regularly monitored (National Geographic, 2006). High-income countries already generally restrict the use of DDT. Globally, much less is used now than previously (Loganathan and Kannan, 1994). Nevertheless, since the ban on OCs, tonnes of DDT have been stockpiled under inappropriate conditions in low-income countries where they pose a risk to environmental and human health (Elfvendahl et al., 2004; Dasgupta et al., 2010). To date, reliable comprehensive data on the production of OCs and the use of old stocks of OCs are not available.

Environmental behavior and occurrence.

The physical and chemical properties of OC insecticides vary considerably. For instance, lindane and its other hexychlorocyclohexane isomers have higher vapor pressures and water solubilities, but lower adsorptions than chlordanes and DDT and, therefore, have less potential for bioaccumulation. However, all OC insecticides are known to persist in environmental systems for extended periods. Table 1 presents the physiochemical properties of significant OC insecticides. Volatile and semi-volatile OCs, such as lindane, persist in the atmosphere. The global climate transports volatile OCs from warmer to colder polar regions where they accumulate in the water and ice (Goldberg, 1975). In contrast, lipophilic compounds accumulate in soils and biota and affect wildlife and humans. Biotransformation eliminates residues slowly (Figure 5). Decades after the ban on OC insecticides, the levels of residues in human and bird adipose tissue are declining very slowly (Loganathan and Kannan, 1994). The top predators, the last links in the food chain, are most affected as a consequence of the enrichment of lipophilic OC insecticides by biomagnification at successive trophic levels (Bro-Rasmussen, 1996). Clearance rates in biota are higher in rivers and lakes than in semi-closed seas, where OC concentrations have slightly decreased, and in oceans, where they have remained constant. In aquatic biota in tropical regions, concentrations of OCs have increased slightly since 1970. The increase in concentrations may be the result of the persistence of OCs and because several of these, mainly DDT, are still used to prevent the spread of vector-borne diseases, such as dengue fever and malaria.

In 2003, OC insecticide concentrations in the Tonghui River, China, ranged from 134.9 to 3788 ng/L. Concentrations of OC insecticides in sediments ranged from 1.79 to 13.98 ng/g dry weight (Zhang et al., 2004). On the east coast of Thailand, oysters contained concentrations of OC insecticides up to 16.71 ng/g wet weight (Cheevaporn et al., 2005). In 2008, Devanathan et al. showed that the concentrations of DDT in breast milk in low- and middle-income countries were higher than those in higher-income countries (Devanathan et al., 2009). In New Delhi the mean level of DDT in human breast milk was 1500 ng/g lipid weight and in Chennai 1200 ng/g lipid weight, while in Malaysia the mean level was 1600 ng/g lipid weight. Breast milk sampled in the Democratic Repu-

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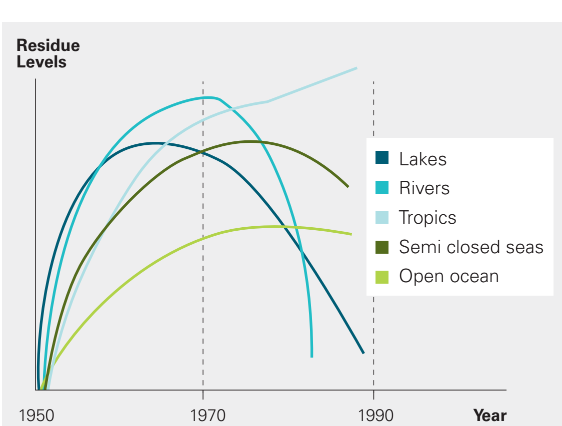
All organochlorine insecticides are known to persist in environmental systems for extended periods. Volatile and semi-volatile organochlorines persist in the atmosphere and accumulate in the water and ice of colder polar regions. Lipophilic compounds accumulate in soils and biota and affect wildlife and humans.

Aquatic Biota



Terrestrial Biota

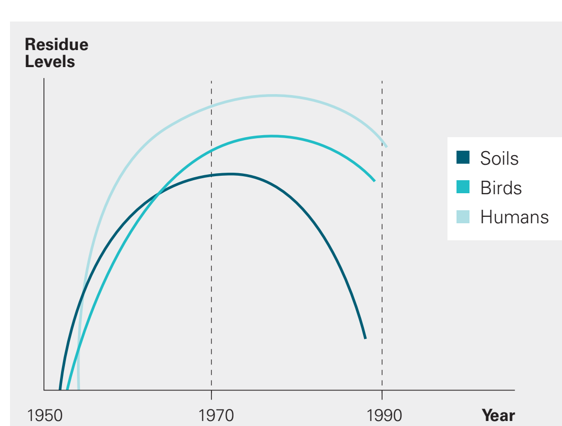


***Figure 5**: Pollution trends of organochlorine insecticides in aquatic and terrestrial biota (Loganathan and Kannan, 1994)*

blic of Vietnam had a DDT concentration (mean value) of 2200 ng/g lipid weight, in China (Hong Kong) it was 2870 ng/g lipid weight, and in Mexico, 4100 ng/g lipid weight. In contrast, human breast milk sampled in the USA had DDT residues of 65 ng/g lipid weight, Germany 240 ng/g lipid weight, Japan 340 ng/g lipid weight, United Kingdom 470 ng/g lipid weight, and Australia 1200 ng/g lipid weight (Devanathan et al., 2009).

Toxicity

OC insecticides have a bad reputation because of their toxic potential. There is evidence of the negative effect of OCs on endocrine activity (Kojima et al., 2004; Lemaire et al., 2004), their carcinogenic potential (Ibarluzea et al., 2004), and their potential to promote neuropsychiatric impairment and diseases such as Parkinson's Disease (Fleming et al., 1994). Furthermore, the DDT metabolite dichlorodiphenyldichloroethylene is known to cause eggshell thinning by impairing or inhibiting prostaglandin synthesis in eggshell gland mucosa (Lundholm, 1997). Bobwhite quail (*Colinus virginianus*) exposed to 60 to 85 µg DDT/g body weight as an oil solution or 300 µg DDT/g body weight in a crystalline form showed acute toxic effects. After chronic exposure (63 days) to 3.07 mg DDT by oral ingestion, 70% of the tested bobwhite quail died (Coburn and Treichler, 1946).

B) Organophosphates (OP) and Carbamates

Continuous application of organophosphates and carbamates increases environmental concentrations especially in lakes, groundwater, and soils, although they degrade more easily than organochlorines.

The most hazardous organophosphates are: Azinphos-methyl, chlorpyrifos, diazinon, dichlorvos, dimethoate, ethephon, malathion, methamidophos, naled, and oxydemeton-methyl. The carbamates aldicarb, aldoxycarb, aminocarb, bendiocarb, carbofuran, dimetan, dimetilan, dioxacarb, methiocarb, methomyl, oxamyl, and propoxur are very toxic. Bufencarb, carbosulfan, pirimicarb, promecarb, thiodicarb, and trimethacarb are moderately toxic carbamates (Morais et al., 2012).

Consumption

Most OPs and carbamates are used in insecticides, herbicides, and fungicides (Table 1). Today, most WHO Class I and II OPs and carbamates are banned in most parts of the world. Large amounts of Class II or lower OPs and carbamates are still widely used (Table 1).

Detecting carbamates is a challenge even when using relatively modern techniques, such as liquid chromatography (LC) with post-column fluorescence detection or LC-diode array ultraviolet (UV) detection.

Environmental behavior and occurrence

Compared to OCs, OPs and carbamates are less persistent and bioaccumulative (Henriques et al., 1997; Klaassen, 2013). Table 1 presents the physiochemical properties of several OPs and carbamates. In soil samples taken in 2002 and 2003 from agricultural areas around Hisar, Haryana (India), the maximum concentrations of the OPs chlorpyriphos, malathion, and quinalphos were 0.172, 0.008, and 0,01 µg/g, respectively (Kumari et al., 2008).

In 2000, groundwater from an agricultural area in the Yaqui Valley, in northwest Mexico, had 5.4 µg/L of the carbamate methiocarb, and surface water had 18 µg/L of the carbamate metabolite of carbofuran, 3-hydroxycarbofuran. In this region, groundwater is an important source of drinking water, especially in rural areas, thus contamination of groundwater by pesticides is a serious health risk for local communities (García de Llasera and Bernal-González, 2001). Consequently, although OPs and carbamates degrade more easily than OCs and have shorter half-lives, these pesticides still occur in water samples at µg/L or ng/L concentrations because of their continuous use in agriculture over months or years (Gruber and Munn, 1998). In low- and middle-income countries, especially in sub-tropical and tropical regions, pesticides may be used throughout the year because there is no winter. Continuous application increases environmental concentrations, especially in standing water (lakes), groundwater, and soils. Inappropriate application of pesticides, applying too much, neglecting to consider wind direction or surface runoff, or applying to agricultural areas near wells or aquifers that are used as drinking water sources, can lead to high concentrations (Wesseling et al., 2005; Pesticide Action Network Asia and the Pacific, 2010). Although large amounts of carbamates are widely used, monitoring data and data on environmental concentrations are not as available as for OCs and OPs, mainly because of the challenge of detecting carbamates. García de Llasera and Bernal-González, (2001) showed that it is even difficult to detect carbamates using relatively modern techniques, such as liquid chromatography (LC) with post-column fluorescence detection or LC-diode array ultraviolet (UV) detection.

Toxicity

Although the chemical structures of OPs and carbamates differ, they act in a similar way. Both inhibit the enzyme acetylcholinesterase. Carbamates are considered to be less toxic than OPs as they bind less tightly to acetylcholinesterase (Henriques et al., 1997). Inhibiting the enzyme acetylcholinesterase kills many insects. However, vertebrates and mammals are also highly susceptible because inhibiting acetylcholinesterase causes neuropsychological sequelae (Fukuto, 1990; Story and Cox, 2001). For instance, in human pesticide poisoning, symptoms of acetylcholinesterase inhibition are miosis, salivation, sweating, lacrimation, rhinorrhea, abdominal cramping, vomiting, diarrhea, urinary incontinence, bronchospasm, dyspnea, hypoxemia, bradycardia, bronchial secretions, pulmonary edema, and respiratory failure (Morais et al., 2012). School children exposed to OPs and carbamates in infancy suffer significant consequential damage. This includes, for example, deficient inhibitory motor control or difficulties in the acquisition phase of verbal learning tasks (Kofman et al., 2006).

In Costa Rica in 2001, drifts of the OP methamidophos, which was being used to prevent agricultural pests, affected 78 children. In 2003 the number was 40 children and in 2004, 61 children were affected (Wesseling et al., 2005). Carbamates and OPs also impair reproduction in vertebrates (Pawar and Katdare, 1984) and mammals (Gosselin et al., 1984) because of their estrogenic potential (Schulte-Oehlmann et al., 2011). Furthermore, carbamates and OPs are suspected of causing cancer (Schlatter and Lutz, 1990). The toxic potential of OPs, and especially carbamates, varies considerably. For instance, aldicarb, aldoxycarb, aminocarb, bendiocarb, oxamyl, and propoxur have an estimated LD_{50} [4] value for humans of less than 50 mg/kg. Bufencarb, carbosulfan, pirimicarb, promecarb, thiocarb, and trimethacarb are moderately toxic with estimated LD_{50} values of from 50 to 200 mg/kg. Fenocarb, carbaryl, and isoprocarb have low toxicity with an estimated LD_{50} of less than 200 mg/kg (Erdman, 2004). From the eco-toxicological point of view, crustaceans are much more sensitive to OPs than to carbamates: *Daphnia magna* and *Hyalella azteca* showed acute LC_{50}s of 0.6 and 0.1 μg/L after exposure to the OP chlorpyrifos for 48 hours, and LC_{50}s of 3990 and 583 μg/L after exposure to the carbamate aldicarb for 48 hours. Vertebrates generally seem to be less sensitive to exposure to OPs and carbamates than crustaceans. The fish *Pimephales promelas* had higher LC_{50} values than crustaceans – 162.7 μg/L after exposure to chlorpyrifos for 48 hours and 8860 μg/L after exposure to aldicarb for 48 hours. Nevertheless, chronic exposure of fish to OPs and carbamates led to alterations in swimming (Matton and LaHam, 1969) and feeding (Bull and McInerney, 1974) behavior, changes in social interactions (Symons, 1973), widened opercula, and increased hyperexcitability (Zinkl et al., 1991). In plants, the herbicide carbamates, for example carbetamide, inhibit cell division by disturbing the nucleic acid metabolism and protein synthesis (Audus, 1976; Ocampo and Barea, 1985; Morais et al., 2012), and they are also known to inhibit photosynthesis (Moreland, 1980).

