Impact of pesticides on environmental, health, and agriculture sustainability

Impacto de los pesticidas en la sustentabilidad ambiental, sanitaria y agrícola

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Abstract

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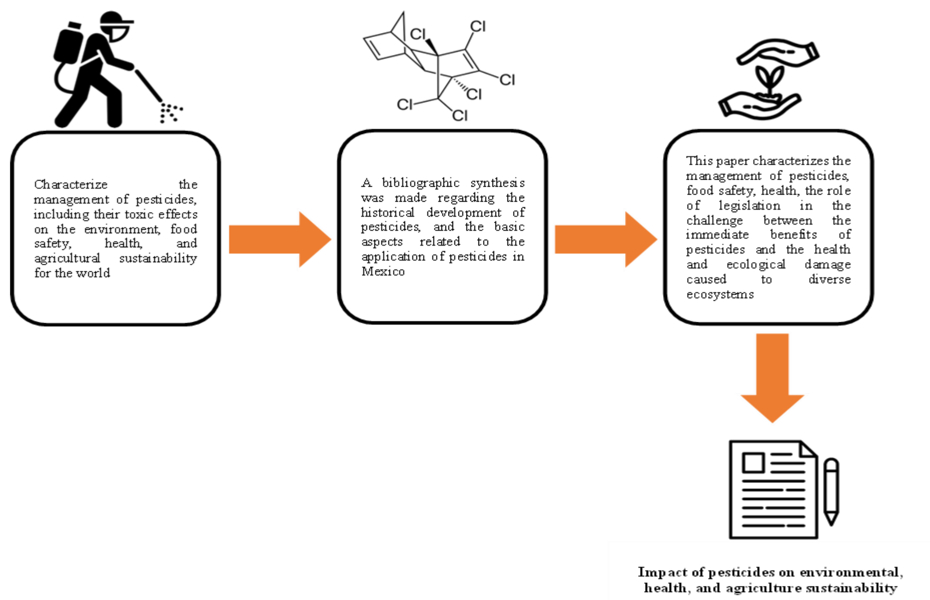
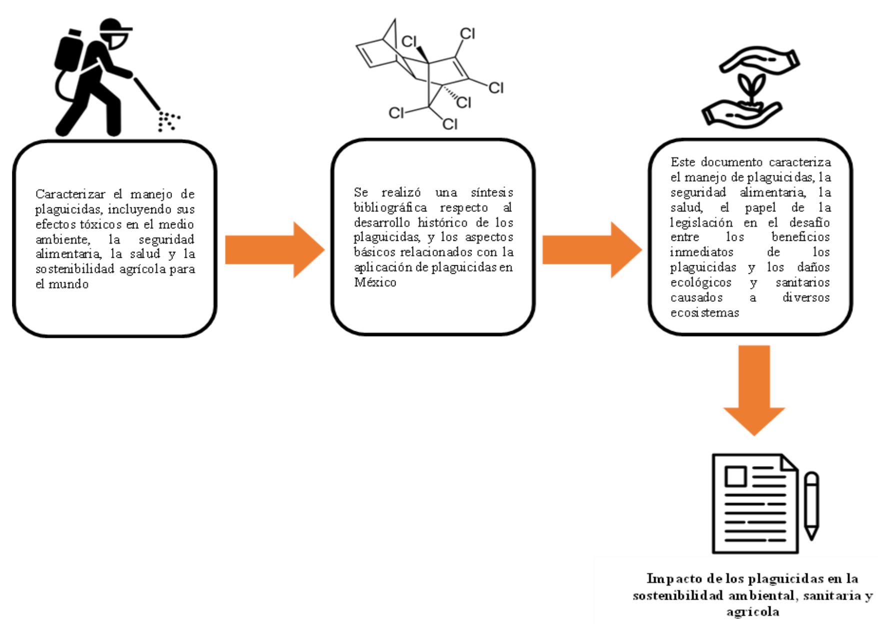


Food security, Agricultural, Sustainability, Legislation, Ecological

Resumen

La agricultura mexicana ha incorporado en gran medida un modelo tecnológico dependiente de plaguicidas. Este manejo y sus efectos tóxicos se evidencian en las zonas de mayor actividad agrícola. El objetivo de este trabajo es caracterizar el manejo de plaguicidas, incluyendo sus efectos tóxicos sobre el medio ambiente, la seguridad alimentaria, la salud y la sostenibilidad agrícola para el mundo. En este sentido, se realizó una síntesis bibliográfica respecto al desarrollo histórico de los plaguicidas, y los aspectos básicos relacionados con su aplicación en México. Este artículo también proporciona evidencia de los efectos nocivos de los plaguicidas en la salud humana y el impacto de su residualidad en ambientes bióticos y abióticos. También analiza el papel de la legislación en el desafío entre los beneficios inmediatos de los plaguicidas, los daños ecológicos causados a diversos ecosistemas y los daños a la salud. La información contenida en él capítulo apoyará a cualquier persona involucrada o relacionada con la producción agrícola sostenible.