C) Triazines

Atrazine, atraton, simazine, prometon, and propazine are members of the triazine-derivate herbicides of environmental concern (Köck-Schulmeyer et al., 2013).

Consumption

The triazine derivate atrazine is one of the most widely used herbicides worldwide (Azevedo et al., 2010). According to a quantitative analysis for atrazine, the EPA estimated that the annual consumption of atrazine was about 35,000 tonne, in 2001 (United States Environmental Protection Agency, 2006). Usually, the herbicide is used to eliminate unwanted plants before the emergence of the crop. Most of it is used before the cultivation of crops such as corn, sugarcane, sorghum, and sweet corn. In addition to its agricultural application it is used in forestry for non-selective plant control on roads, railway lines, and industrial areas (United States Environmental Protection Agency, 2006; Azevedo et al., 2010).

Environmental behavior and occurrence

The investigations of Köck-Schulmeyer et al. (2013) showed that triazines, triazine- derivates, and the transformation products atrazine, desethylatrazine,deisopropylatrazine, simazine, and terbuthylazine are hard to remove from water systems. Given their nitrogen and chlorine atoms, triazines have polar and persistent characteristics.

The physicochemical properties of atrazine are presented in Table 1. From 2007 to 2009, Köck-Schulmeyer et al. (2013) measured concentrations of triazines, its derivates, and its metabolites ranging from 20 to 169 ng/L (mean values) in the effluents of wastewater treatment plants (WWTPs) from Catalonia (north-east Spain), although they have been banned in the EU since 2003 (Sass and Colangelo, 2006). In addition, the maximum concentration of 1990 ng/L simazine was measured in effluents from one Catalonian WWTP (Köck-Schulmeyer et al., 2013). In addition to these high environmental concentrations in Spain, triazines occur in water samples in other countries and in low- and middle-income countries as well. These herbicides are still in use in the USA and various low- and middle-income countries (Gfrerer et al., 2002; Sass and Colangelo, 2006; Kesavachandran et al., 2009). For instance, in 2002, in the Liaoning Province, eastern China, atrazine concentrations of up to 1600 ng/L were detected in Liao-He River water (Gfrerer et al., 2002). Furthermore, according to the environmental relevance of pesticides from wastewater treatment plants index (ERPWI), atrazi-

Vertebrates and mammals are also highly susceptible to carbamates, as inhibiting acetylcholinesterase causes neuropsychological pathological conditions.

The triazine derivate atrazine is one of the most widely used herbicides worldwide. Although banned in the EU since 2003 triazines are still in use in the USA and many low- and middle-income countries.

[4] LD_{50} is a standardized measure for expressing and comparing the toxicity of chemicals.

ne and simazine, as well as diazinon and diuron, were listed as the most problematic compounds within the scope of their study. The ERPWI considers the occurrence and removal of pesticides in wastewater treatment installations and the toxicity of pesticides to algae, daphnia, and fish (Köck-Schulmeyer et al., 2013).

Toxicity

Triazines act as strong herbicides by inhibiting photosynthesis. Accordingly, processes that are correlated with photosynthesis, for example, stomatal movement, transpiration, ion movement, and other energy-dependent processes, are affected by triazines as well (Ebert and Dumford, 1976). Furthermore, animal tests with rats showed that exposure to triazines causes neuroendocrine development and reproduction impairments because of the antiandrogenic properties (Stevens et al., 1994; McMullin et al., 2004). The uptake of atrazine leads to the suppression of the luteinizing hormone surge in ovariectomized estrogen-primed adult female rats, and it was shown that atrazine has antiandrogenic properties after conducting *in vitro* and *in vivo* studies. Moreover, it was revealed that these herbicides affect parts of the central nervous system, for example, causing hypothalamic dysfunction and disrupting the pituitary function (McMullin et al., 2004). Other effects on humans and wildlife include changes in organ weights and damage to the heart and liver. Tremors were observed as well (Fishel, 2015). Because of the adverse effects of the triazine compound atrazine, the EPA recommended that atrazine concentrations in drinking water should not exceed 3 µg/L to prevent chronic effects on humans and animals (Fishel, 2015). For the algae *Chlamydomonas reinhardtii* and *Pseudokirchneriella subcapitata*, mean EC_{50} values (96 hour), ranged from 176 to 117 µg atrazine/L. The triazine metribuzin seems to be more toxic by showing lower EC_{50} mean values ranging from 23 to 43 µg/L when used with the same algae. For the macrophytes *Ceratophyllum* demersum and *Lemna minor*, EC_{50} values of 22 and 92 µg/L were measured for atrazine and 14 and 36 µg/L for metribuizin (Fairchild et al., 1998). Invertebrates are much less sensitive to triazines. For example, for zebrafish *(Danio rerio*) embryos, a LC_{50} (48 hour) value of 36.8 mg/L was determined (Wiegand et al., 2000).

Effects on humans and wildlife by triazines include changes in organ weights and damage to the heart and liver.

D) Bipyridylium herbicides

Diquat and paraquat are the most popular bipyridylium herbicides (Pesticide Action Network UK, 1996).

Consumption

These are non-selective contact herbicides, causing wilting of foliage as a result of the rapid destruction of plant cell membranes even after a few hours of exposure (Fishel, 2014a). Diquat is mainly used for agricultural purposes to desiccate certain crops, for example, alfalfa, clover, potato, grain sorghum, and soybean, to simplify harvesting. It is used to control free-floating and submerged weeds in aquatic systems as well (Food and Agriculture Organization and World Health Organization, 1995). Paraquat is mostly used as a desiccant prior to harvesting of plants or it is applied as a weed killer to quickly eliminate unwanted plants before favored crops are sown (Fishel, 2014a).

Environmental behavior and occurrence

The distribution patterns of diquat and paraquat are quite similar. Given their low vapor pressures and their relatively high solubilities in water, they do not have the tendency to evaporate out of the water phase (Food and Agriculture Organization and World Health Organization, 1995; Rodriguez Jr et al., 2002; Sigma-Aldrich, 2014b). Paraquat and diquat are stable under neutral and acidic conditions, but in alkaline environments (pH > 12) they are hydrolyzed (Roberts et al., 2002). However, although they are soluble in water, they more likely adsorb to organic material and accumulate in soils and sediments. Because of their high affinity to bind to soil surfaces and their, therefore, lower availability in the soil pore water, their potential for microbial degradation is limited (Riley et al., 1976; Roberts et al., 2002; Fishel, 2014a). Regardless of these limitations for microbial degradation, there are some microbial species and fungi that are able to metabolize these herbicides alone or through co-metabolism processes (Funderburk and Bozarth, 1967; Carr et al., 1985; Roberts et al., 2002). Nevertheless, these herbicides pose a risk to aquatic environmental health mainly because of continuous exposure. Agricultural surface runoff transports these substances into flowing and still water systems, harming aquatic organisms, particularly algae and macrophytes (Sáenz et al., 1997; Sigma-Aldrich, 2014b). However, because of its adsorption to soils, it is not transported into ground water aquifers (Roberts et al., 2002). Fortunately, these compounds are not extensively transferred into plants (Fuerst and Vaughn, 1990), they can be removed quite easily from plant surfaces and water through sunlight and photo-degradation processes, or they can be removed through absorption to the soil (Slade, 1965, 1966; Roberts et al., 2002). Nevertheless, it has to be noted that these herbicides are much disputed, especially for use in low- and middle-income countries, because of their high acute toxicity (Wu et al., 2012a). In these regions, no data about environmental concentrations are available.

Toxicity

According to the material safety data sheets of Sigma-Aldrich, these agents are categorized as Category 1 chemicals, which have chronic aquatic toxicity (Sigma-Aldrich, 2014a, b) and are particularly known for their high acute toxicity as well (Sigma-Aldrich, 2014a, b). The toxic effects of these compounds are caused by several steps:

- After the exposure of plants and animals to bipyridylium herbicides (paraquat and diquat) the compounds are reduced, leading to the formation of radicals

- These radicals then reduce the molecular oxygen and promote formation of superoxide radicals

- Through further complex processes and reactions, other toxic oxygen species are formed, for example, hydroxyl radicals, hydrogen peroxides, and singlet oxygen

- The formation of these toxic species, lipid peroxidation, and the adverse effects to cell membrane integrity, results in fast dehydration (Fuerst and Vaughn, 1990).

Vertebrates and crustaceans seem to be less sensitive to exposure of bipyridylium herbicides. For instance, studies show that the LC_{50} of paraquat for the fish *Lepomis macrochirus* is 13 mg/L after 96 hours of exposure and the EC_{50} for *Daphnia magna* after 48 hours of exposure is 2.8 mg/L (Sigma-Aldrich, 2014b). For the algae *Selenastrum capricornutum* and *Chlorella vulgaris* even very low mean EC_{50} values (96 hour) of 670 and 140 μg paraquat/L were determined for the endpoint growth (Sáenz et al., 1997).

Although paraquat and diquat are known for their potential for geo-accumulation, they are not suspected to bio-accumulate in fruits and food because of their high potential for photochemical degradation (Food and Agriculture Organization and World Health Organization, 1995). To humans and mammals, the acute toxicity of diquat and paraquat is high (Category 2; Sigma-Aldrich, 2014a, b), especially the dermal uptake, and uptake through inhalation during application is life-threatening. The uptake of these agents causes organ damage, particularly to lungs and skin (Clark et al., 1966; Sigma-Aldrich, 2014a, b). Malfunctions of the respiratory system and adverse effects to the nervous system and kidneys are caused when these herbicides are inhaled. Exposure to high volumes causes progressive pulmonary fibrosis and epithelial proliferation that can lead to death (Rodriguez Jr et al., 2002). The LD_{50} of paraquat for rats through oral uptake is 57 mg/kg body weight, whereas the LD_{50} through dermal uptake for rabbits is 325 mg/kg (Sigma-Aldrich, 2014b). Furthermore, these substances are well-known for causing damage to the central nervous system (Clark et al., 1966; Wu et al., 2012a; Prakash et al., 2013) and paraquat is even suspected to cause Parkinson's disease (Wu et al., 2012a; Moretto and Colosio, 2013). According to the EPA, the maximum concentration of diquat and paraquat in drinking water, 20 μg/L or 3 μg/L, respectively, should not be exceeded (Rial-Otero et al., 2006). For humans the highest risk is through accidental uptake or skin contact during unsafe application of these herbicides. Unsafe applications include the use of inappropriate methods, not using personal protective equipment, or occupational accidents.

Mainly because of its high acute toxicity and its potential to endanger aquatic systems, paraquat has gained a bad reputation – during the last decades it has become one of the most controversial herbicides worldwide (Dinham, 2003). In addition, paraquat was being used very frequently to commit suicide, especially in developing countries (Dinham, 2003). Several public organizations, such as the Berne Declaration of Switzerland, Swedish Society for Nature Conservation, Foro Emaús of Costa Rica, Pesticide Action Network of Asia and the Pacific (PANAP), and Pesticide Action Network (PAN) UK, support a phasing out of paraquat. They emphasize that paraquat is mainly used in low- and middle-income countries in Asia and Central and South America, where proper handling of these hazardous herbicides cannot be guaranteed because of a lack of knowledge of the safe handling of pesticides and regulations governing its use (Dinham, 2003). Furthermore, it is questionable why, when paraquat is banned in several countries (including Austria, Denmark, Finland, Germany, Hungary, Slovenia, Sweden, and Switzerland), its use in low- and middle-income countries is still permitted.

E) Pyrethroids

The pyrethroids can be classified into two types, Type I without and Type II with cyano groups. The cyano-pyrethroids (Type II pyrethroids) – cyhalothrin, cypermethrin, deltamethrin, cyfluthrin, fenvalerate, flucythrinate, and

Bipyridylium herbicides are more likely to adsorb to organic material and accumulate in soils and sediments. Their high affinity to bind to soil surfaces and lower availability in the soil pore water limits their potential for microbial degradation.

The uptake of diquat and paraquat through the skin, and inhalation during application is acutely life threatening to humans and mammals.

fluvalinate – are the pyrethroids of higher concern because they are more toxic than the Type I pyrethroids (Roberts and Reigart, 2013).

Consumption

After application, pyrethroids adsorb to particles and organic matter and are transferred to rivers and streams with surface runoff and erosion.

Pyrethroids are synthetic analogues of natural pyrethrins obtained from chrysanthemum flowers (*Chrysanthemum cinerariaefolium)*. They are modern insecticides. Compared to natural pyrethrins, pyrethroids are designed to have an increased toxicity to targeted insects, have more persistence in the environment, and to have a good knockdown activity to pests. At the same time, they are designed to have a lower mammalian toxicity than other pesticides (Palmquist et al., 2012). Nevertheless, since synthetic pyrethroids became popular as substitutes for banned OCs, OPs, and carbamates, their application and the accompanying concern caused by these substances has constantly increased (Sayeed et al., 2003). Today, they are often used in agriculture, homes, and gardens, and for the treatment of ectoparasitic diseases in humans and animals. In some products, they are often combined with other strong OP or carbamate insecticides to enhance their effects (Roberts and Reigart, 2013).

Environmental behavior and occurrence

These synthetic compounds are known for their lipophilic characteristics, their persistence, and their high stability to photolytic degradation. Their low vapor pressures and high octanol-water coefficients show that they have a low potential to volatilize, but they have a high affinity to adsorb to organic matter and soils (Weston and Lydy, 2010; Palmquist et al., 2012; Lewis et al., 2015). Therefore, according to their physicochemical properties (Table 1) pyrethroids are most likely adsorbed to organic matter and particles. After application, these pesticides are transferred to rivers and streams by sediment movement through surface runoff. Investigations have shown that these pesticides occurred significantly in eroded sediments (Gan et al., 2005), which is indicative of their high potency for sorption to soil and organic particles (Luo and Zhang, 2011). For instance, in the Ubombo and Ingwavuma districts in KwaZulu-Natal province, South Africa, the maximum concentration of the pyrethroid cypermethrin found in the soil of the Makhathini flat was 1651 µg/kg and the maximum concentration found in the water of the same area was 40.7 µg/L. In the Ndumo agricultural area, concentrations of up to 467.3 µg/kg were measured in soil samples, while concentrations in the water samples were 23.19 µg/L. In Ophansi, 261 µg/kg of cyfluthrin was detected in soils, whereas in the water no cyfluthrin could be detected. Even in Tembe Elephant Park, a nature reserve, surprisingly high concentrations – up to 467.3 µg/kg – of cyfluthrin were found although, officially, no pesticides have been applied in this region (Sereda and Meinhardt, 2005). These concentrations confirm that these compounds tend to sorb to organic matter, soil, and suspended sediments because the concentrations in soils exceed those found in the water samples. The concentrations found in water and sediments are both of environmental concern.

Fish and invertebrates seem to be highly susceptible to exposure to pyrethroids.

Toxicity

In contrast to the OPs, the pyrethroids do not impair the central nervous system of animals exposed to them, but, rather, they affect the functioning of the peripheral nervous system. Pyrethroids prolong the opening time of voltage-gated sodium channels on nerves. Consequently, this alteration in nerve function leads to a series of short bursts or a prolonged burst, caused by repeated stimulus-dependent nerve depolarization or discharges of nerve signals (Soderlund and Bloomquist, 1989). For humans, exposure to Type I pyrethroids causes effects like restlessness, hyperexcitation, prostration, and body tremors. Exposure to Type II pyrethroids leads to hyperactivity, incoordination, convulsions, and writhing (Soderlund and Bloomquist, 1989; Fishel, 2014b). The pyrethroids are well-known for being less toxic to mammals and birds, because they do not have a high potential for bioaccumulation and they are easily degradable through the liver systems of mammals and birds. However, in contrast, non-target insects, invertebrates, and fish are highly susceptible to these chemicals (Fishel, 2014b).

On the one hand, as described before, pyrethroids are less toxic to mammals and birds than most of the other pesticides, for example, carbamates, OCs, and OPs, because they are more selective to insects and they are more easily metabolized. On the other hand, fish and invertebrates seem to be highly susceptible to exposure to pyrethroids. For instance, for the fish *Danio rerio,* the LC_{50} values range from 1.9 to 27.6 µg/L after exposure to permethrin for 2 days (United States Environmental Protection Agency, 2014a)

For crustacean invertebrates, the 10 day LC50 values for pyrethroids in general ranged from 2 to 140 ng/L in water samples (for *Americamysis bahia* and *Ceriodaphnia dubia*) and from 4 to 110 ng/L (for *Hyalella Azteca*) in sediments (Hladik and Kuivila, 2009). In summary, given their photolytic stability, their high lipophilic characteristics, and their high acute toxicity to fish and invertebrates, pyrethroids pose a risk to environmental health and especially to aquatic systems.

Table 1: Selection of hazardous pesticides used in low- and middle-income countries

Name [A]	Type/ chemical family	WHO toxicity classi-fication [B] (World Health Organization, 2010b)	Use trend [C]	Henry's law constant (at 25°C)	Log K_{OW} (at 25°C)	Water solubility [g/L]	LD_{50} for rats [mg/kg body weight] (World Health Organization, 2010b)	Environmental quality standard (in surface water bodies) AA-EQS/ MAC-EQS [µg/L]
BIPYRIDILS								
Paraquat	Herbicide	II	→	$1.23*10^{-12}$ (Lewis et al. 2015)	-4.5 (20°C) (Lewis et al. 2015)	620 (20°C) (Lewis et al. 2015)	150	NA/NA
CARBAMATES								
Carbaryl	Insecticide	II	→	$3.3*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.4 (Gramatica and Di Guardo, 2002)	0.120 (27°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	300 [D]	0.23/NA (National Institute for Public Health and the Environment - RIVM, 2008)
Carbendazim	Fungicide	IV	↑	$2.1*10^{-11}$ (Gramatica and Di Guardo, 2002)	1.5 (Gramatica and Di Guardo, 2002)	0.008 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	> 10,000	0.34/0.57 (Ecotox Centre, 2015)
Carbofuran	Insecticide	Ib	↓	$3.1*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.3 (Gramatica and Di Guardo, 2002	0.320 (25°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	8	0.02/NA (Institut National de l'Environ-nement Industriel et des Risques - INERIS, 2008a)
Carbosulfan	Insecticide	II	↓	$1.83*10^{-5}$ (Lewis et al. 2015)	7.42 (Lewis et al. 2015)	0.00011 (20°C) (Lewis et al. 2015)	101 (Lewis et al. 2015)	NA/NA
Fenobucarb	Insecticide	II	→	$5.9*10^{-8}$ (Gramatica and Di Guardo, 2002)	2.8 (Gramatica and Di Guardo, 2002)	Practically not soluble (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	620	NA/NA
Mancozeb	Fungicide	IV	↑	$1.76*10^{-10}$ (20°C) (Lewis et al. 2015)	1.8 (European Commission, 2015)	0.000006 (25°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	>8000	0.07/0.7 (European Commission,2015)
ORGANOCHLORINES								
2,4-D	Herbicide/ Alkyl chloro-phenoxy	II	↓	$1.40*10^{-9}$ (20°C) (Lewis et al., 2015)	2.8 (Travis and Arms, 1988)	23.180 (25°C) (European Commission, 2015)	425-764 (European Commission, 2015)	0.2/1.3 (Ecotox Centre, 2015)
Butachlor	Herbicide	III	↓	$5.1*10^{-8}$ (Gramatica and Di Guardo, 2002)	4.5 (Gramatica and Di Guardo, 2002)	0.020 (20°C) (Lewis et al., 2015)	2200	NA/NA
Chlorothalonil	Fungicide	IV	→	$1.36*10^{-5}$ (20°C) (Lewis et al., 2015)	2.9 (Institut für Arbeits-schutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	0.0006 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	>10.000	0.035/1.2 (Maycock et al., 2012a)
Clomazone	Herbicide/ oxazolidone	II	→	$1.67*10^{-6}$ (Lewis et al., 2015)	2.54 (Lewis et al., 2015)	1.102 (20°C) (Lewis et al., 2015)	1369 (Lewis et al., 2015)	2/NA (Institut National de l'Environnement Industriel et des Risques - INERIS, 2008b)
DDT	Insecticide	II	↓	$8.3*10^{-6}$ (Gramatica and Di Guardo, 2002)	6.9 (Gramatica and Di Guardo, 2002)	0.000001 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	113	0.025/NA (European Commission, 2008)

The human toxicological potential of substances is indicated by the LD_{50} values for rats and the eco-toxicological potential by the environmental quality standards. AA-EQS (annual average concentration) and MAC-EQS (maximum allowable concentration) are the chronic and acute environmental concentrations of chemical agents which affect water organisms significantly.

NA: not applicable
A: (green) = Approved in EU; (orange) = Not approved in EU (European Commission, 2015)
B: Ia: Extremely hazardous; 1b: Highly hazardous; II: Moderately hazardous; III: Slightly hazardous; IV Unlikely to present acute hazard in normal use.
C: ● Presumable decreasing trend in use; ● Trend in use is uncertain – approximation is difficult; ● Presumable increasing trend in use.
D: The LD_{50} was not a single value, but rather a value within the wider than usual range adopted for the WHO's recommended classification of pesticides by hazard.
E: Usually, the LD_{50} values for oral uptake are taken. E indicates that the LD_{50} values are for dermal uptake.
F: Converted from Henry's constant $k_H{}^{cp}$ [atm m³/mol] to $k_H{}^{cc}$ [dimensions less] using the EPA online tools for site assessment calculation (United States Environmental Protection Agency, 2015b).
G: Approximated by and ad hoc value; less data available.

Name [A]	Type/ chemical family	WHO toxicity classification [B] (World Health Organization, 2010b)	Use trend [C]	Henry's law constant (at 25°C)	Log K_{OW} (at 25°C)	Water solubility [g/L]	LD_{50} for rats [mg/kg body weight] (World Health Organization, 2010b)	Environmental quality standard (in surface water bodies) AA-EQS/ MAC-EQS [µg/L]
ORGANOCHLORINES								
Difenoconazole	Fungicide	II	→	$7.31*10^{-10}$ (20°C) (Lewis et al., 2015)	4.4 (Mensink, 2008)	0.015 (25°C) (Schummer et al., 2010)	1453	0.76/7.8 (National Institute for Public Health and the Environment - RIVM, 2008)
Endosulfan	Insecticide	II	↓	$6.5*10^{-5}$ (Gramatica and Di Guardo, 2002)	3.8 (Gramatica and Di Guardo, 2002)	0.00033 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	80	0.005/0.01 (European Commission, 2008)
Fipronil	Insecticide	II	→	$1.60*10^{-7}$ (20°C) (Lewis et al., 2015)	4.0 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.0024 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	92	0.012/NA (Biocidal Products Committee, 2011)
Imidacloprid	Insecticide	II	→	$4.10*10^{-11}$ (20°C) (Lewis et al., 2015)	0.33 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.61 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	450	0.067/0.2 (National Institute for Public Health and the Environment - RIVM, 2008)
MCPA [G]	Herbicide	II	→	$1.10*10^{-8}$ (Lewis et al., 2015)	2.56 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.3 (25°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	700 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	1.34/15.2 (Ecotox Centre, 2015)
Niclosamide	Fungicide	IV	→	$2.15*10^{-12}$ (20°C) (Lewis et al., 2015)	4.56 (20°C) (Lewis et al., 2015)	0.005 (20°C) (Lewis et al., 2015)	5000	NA/NA
Propanil	Herbicide/ anilide	II	→	$1.82*10^{-8}$ (Lewis et al., 2015)	2.29 (Lewis et al., 2015)	0.095 (20°C) (Lewis et al., 2015)	960 (Lewis et al., 2015)	NA/NA
Propiconazole	Fungicide	II	→	$4.2*10^{-9}$ (Gramatica and Di Guardo, 2002)	3.7 (20°C) (Lewis et al., 2015)	0.15 (20°C) (European Commission, 2015)	1520	1.0/NA (Marion Junghans (Ecotox Centre); personal communication)
ORGANOPHOSPHATES								
Acephat	Insecticide	II	↓	$2.15*10^{-11}$ (Lewis et al., 2015)	-0.85 (Lewis et al., 2015)	790 (20°C) (Lewis et al., 2015)	945 (Lewis et al., 2015)	57/570 [I] (Marion Junghans (Ecotox Centre); personal communication)
Chlorpyrifos	Insecticide	II	→	$3.0*10^{-6}$ (Gramatica and Di Guardo, 2002)	5.0 (Gramatica and Di Guardo, 2002)	0.001 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	135	0.03/0.1 (European Commission, 2008)
Dichlorvos [G]	Insecticide	Ib	↓	$1.50*10^{-2}$ (20°C) (Lewis et al., 2015)	1.43 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	10 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	17 (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	0.0006/0.0007 (European Parliament and Council of the European Union, 2013)

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C: ● (orange) Presumable decreasing trend in use; ● (yellow) Trend in use is uncertain – approximation is difficult; ● (green) Presumable increasing trend in use.

D: The LD_{50} was not a single value, but rather a value within the wider than usual range adopted for the WHO's recommended classification of pesticides by hazard.

E: Usually, the LD_{50} values for oral uptake are taken. E indicates that the LD_{50} values are for dermal uptake.

F: Converted from Henry's constant $k_H{}^{cp}$ [atm m³/mol] to $k_H{}^{cc}$ [dimensions less] using the EPA online tools for site assessment calculation (United States Environmental Protection Agency, 2015b).

G: Approximated by and ad hoc value; less data available.

Name [A]	Type/ chemical family	WHO toxicity classi-fication [B] (World Health Organization, 2010b)	Use trend [C]	Henry's law constant (at 25°C)	Log K_{OW} (at 25°C)	Water solubility [g/L]	LD_{50} for rats [mg/kg body weight] (World Health Organization, 2010b)	Environmental quality standard (in surface water bodies) AA-EQS/ MAC-EQS [µg/L]
ORGANOPHOSPHATES								
Dimethoate	Insecticide	II	→	$1.0*10^{-10}$ (Gramatica and Di Guardo, 2002)	0.8 (Gramatica and Di Guardo, 2002)	39.8 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	150 [D]	0.07/0.977 (Ecotox Centre, 2015)
Fenthion	Insecticide	II	→	$1.4*10^{-6}$ (Gramatica and Di Guardo, 2002)	4.1 (Gramatica and Di Guardo, 2002)	0.055 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	586[E]	0.003/NA (National Institute for Public Health and Environment - RIVM, 2008)
Glyphosate	Herbicide	III	↑	$8.5*10^{-11}$ (European Commission, 2015)[F]	-3.2 (European Commission, 2015)	10.5 (20°C) (European Commission, 2015)	4230	196/389 (Maycock et al., 2012b)
Malathion	Insecticide	III	↑	$4.9*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.4 (Gramatica and Di Guardo, 2002)	0.145 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	2100 [D]	0.013/NA (National Institute for Public Health and the Environment - RIVM, 2008)
Monocrotophos	Insecticide	Ib	↓	$6.5*10^{-13}$ (Gramatica and Di Guardo, 2002)	-0.2 (Gramatica and Di Guardo, 2002)	818 (20°C) (Lewis et al., 2015)	14	0.00008/NA (National Institute for Public Health and the Environment - RIVM, 2008)[I]
Parathion-methyl	Insecticide	Ia	↓	$2.30*10^{-6}$ (20°C) (Lewis et al., 2015)	3.0 (20°C) (Lewis et al., 2015)	0.55 (20°C) (Lewis et al., 2015)	14	0.011/NA (National Institute for Public Health and the Environment - RIVM, 2008)
Phenthoate	Insecticide	II	→	$6.34*10^{-5}$ (Lewis et al., 2015)	3.69 (Lewis et al., 2015)	0.011 (20°C) (Lewis et al., 2015)	249 (Lewis et al., 2015)	NA/NA
Phorate	Insecticide	Ia	↓	$4.4*10^{-6}$ (Gramatica and Di Guardo, 2002)	3.6 (Gramatica and Di Guardo, 2002)	0.050 (20°C) (Lewis et al., 2015)	2	0.000165/NA (National Institute for Public Health and the the Environment - RIVM, 2008)[I]
Phosphamidon	Insecticide	Ia	↓	$6.5*10^{-12}$ (Gramatica and Di Guardo, 2002)	0.4 (Gramatica and Di Guardo, 2002)	Completely mixable (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	7	0.03/NA (National Institute for Public Health and the Environment - RIVM, 2008)[I]
Profenofos	Insecticide	II	→	$2.2*10^{-8}$ (Gramatica and Di Guardo, 2002)	4.7 (Gramatica and Di Guardo, 2002)	0.02 (25°C) (United States Environmental Protection Agency, 2000)	358	NA/NA
Quinalphos	Insecticide	II	→	$2.38*10^{-6}$ (20°C) (Lewis et al., 2015)	4.44 (20°C) (Lewis et al., 2015)	0.0178 (20°C) (Lewis et al., 2015)	62	NA/NA
Triazophos	Insecticide	Ib	↓	$1.30*10^{-6}$ (20°C) (Lewis et al., 2015)	3.55 (Lewis et al., 2015)	0.035 (20°C) (Lewis et al., 2015)	82	0.001/0.02 (National Institute for Public Health and the Environment - RIVM, 2008)
PYRETHROIDS								
Cyfluthrin	Insecticide	Ib	↑	$7.78*10^{-5}$ (20°C) (Lewis et al., 2015)	6.0 (European Commission, 2015)	0,000002 (20°C) (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung, 2013)	15 [D]	0.0006/NA (Andersson and Kreuger, 2011)
Cyhalothrin	Insecticide	II	→	$4.62*10^{-11}$ (20°C) (Lewis et al., 2015)	6.85 (Ochiai et al., 2004)	0.000004 (20°C) (Lewis et al., 2015)	144 [D]	0.00002/0.00047 (National Institute for Public Health and the Environment - RIVM, 2008)
Cypermethrin	Insecticide	II	↑	$3.70*10^{-6}$ (20°C) (Lewis et al., 2015)	5.3 (20°C) (Lewis et al., 2015)	0.000009 (20°C) (Lewis et al., 2015)	250 [D]	0.00008/0.0006 (Ecotox Centre, 2015)
Deltamethrin	Insecticide	II	↑	$4.20*10^{-6}$ (20°C) (Lewis et al., 2015)	6.2 (European Commission, 2015)	<0.0001 (20°C) (European Commission, 2015)	135 [D]	0.0000031/0.0003 (National Institute for Public Health and the Environment - RIVM, 2008)
Esfenvalerate	Insecticide	II	↑	$1.01*10^{-6}$ (Lewis et al., 2015)	6.24 (Lewis et al., 2015)	0.000001 (20°C) (Lewis et al., 2015)	88.5 (Lewis et al., 2015)	0.0001/0.0009 (National Institute for Public Health and the Environment - RIVM, 2008)

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TRIAZINES								
Atrazine	Herbicide	III	→	$2.3*10^{-9}$ (Gramatica and Di Guardo, 2002)	2.6 (Gramatica and Di Guardo, 2002)	0.035 (22°C) (Agency for Toxic Substances and Disease Registry, 2003)	2000 [D]	0.6/2 (European Parliament and Council of the European Union, 2008)
OTHERS								
Cymoxanil	Fungicide/ urea derivative	II	↑	$1.53*10^{-8}$ (Lewis et al., 2015)[F]	0.67 (Lewis et al., 2015)	0.78 (20°C) (Lewis et al., 2015)	760 (Lewis et al., 2015)	3/NA (Andersson and Kreuger, 2011)
Dinocap [G]	Fungicide/ dini-trophenol	II	→	$5.96*10^{-6}$ (Lewis et al., 2015)	6.5 (20°C) (Lewis et al., 2015)	0.000183 (20°C) (Lewis et al., 2015)	766 (Institut für Arbeits-schutz der Deutschen Gesetzlichen Unfall-versicherung, 2013)	NA

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G: Approximated by and ad hoc value; less data available.

Input pathways of pesticides

The input pathways of pesticides in low- and middle-income countries and higher-income countries have similarities and differences.

In high-, and low- and middle-income countries, pesticides after application can leach into the subsoil and groundwater aquifers through irrigation or they can be transported into rivers, streams, and groundwater systems through surface runoff after rainfall events, thus posing risk to environmental and human health. However, in high-income countries, ground water and surface waters are more strictly controlled and wastewater treatment facilities for surface water purification are common. In contrast, in most of the low- and middle-income countries, water controls and wastewater treatment facilities are lacking or not available. This results in higher environmental concentrations of pesticides, especially if contaminated and untreated river water is used for irrigation over several years (Clarke et al., 1997; Corcoran et al., 2010; Heeb et al., 2012; Ismail et al., 2012; Sapari and Ismail, 2012).

In addition, the amounts of pesticides released into the environment through individual input sources differ to a greater extent between high- and low- and middle-income countries. For example, in high-income countries with their more strict controls and regulations and improved education in pesticide handling and storage, less cases of acute pesticide poisoning are observed during application and, presumably, smaller amounts of pesticides are exposed and released to the environment (Jeyaratnam and Chia, 1994; Kesavachandran et al., 2009). Consequently, smaller amounts accumulate in soil/sediments, biota, and food (crops, fruits). For instance, the amount of DDT found in human breast milk is much higher in low- and middle-income countries than in high-income countries (Devanathan et al., 2009). However, it must be noted that reliable, comprehensive, and comparative data about the amounts of pesticides released in high- and in low- and middle-income countries are not available yet. Even in high income countries, studies of the environmental distribution and the individual sources of pesticides need to be conducted to gain a better understanding of their environmental behavior and their risk to environmental and human health (Wittmer et al., 2010).

In private gardens in urban regions of high-income countries, pesticides are mainly used to protect plants. Herbicides, fungicides, and algaecides are applied to terraces and floors or they are contained in wall paints and renderings to get rid of unwanted plants or to prevent plants, algae, and fungi growing for aesthetic reasons (Wittmer et al., 2010, 2014). In private households in several urban regions located in low- and middle-income countries, pesticides are used for cultivating plants for private purposes. Or they are used as vector control agents against malaria and other pathogenic diseases that are transferred by insects. In that case, more hazardous and persistent pesticides – carbofuran, DDT, dichlorvos, endosulfan, monocrotophos, profenofos, etc., which are banned in Europe or most other high-income countries – are often used (Mabaso et al., 2004; National Geographic, 2006). In high- and low- and middle-income countries, inappropriate disposal and cleaning of contaminated equipment can act as additional point sources of pesticide pollution, as well (Pesticide Action Network Asia and the Pacific, 2010; Wittmer et al., 2010). In low- and middle-income countries, inappropriate stockpiles of obsolete pesticides, originating from industrial countries, are acting as additional point sources of high amounts of hazardous pesticides (Elfvendahl et al., 2004; Dasgupta et al., 2010).

Hazardous and persistent pesticides - carbofuran, DDT, dichlorvos, endosulfan, monocrotophos, profenofos, etc. - are often used for control of disease transmitting vectors in low- and middle-income countries.

Use of pesticides and pollution trends and impacts

Data availability

It is generally difficult to obtain reliable data on pesticide use. In addition, comprehensive data about the production of pesticides is even more difficult to get hold of. This is true for high-income countries and it is particularly problematic for low- and middle-income countries. In general, according to the National Health Surveillance Agency and the Observatory of Pesticides of the Universidade Federale do Paraná, Brazil, it is safe to assume that during the last decade, the world pesticide market increased by 93%. The Brazilian market alone increased by 190% (Carneiro et al., 2012). Apart from that, in low- and middle-income countries, weakly implemented regulations and policies governing pesticide use and import, the stockpiling of obsolete pesticides, and poor education in pesticide storage and handling, have led to a high risk of occupational acute and chronic pesticide poisoning. These issues make it more difficult to assess data about pesticide production, import, and use. Currently, it is not possible to reliably assess the number of people affected by pesticide poisoning. Nevertheless, the WHO estimates that every year, around 3 million people globally might suffer from severe pesticide poisoning and the estimated number of unreported cases seems to be unpredictably high (Kesavachandran et al., 2009). In low- and middle-income countries it is impos-

Currently, it is not possible to reliably assess the number of people affected by pesticide poisoning. Nevertheless, the WHO estimates that every year, around 3 million people globally might suffer from severe pesticide poisoning and the estimated number of unreported cases seems to be very high.

sible to document systematic and authentic data about pesticide poisoning for many reasons. These include the lack of medical facilities, the farmers' lack of knowledge of the symptoms of pesticide poisoning, and the uncontrollable use of pesticides, particularly in remote small agricultural establishments.

In general, it can be said that worldwide, from 2 million to 2.4 million tonne of pesticides are consumed annually (Gupta, 2004; United States Environmental Protection Agency, 2011). According to the studies of Kesavachandran et al. (2009) and Gupta (2004) around 45% of this is consumed in Europe alone, 25% in the USA, and about 20–25% in low- and middle-income countries. Of all pesticides, the consumption of herbicides is highest, representing 47.5%, followed by insecticides at 29.5%. Fungicides account for 17.5% and others for 5.5% (Gupta, 2004). In our report, we focus mainly on the pesticides most used, and the pesticides having the highest negative effects on environmental and human health – herbicides and insecticides. Nevertheless, although such data is not readily available, some hot spots with high use of those pesticides can be identified (Figure 6).

Future trends and hot spots

The list of pesticides presented in Table 1 and the investigations of Roberts et al. (2003) show that exposure to OPs, OCs, bipyridylium herbicides, and carbamates poses high risks to human and environmental health. Several publications of international organizations and research institutes show that there are serious issues, especially in low- and middle-income countries, related to policies and regulations, application, storage, and disposal of pesticides (El Sebae, 1993; Eddleston et al., 2002; Pesticide Action Network Asia and the Pacific, 2010; United Nations Environment Programme and Food and Agriculture Organization, 2013; United Nations Environment Programme, 2013c, 2014). Today, the WHO Class II pesticides (as shown in Table 1) seem to be the most used and most hazardous ones, since the production of WHO Class I pesticides is being phased out and their use and trade abolished in the most parts of the world (Roberts et al., 2003). Implementation of the Rotterdam and Stockholm Conventions has resulted in the international trade in several obsolete and dangerous pesticides being abolished and has triggered a phasing out of the most toxic and persistent Class I and several Class II (WHO classification) pesticides. These include aldrin, chlordane, chlordecone, dieldrin, endrin, heptachlor, hexachlorobenzene, hexachlorocyclohexane, lindane, mirex, pentachlorbenzene, endosulfan, and toxaphene. In future, the consumption of OCs will decrease because of restrictions on and prohibitions of these compounds. This is because of their high persistence and their high toxicologic and bioaccumulative potentials. However, the use of pyrethroids will increase as they are used as substitutes for the banned OCs, OPs, and carbamates because of their lower toxicity to mammalian species (Fishel, 2014b; Luo and Zhang, 2011; Palmquist et al., 2012). Furthermore, the use of the lower toxic OPs and carbamates of WHO Class III or Class IV pesticides will increase as well.

Research shows that there are serious issues related to policies and regulations, application, storage, and disposal of pesticides, especially in low- and middle-income countries.

Figure 6 presents the worldwide average annual use of pesticides. Between 2001 and 2010, this ranged from 0 to 80 kg pesticide/ha of arable land according to data available from FAO (Food and Agriculture Organization, 2013). According to the datasets, the hot spots for pesticide application, with dosages ranging from 5.2 to 76 kg pesticides per ha of arable land, are the Bahamas, Maureta-

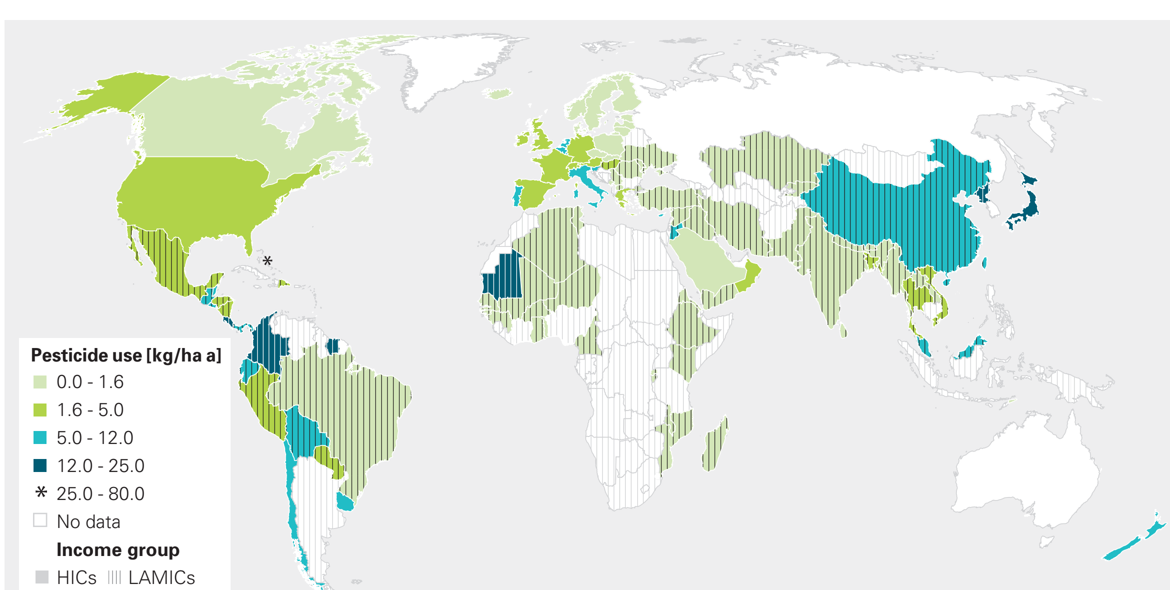


***Figure 6**: Average annual pesticide use for the period 2001–2010 ranged from 0 to 80 kg pesticide/ha of arable land (Food and Agriculture Organization, 2013). The shaded areas represent low- and middle-income countries.*

nia, Costa Rica, Colombia, North Korea, Suriname, China, Belize, Panama, Jordan, Ecuador, Guatemala, Malaysia, Bolivia, and El Salvador, in descending order of rate of application. However, these data have to be treated with caution since for several regions, especially Africa, South America, and Asia, there is a lack of data. This is especially the case for the rural regions and smaller agricultural communities in low- and middle-income countries where it is difficult to estimate the real amounts of pesticides applied. Often farmers in these regions are buying their pesticides unofficially and they do not really know the concentrations of the pesticides applied on their fields. For this reason, the amounts of pesticide applied may be underestimated for several regions (Pesticide Action Network Asia and the Pacific, 2010).

Figure 6 shows the average annual pesticide use for the period 2001–2010 and this forms the base layer for the components of Figure 7.

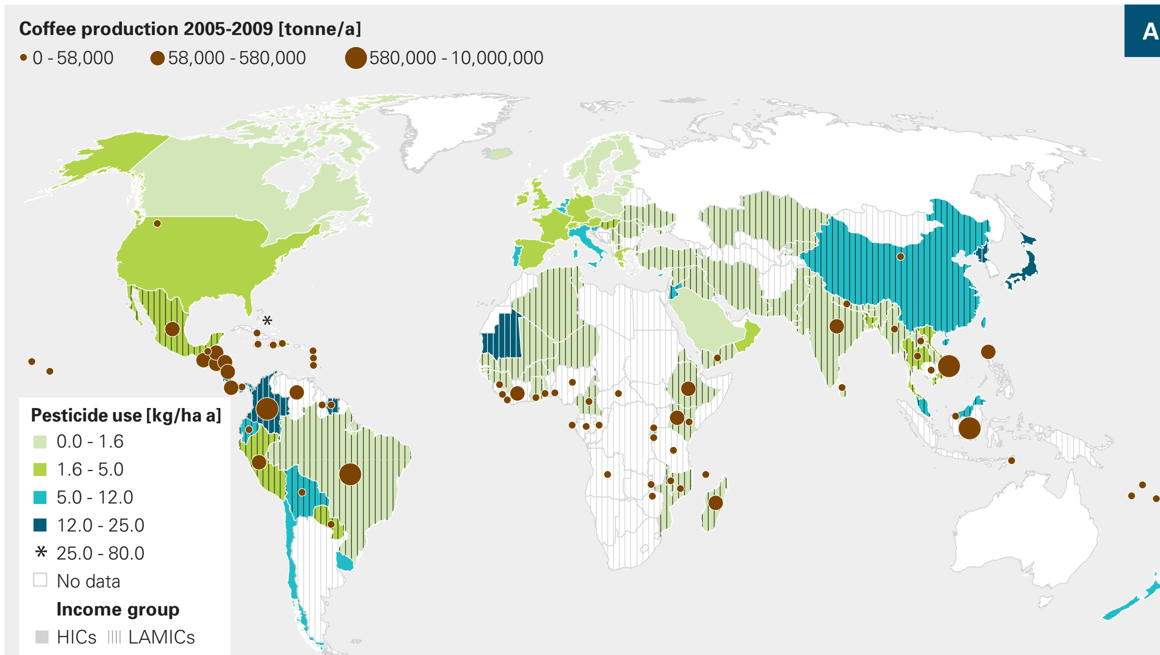
Figure 7 shows the worldwide average use of pesticides per hectare of arable land along with the annual average production (2005–2009) of crops requiring high volumes of pesticides. These include the permanent crops coffee (Rama and Jaga, 1992; Yang et al., 2011) and lemons and limes (Ortelli et al., 2005), and the temporary crop soybeans (Pizzutti et al., 2007) as the top layer (data from FAO; Food and Agriculture Organization, 2013). Although for the cultivation of palm trees (a permanent crop) less pesticides are required, as compared to most other commodities, data about palm oil production is shown as well. Mainly this is because it is well-known that for the cultivation of palm trees, large amounts of the extremely acutely toxic herbicide paraquat are used. In addition, these tropical trees are commonly cultivated in many different low- and middle-income countries (Teoh, 2010). By considering these data on crop production, it can be assumed that in middle America, northern and southern South America, west central Africa, southeast Africa, South Asia, and Oceania, higher amounts of pesticides might be used for the cultivation of these agricultural commodities than is suggested by the average pesticide use.

Impacts on environmental and human health

Pimentel (1995) predicted that of the amount of pesticide applied, only 0.1% to 0.3% comes into contact with the target pests directly or indirectly. Thus, 99.7 to 99.9% of the applied pesticide is dispersed into the environment and reaches non-target organisms, including humans. This might certainly be the case if obsolete methods and equipment are used in applying the pesticides. Mostly, pesticides can be dispersed into the environment through the air. If they are sprayed manually using a backpack spray tank or mechanically by a lawn sprinkler system, a plane, or a tractor, the unintentional drift of these substances can range from hundreds of meters up to several kilometers (Pimentel, 1995) depending on the method, weather conditions, and the degree of education of the person applying the pesticide. Afterwards residues of the pesticides remain and adsorb to plants, soils, and sediments, given their high potential for bioaccumulation. Additionally, pesticides can be leached out into drinking water aquifers by the rain and irrigation water or they can be transported by surface runoff into river systems. Humans can take up hazardous pesticides directly by inhaling the pesticide spray or ingest them by drinking or eating contaminated water or food. Some pesticides, such as paraquat, can even be absorbed directly through the skin during the preparation of the pesticide solution, through handling, or during the mixing process (Wester et al., 1984; Dinham, 2003).

Of the amount of pesticide applied, only 0.1% to 0.3% comes into contact with the target pests directly or indirectly. Thus, 99.7 to 99.9% of the applied pesticide is dispersed into the environment and reaches non-target organisms, including humans.

After exposure, pesticides often have adverse impacts on human health. Most of them, particularly the OPs, OC, and carbamates, are known to cause malfunctions in the brain and peripheral nervous system. Chronic exposure can lead to neurological, neurobehavioral, and psychiatric diseases and diminish intelligence (Salvi et al., 2003; Wu et al., 2012a). The pesticides which cause inhibition of cholinesterase – OCs, OPs, and carbamates – can affect the respiratory system. An affected respiratory system can be indicated by symptoms like coughing, discharging phlegm, and wheezing. In addition, pesticides can cause contact allergies and skin eruptions (Kesavachandran et al., 2009). Furthermore, OPs, OCs, and carbamates are known for causing malfunctions in reproduction through their endocrine disruptive potential. Moreover, there is evidence that chronic pesticide exposure can lead to several forms of cancer (López et al., 2007; Kesavachandran et al., 2009; Bedi et al., 2013). There are a many examples of private and occupational accidents involving pesticide poisoning in low- and middle-income countries that have led to adverse effects on human health or even to death. For instance, in the state of Mato Grosso do Sul,



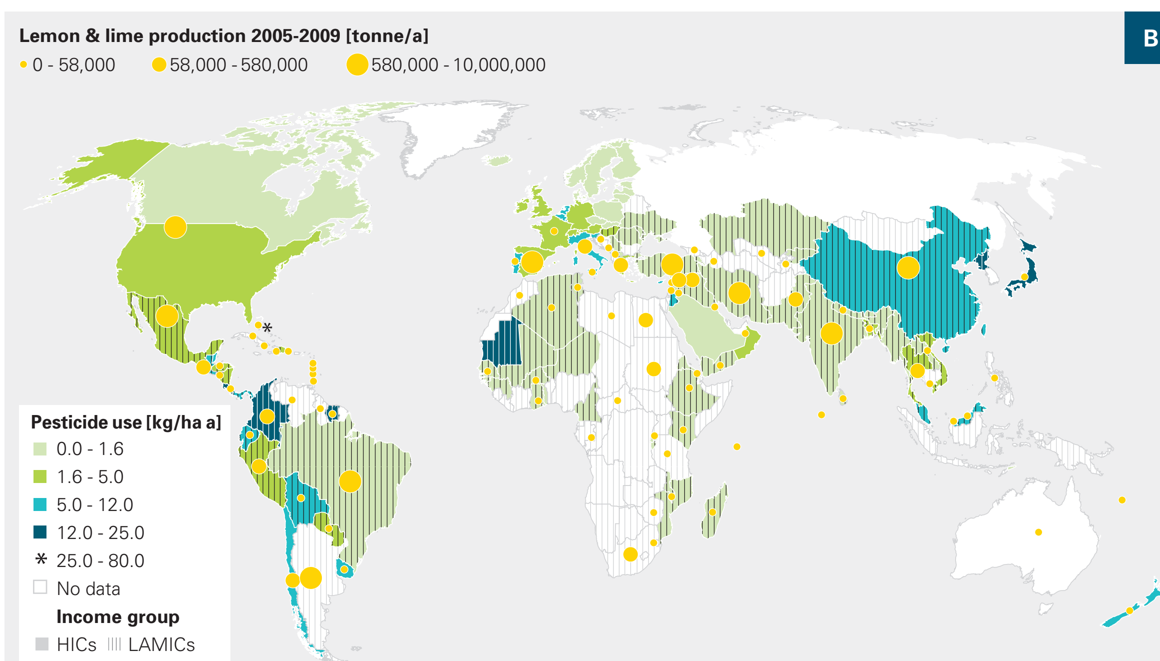
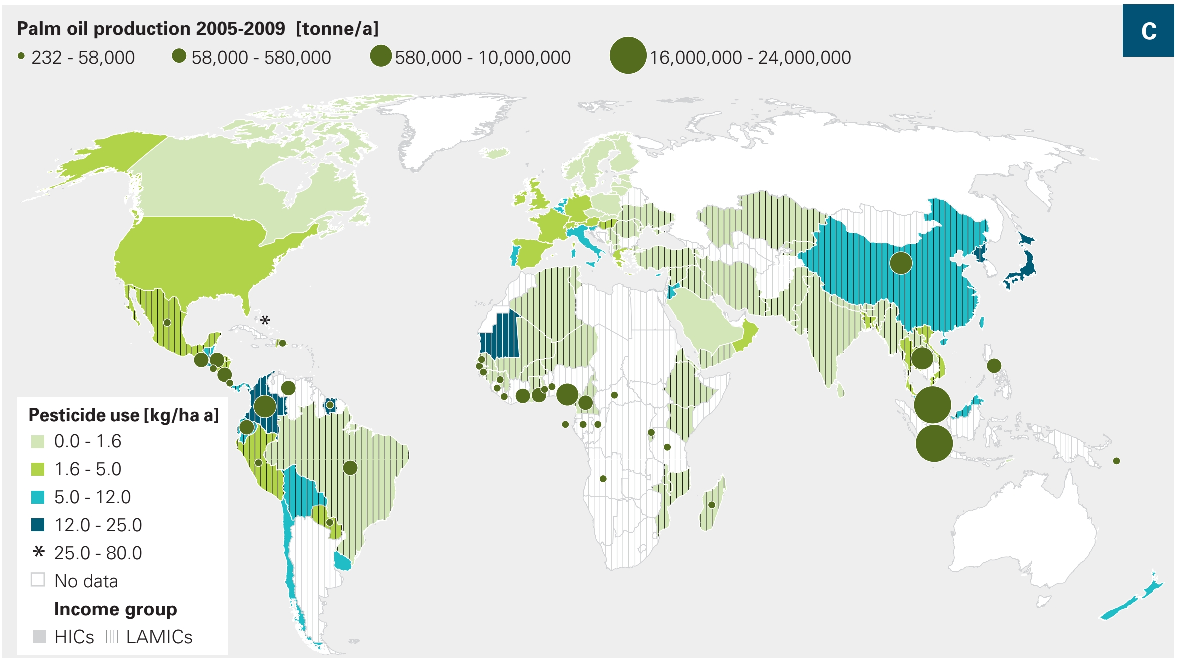
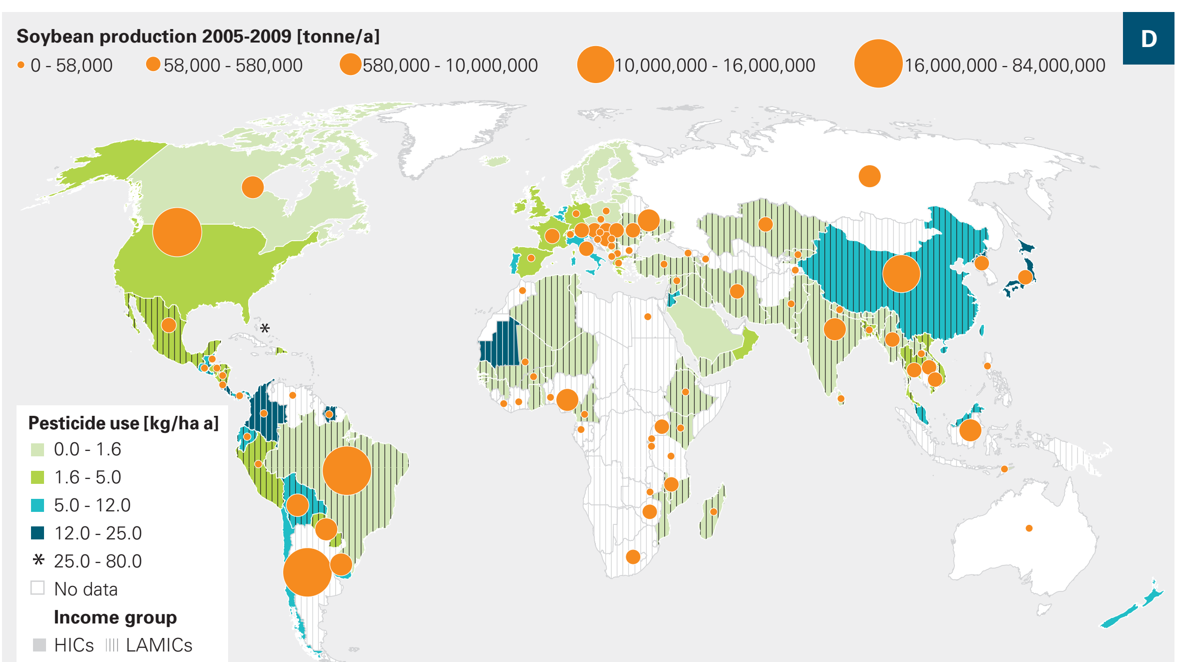


Figure 7*: Average annual pesticide use in 2001–2010 and the average annual A) coffee, B) lemon and lime, C) palm oil, and D) soybean production. For the period 2005–2009 production ranged from 0 – 84 million tonne (Food and Agriculture Organization, 2013). The shaded areas represent low- and middle-income countries.*

Brazil, between 1992 and 2002, about 123 persons suffered from acute pesticide poisoning. Of these, 46% were intentional self-poisonings and the rest were poisoned as a result of occupational and private incidents. In Brazil as a whole, 5185 people suffer pesticide poisoning annually. Of these, 31.1% are intentional and 68.9% unintentional poisonings (Recena et al., 2006). In the Warangal district in Andhra Pradesh, southern India, more than 1000 pesticide poisoning cases have been observed annually, leading to 200–400 deaths. In 2002, the majority of deaths were caused by the pesticides monocrotophos and endosulfan (Srinivas Rao et al., 2005). A recent headline event covering pesticide poisoning concerned 23 school children who died after eating a school lunch in eastern India. Forensic tests revealed that the meal was contaminated with oil containing residuals of the WHO Class Ib OP, monocrotophos. This is a product that has been banned already in many countries (ABC News Online, 2013).

Besides the observed adverse health impacts to humans, exposure to pesticides can have disastrous consequences for the health of the environment as well. Vertebrates and mammals are often highly susceptible to pesticides. For instance, OCs cause eggshell thinning in birds (Lundholm, 1997). OPs and carbamates are posing high risks to mammals (Kwon et al., 2004) and herpetofauna be-





cause of their high toxicity, their large-scale application in agriculture (Story and Cox, 2001), and, especially, their inhibition of acetylcholinesterase activity. Furthermore, these pesticides and the pyrethroids affect the reproduction of amphibians as well because of their estrogenic activity (Pawar and Katdare, 1984; Kojima et al., 2004). The pyrethroids are less toxic to mammals than the OCs, OPs, and carbamates (Palmquist et al., 2012). Other pesticides act as endocrine disruptors as well. Tests with animals showed that the triazine herbicides can hinder the reproduction of mammals because of their antiandrogenic activity (Stevens et al., 1994; McMullin et al., 2004). Because of their high toxicity, potential to adsorb to organic material, soils, and sediments, or their persistence in water systems, OPs, carbamates, triazines, bipyridylium herbicides, and pyrethroids harm non-targeted invertebrates located close to pesticide treated areas (Fukuto, 1990; Köck-Schulmeyer et al., 2013). At present, there are plenty of publications about other non-target organisms that are affected by exposure to pesticides. For instance, in several regions, honey bee (*Apis mellifera*) populations are endangered. It has been proven that pesticides are causing significant delays in the development of bees. Furthermore, the exposure to pesticides is making bees more susceptible to viral, spore, and bacterial infections and these are showing sub-lethal effects (Wu

Organochlorines cause eggshell thinning in birds; organophosphates, carbamates and pyrethroids affect the reproduction of amphibians because of their estrogenic activity; triazine herbicides can hinder the reproduction of mammals because of their antiandrogenic activity; organophosphates, carbamates, triazines, bipyridylium herbicides, and pyrethroids harm nontargeted invertebrates located close to pesticide treated areas (e.g. honey bees).

Worldwide, 400,000 to 500,000 tonne of obsolete pesticides are stockpiled in low- and middle-income countries.

et al., 2011a). Bees and other pollinators are very important in most terrestrial ecosystems. They guarantee genetic variation in the plant community and flora diversity, specialization, and evolution. The production of seeds, nuts, and fruits relies on pollination; in the absence of bees and other pollinators, many species of plants and animals would not be able to survive (Bradbear, 2009).

Also, other invertebrates are affected adversely by contamination with of pesticides. For instance, the crustacean *Americamysis bahia* and the branchiopoda *Ceriodaphnia dubia* are sensitive to pyrethroids, having a low LC_{50} after 10 days of exposure, ranging from 2 to 140 ng/L. The amphipod crustacean *Hyalella azteca* has a low LC_{50} after 10 days of exposure of from 4 to 110 ng/L (Hladik and Kuivila, 2009). The carbamates, bipyridylium, and triazine herbicides are known to cause inhibition of nucleic acid metabolism and protein syntheses and affect photosynthetic activity (Audus, 1976; Ebert and Dumford, 1976; Moreland, 1980; Ocampo and Barea, 1985; Morais et al., 2012). The non-selective bipyridylium herbicides are known to promote oxidative stress as a result of producing reactive oxygen species (Pasternak et al., 2007) or for destroying plant cell membrane (Fishel, 2014a).

For instance, 0.5 mg/L atrazine completely inhibits the autotrophic growth of *Chlamydomonas reinhardtii* (Helling et al., 1971) and 1 mg/L of atrazine, paraquat, or diquat is able to inhibit photosynthesis and growth or kill the cyanobacteria *Anabaena azollae* after 10 days of exposure (Holst et al., 1982). In addition, although the amounts of atrazine that are affecting the growth of *Chlamydomonas reinhardtii* are quite high, field studies showed that atrazine concentrations of even 50 µg/L or greater were ecologically relevant (Solomon et al., 1996). The primary producers (algae, cyanobacteria, and other plants) are important for sustaining the high quality of the aquatic habitat, which enables other organisms, such as invertebrates and vertebrates, to survive and settle down. Chronic exposure to herbicides may lead to a reduction of primary production which consequently can have adverse effects on the survival, growth, and reproduction of herbivores and predators, leading to disruptions of the food chain (Solomon et al., 1996). According to data obtained by FAO (Food and Agriculture Organization, 2013), the highest risk areas for environmental and human health from exposure to pesticides seem to be in middle America, northern and southern South America, west, central and southeast Africa, and south and east Asia. This assessment is based on the annual amounts of pesticide used (kg per ha of arable land) and the amount of crops produced that require large amounts of pesticides (or highly toxic ones) for their growth.

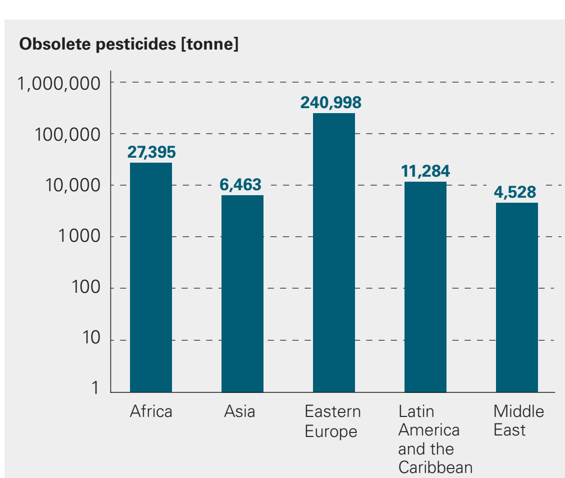


Figure 8: *Volumes of obsolete pesticides stockpiled in different areas of the world (Food and Agriculture Organization, 2015a)*

Issues of special concern

Inadequate storage

The stockpiling of obsolete pesticides is a serious problem in many low- and middle-income countries (Elfvendahl et al., 2004; United Nations Environment Programme, 2013c). After they were banned, their registrations withdrawn, or because of international policy decisions and conventions, several stocks of highly toxic and persistent pesticides, which were being phased out, were transferred from high-income countries and deposited in low- and middle-income ones. For instance, DDT, lindane, aldrin, atrazine, endosulfan, chlordane, heptachlor, metazachlor, and pendimethalin are examples of these obsolete pesticides that have been transferred. Today, these unwanted pesticides are often a severe source of pollution because they are stored under inadequate and unsafe conditions, thus posing high risks to human and environmental health (Elfvendahl et al., 2004). Examples of these stockpiled obsolete pesticides were found in low- and middle-income countries all over the world (García de Llasera and Bernal-González, 2001; Haylamicheal and Dalvie, 2009; Dasgupta et al., 2010). FAO published data about the volumes of pesticides which were disposed of inappropriately and under unsafe conditions (Figure 8). At present, they estimated that, worldwide, 400,000 to 500,000 tonne of obsolete pesticides are stockpiled in low- and middle-income countries (Food and Agriculture Organization, 2001). Of this amount, about 50,000 tonne are found in Africa alone (United Nations Environment Programme, 2003, 2013). Figure 8 shows that the highest amounts of stockpiled pesticides can be found in eastern Europe; Russia, Macedonia, Ukraine, and Uzbekistan have the highest volumes. Africa has the second highest volume with Mali, Tanzania, and Tunisia holding the highest amounts of these pesticide legacies. It is estimated that it would need US$1.25 billion to clean up this amount of obsolete pesticides (Food and Agriculture Organization, 2015a).

Case study of obsolete pesticide stockpiles

One good example of a country with a legacy of obsolete pesticides is Tanzania. There, according to estimates of the Food and Agriculture Organization of the United Nations, about 1500 tonne of obsolete pesticides were stockpiled in the whole country in 2008 (Food and Agriculture Organization, 2015b). In Arusha and Tanga, 470 L of atrazine, 10 kg pirimiphos methyl + permithrin, 11 kg benomyl, 40 tonne DDT, 8 tonne endosulfan and 3000 L dinitro-ortho-cresol were found (Rwazo, 1997). In 1989 in the Co-operative and Rural Development Bank warehouse in Mikocheni, about 11,000 L and 350 kg of the OPs Damfin P (methacrifos) and phosphamidon and the fungicide Thiovat (sulfur) were found. In 1993, according to a survey conducted by the Tanzania-Germany Project on Integrated Pest Management 40,000 L of obsolete pesticides – endosulfan, flumeturon, atrazine, malathion, methidathion, and DDT – were found in Mwanza and Shinyanga in the southern region close to the Lake Victoria. Additionally, 50 tonne of DDT, lindane, aldrin, chlordane, heptachlor, and endrin were located at Vikunge farm (Rwazo, 1997). Today, after removal of the obsolete pesticides at Vikunge farm, there are still high concentrations of pesticides found in this region. Soil samples taken to a depth of from 0 to 5 cm contained 12 to 282 g DDT and 23 to 63 g lindane per kg dry weight. Even after a cleanup of obsolete pesticides, these storage areas are often highly contaminated with pesticide residuals. Tap water at Vikunge farm was contaminated for years after the pesticide cleanup. In 2000, it was showing pesticide concentrations of 0.95 μg/L lindane and 1.7 μg/L DDT. Often only the visible remains of pesticides, the tanks and packages, are removed instead of a systematic removal of the soils within the contaminated areas (Elfvendahl et al., 2004).

Inadequate handling and lack of education

Inadequate handling and inappropriate application of pesticides poses another risk to human and environmental health in low- and middle-income countries (Eddleston et al., 2002; Kesavachandran et al., 2009). Often no personal protective equipment, such as rubber gloves, boots, breathing masks, googles, and coats, are worn because they are too expensive and uncomfortable to wear in the heat and high humidity present in tropical regions. In addition, the agricultural workers are not well educated in handling pesticides. In these countries the level of illiteracy is quite high and farmers are often not able to read or understand the safety precautions printed on the pesticide packages. Up to one-third of agricultural workers in low- and middle-income countries read the safety instructions on the packages, while only 1.5% understand the color coding system that presents information about the toxicity of the pesticide being used (Kesavachandran et al., 2009). These workers are not aware of the consequences resulting from acute or chronic exposure to hazardous pesticides. Often, untrained farmers were blending several hazardous pesticides together trying to increase their effect without knowing if these mixtures are useful or not. A lot of agricultural workers in low- and middle-income countries are continuously exposed to pesticides in several processes, like mixing pesticides (as mentioned previously sometimes pesticides were even blended together by hand), cleaning, and loading spray equipment. They are also exposed through inadequate manual application, by not considering the wind direction when spraying, or by wearing contaminated clothes for days. They are in direct contact with pesticides and they are often not able to wash off pesticide spillages because water is not always available (Eddleston et al., 2002; Kesavachandran et al., 2009; Pesticide Action Network Asia and the Pacific, 2010; United Nations Environment Programme, 2013c). Furthermore, pesticides are stored in their kitchens and living rooms posing risks to human health, especially to children and pregnant women (Pesticide Action Network Asia and the Pacific, 2010). Deliberate self-poisoning through pesticide ingestion is a big problem as well. This comes about because of the easy access to highly toxic pesticides. In the event of contamination, especially in rural regions, there is not much knowledge of how to interpret the symptoms of pesticide poisoning. In addition, there are few or no medical services accessible. In these regions there are too many patients and too few medical facilities, pharmaceuticals, antidotes, and doctors. There is little evidence that people know how to treat poisoned patients properly (Eddleston et al., 2002; Pesticide Action Network Asia and the Pacific, 2010).

A lot of agricultural workers in low- and middle-income countries are continuously exposed to pesticides during mixing of pesticides, cleaning, or loading of spray equipment. Workers are neither aware of the risks nor of the consequences resulting from acute or chronic exposure to hazardous pesticides.

Case study of inadequate pesticide handling

A survey conducted by PANAP (Pesticide Action Network Asia and the Pacific, 2010) in eight Asian countries (Cambodia, India, Sri Lanka, Indonesia, Philippines, Vietnam, Malaysia, and China) showed that farmers and agricultural workers in those regions are often not well educated in the adequate handling of and appropriate application methods for pesticides. The survey showed that mostly the workers are not wearing adequate protective clothing. For instance, in most of the regions surveyed (An Gian, Andhra Pradesh, Digos, Orissa, and Yunnan) only 1–5% of the farmers wore gloves when applying pesticides. In An Gian, Andhra Pradesh, Digos, Orissa, Prey Veng, Sri Lanka, and Yunnan only 0–13% wore overalls and in most of the regions (An Gian, Andhra Pradesh, Orissa, Sri Lanka, and Yunnan) only 0–19% were equipped with masks during pesticide application.

The survey showed that the blending of different hazardous pesticides is another issue. For example in Prey Veng, Cambodia, farmers blended from three to eight different pesticides together. In Hai Van, Vietnam, about three different pesticides were blended together. Often the field workers had no idea which kind of pesticides they were using. Furthermore, the survey revealed that in most of the regions (Andhra Pradesh, Orissa, Nam Dinh, Prey Veng, Sarawak, Sri Lanka, Yunnan) from 77% to 90% of the agricultural workers have never received any training on the pesticides they use in their fields. According to that it would appear that they are often not aware of the toxicity of these pesticides and that they follow bad practices when using pesticides.

Inappropriate regulation and implementation

Another critical point is the inappropriate implementation of government and international regulations and restrictions on pesticides in low- and middle-income countries. In these regions, the governments do not have the resources to enforce and control the availability and the use of pesticides, in part because there is a lack of pesticide registration processes and government infrastructure. Where there are regulations and restrictions governing pesticide use, they often differ markedly between countries. This encourages the illegal import of more toxic, but less expensive pesticides from neighboring countries (Roberts et al., 2003). Strengthening international regulations and initiating additional international conventions, like the Stockholm and Rotterdam ones, would solve this problem. The responsibility for controlling the circulation, safety, and use of hazardous pesticides should rest more on the importers, exporters, manufacturers, and the pesticide industry in general (Eddleston et al., 2002).

Best practices

A more sustainable and secure use of pesticides is required. Currently, there are several government and non-governmental initiatives to control and improve the use of toxic pesticides. Some theoretical approaches as well as some methods that have been implemented already are described below.

Implemented examples

Initiatives and conventions in sound chemical management and consumption

Currently, there are several approaches to achieving more sustainable and ecological agriculture. For instance, the main goal of the Rotterdam Convention is to control and ban the international trade in certain hazardous chemicals, including 32 pesticides. It also seeks to avoid the stockpiling of obsolete pesticides in low- and middle-income countries to prevent environmental and human health hazards. In addition, another objective is to guarantee the sound use of chemicals by giving information about chemical characteristics and labeling toxic chemicals with safety instruction and pictograms (United Nations Environment Programme and Food and Agriculture Organization, 2013). The Stockholm Convention is an international agreement which focuses on abolishing highly persistent, bioaccumulative, and toxic chemical compounds (United Nations Environment Programme, 2013d). In addition there are several non-governmental organizations (NGOs), such as Global Good Agricultural Practices (GlobalGAP) and the PAN organizations, trying to improve or enforce the sound use of pesticides. GlobalGAP is a European non-profit organization that defines voluntary standards for the certification of production processes for agricultural products worldwide. This organization was established to show consumers that agricultural commodities were being produced using sustainable production techniques and smaller amount of pesticides and other agro-chemicals, and to ensure that the working conditions and the animal husbandry practices were fair and safe (GlobalGAP, 2016). PAN is a network, including over 600 participating NGOs, individuals, and institutions, operating in more than 90 countries. Its main objective is to reduce and replace the use of hazardous pesticides with ecologically sound approaches. It has five independent collaborating regional centers located in North America, Latin America, Europe, Africa, and Asia and the Pacific region (Pesticide Action Network International, 2014). For example, PAN Asia and the Pacific conducted a community monitoring study to investigate the effects of pesticides in 12 communities in eight Asian countries. They interviewed 1304 people from the agricultural sector, including vegetable, paddy, and cotton farmers and workers in crop fields and palm oil plantations. They studied which of them used pesticides and which pesticides were the most toxic (paraquat, endosulfan, monocrotophos, etc.). They investigated, if the workers had been educated in the handling, use, and storage of pesticides and if they wore personal protective equipment. Studies like this are helping us to understand and highlight issues in pesticide use and, consequently, to find some solutions to these problems. Furthermore, they are teaching workers how to handle pesticides and what alternative methods could be used for agriculture, for example keeping away unwanted pests by using traps or pheromone traps or predators of the pests (Pesticide Action Network Asia and the Pacific, 2010).

The investigations of Roberts et al. (2003) showed that establishing regulations alone will not always be sufficiently effective to minimize the risks of hazardous pesticides to human and environmental health. For instance, at the beginning of the ban of WHO Class I pesticides in 1995, in Sri Lanka the number of deaths decreased significantly. Three years after this ban, the Class I OPs were substituted with endosulfan and carbamates causing even more deaths than before. This Sri Lankan case indicates that more adjustments and arrangements have to be made than just changing regulations to achieve significant improvements in the long term. Occupational and intended pesticide poisonings could be reduced according to a three step system.

1. eliminate the most hazardous pesticides using regulations and controls and introduce alternative and more sustainable methods to reduce the infestations of pests
2. have people who are trained in the handling of pesticides administer the controls. Only workers who are trained should be allowed to apply pesticides. Pesticides should never be stored at home. They should be stored in community stores with lockers available only to trained individuals. In addition, pesticide exposure should be monitored and controlled regularly
3. personal protective equipment should be used to guarantee safe and healthy working conditions and the medical management of pesticide poisonings needs to be improved to minimize the sequelae of pesticide poisoning (Murray and Taylor, 2000; Roberts et al., 2003).

Extension of data collection

It is important to collect more data about the spatio-temporal distribution of pesticides among the environmental compartments air, water, soil, and biota. This is necessary to obtain more detailed information about the toxicity of pesticides used in the past, present, and future. In future, it will be relevant to investigate the combined effect on environmental and human health of different pesticides or mixtures of pesticides and other anthropogenic agents. Chemicals can be measured directly in soils (Elfvendahl et al., 2004), air, and water (Karlsson et al., 2000) and pesticide residues can be measured indirectly in fruits and vegetables or in animal and human blood samples. For instance, Lehotay et al. (2005) developed a quick, easy, cheap, effective, rugged and safe method based on gas chromatography coupled with mass spectrometry with an ion trap instrument to identify different pesticides in lettuce and oranges. In addition, PAN, together with the European Food Safety Authority and the Swedish Chemicals Agency, are highlighting a selection of endocrine disrupting pesticides found in fruits, vegetables, milk, and eggs (Pesticide Action Network Europe, 2013). Dulaurent et al. (2010) developed a general screening method to determine and quantify pesticides in blood samples. To obtain their measurements they used LC coupled with a single linear ion trap mass spectrometer. With their method it is possible to detect more than 320 different pesticides and metabolites in blood, serum, plasma, and urine samples (Dulaurent et al., 2010).

Low cost approaches

To reduce the number of deaths caused by pesticides in low- and middle-income countries it is important to find cheap and easy methods, which are available in these countries, to monitor pesticide contaminations or for fast diagnosis of poisoning. For instance, the Securetec Detektions-Systeme AG company, Brunnthal, developed, in cooperation with the Bundeswehr Institute of Pharmacology and Toxicology, a rapid and cheap (about €3770 for the applicator and 100 test kits; Mark Johnson (Securetec), personal communication *in vitro* detector which can give information about poisoning by OPs, carbamates, or other nerve agents. Detection is based on the photometric analysis of acetylcholinesterase (AChE) or butyrylcholinesterase (BChE) activity. The inhibition of AChE and BChE is the predominant indicator of poisoning caused by OPs and carbamates. With this tool it is possible to get results within several minutes. The tool is easy to handle and it can be used in the laboratory or in field studies at temperatures ranging from 10° to 50°C (Securetec AG, 2013).

More data and analysis on the spatio-temporal distribution of pesticides and the combined effect on environmental and human health of different pesticides or mixtures of pesticides and other anthropogenic agents is needed.

García-Santos et al. (2011) introduced a low cost method to monitor the drift of airborne pesticides after application using a knapsack sprayer. For their studies, they used a test field of 380 m^2 in Tunja, Columbia. To measure the air born drift of pesticides, highly absorbent papers were fixed at various distances up to 20 m downwind and next to the treated area. Droplet deposition inside the test field and on the applicator was determined as well by installing highly absorbent paper inside the test field and on the applicator. The test solution (for instance water) was sprayed by a farmer under stable weather conditions at low radiation intensity. Afterwards, the distribution and the deposition of potential airborne pesticides in exposed fields next to the test one, inside the test field, and directly at the applicator were determined. This was achieved using a cheap and simple weight method – absorbent papers were weighed directly before and after the application of the test substance. These results were evaluated according to a simple mass balance approximation. In the end, they showed that by using the weight method they were able to explain about 86% of the airborne drift and deposition variance (García-Santos et al., 2011).

Theoretical examples

Improvement of existing regulations

As already mentioned in the chapter "Input pathways of pesticides", internationalizing and generalizing regulations on pesticide use, export, import, and production would help to interrupt the circulation of highly toxic and illegal pesticides. Although there are some international conventions about pesticide use, as a status quo they do not seem to be effective enough. Furthermore, hazardous pesticides, the application of which requires the use of proper and expensive personal protective equipment (overalls and respirators) – especially the majority of the phase I and II pesticides – should be prohibited in low- and middle-income countries, where the appropriate application of the pesticide cannot be guaranteed (Roberts et al., 2003). In addition, there should be more investigation of chronic exposure of humans, animals, and the environment to pesticides. Mostly, the toxicity of pesticides is determined and classified through the investigation of acute animal tests (World Health Organization, 2010b). However, the effects of a long-term exposure of the environment, animals, and humans to pesticides are quite unclear. Moreover, the research on and the use of improved and more specific pesticides, which are potentially less bioaccumulative and toxic, such as most of the pyrethroids, should be promoted and extended. Maybe funding for the use of less toxic pesticides and/or the application of organic agricultural practices could help to reduce the production and the use of pesticides with high toxicity.

More data on the production, application, uses, and distribution of pesticides are required. Often in low- and middle-income countries, monitoring and risk assessment is challenging or impossible because of the scarcity of data and the uncontrolled use of unregistered pesticides. If comprehensive data about

- pesticide use (use rates and concentrations)
- application (application rates and which pesticides are used in which region for each crop)
- crop and pesticide production
- the import and export of pesticides

were available, it might be possible to conduct preliminary risk assessment studies. These would localize high risk areas where further investigation was needed to mitigate the risks to human and environmental health associated with exposure to pesticides.