Seguridad alimentaria, Agrícola, Sostenibilidad, Legislación, Ecológico

Introduction

The term pesticide is generally used to identify agrochemicals to prevent, control, or destroy unwanted species that interfere with the production, storage, transportation, and drying of food, wood, and wood products (Pereira *et al.*, 2021; Tudi *et al.*, 2021). Pesticides can be grouped into different chemical families, such as: Organochlorines (**OCPs**); organophosphates(**OPPs**); organofluorines; carbamates; pyrethroids; bipyridyl herbicides; triazine herbicides; triazoles; and chloroacetanilide herbicides (Tudi *et al.*, 2021). Globally, about 2 million t of pesticides are utilized each year (Bhattu *et al.*, 2021). Their functions are expressed with varying degrees of toxicity that are related to the Median Lethal Dose (**LD_{50}**) parameter (Weis *et al.*, 2019), and for field handling, the container is identified with a color (Kaur *et al.*, 2019). The chemical nature and physical properties of these compounds make them especially toxic by altering structures and functions of fundamental biomolecules (Nagy *et al.*, 2020), consequently blocking cellular homeostasis and damaging vital processes (Machado and Martins, 2018). They are abundantly used in agriculture to control pests (Afshari *et al.*, 2021), in industry as solvents (Musarurwa and Tavengwa, 2021), in petroleum additives (Purkait and Hazra, 2020), and in treatment of green areas, water reservoirs. and cleaning of physical spaces (Wang *et al*., 2021). It is estimated that, by 2023, there will be 1,600 Active Ingredient (**a.i.**) (Zhang and Yang, 2021), which will generate more than 50,000 products registered as pesticides in the world (Kalyabina *et al.*, 2021). The World Health Organization (2022) has estimated that about 3 million workers in developing countries experience severe poisoning from pesticides each year, of which approximately 18,000 of those affected eventually die. This paper will review, in greater depth: i) the historical development of pesticides; ii) the application of pesticides in Mexico; iii) the harmful effects of pesticides on human health; iv) the harmful effects of pesticides on biotic and abiotic media; and v) legislation on the use of pesticides.

1. Historical development of pesticides

Pesticides are any substance or mixture of substances which purpose is to prevent, destroy, repel, or control a pest (Pesticide Action Network, 2017). There are different types of pesticides, and each serves to combat specific pests. For example: i) insecticides to control insects; ii) herbicides to kill or inhibit the growth of unwanted plants (also known as weeds); and iii) fungicides to control fungal problems, such as mold, mildew, and rust (Silveira *et al.*, 2018; Pesticide Action Network in Mexico, 2022) (Table 1):

Box 1

Table 1

General classification of the most frequently used pesticides worldwide

Pesticide	Class: Substance
Insecticide	Carbamate: Aldicarb, Pirimicarb, Carbofuran, Carbary1, Propoxur, Oxamyl, Terbucarb
	Neonicotinoid: Acetamiprid, Thiamethoxam
	OCPs: Endosulfan, Lindane, DDT, Dieldrin
	OPPs: Diazinon, Fenthion, Malathion, Ethion, Parathion, Phosphamidon, Dimethoate, Dichlorvos, Chloropyrifos, Mevinphos, Oxydemeton-methyl, Methamidophos, Monocrotophos, Disulfoton, Isofenphos, Carbophenothion
	Phenylpyrazole degradate: Aldicarb sulfoxide
	Pyrethroid: Deltamethrin, Fenpropathrin, Permethrin
Herbicide	Aminophosphonates: Glyphosate
	Benzamide: Fluopicolide, Zoxamide
	Cloroacetamide: Alaclor, Butachlor, Dimethenamid, Metolachlor
	Quaternary nitrogens: Paraquat dichloride
	Substituted urea: Diuron
	Triazine: Atrazine, Cyanazine
Fungicide	Carboxamide: Boscalid, Captofol
	Chlorinated hydrocarbon: Hexachlorbenzene
	Chlorophenyl: Dichloran, Quintozene
	OPPs: Edifenphos, Iprobenfos

OCPs: organochlorines; OPPs: organophosphates.

(Pesticide Action Network in Mexico, 2022)

There are also other types of pesticides with less global use, such as algaecides to kill algae and/or slow their proliferation, and rodenticides to kill rodents, such as mice and rats (Pesticide Action Network, 2016). The chemical synthesis of pesticides, as well as their applications, got a significant boost from the study done by the Food and Agriculture Organization (**FAO**) in 1995 to analyze losses due to pathologies, pests, and weeds in 60 crops (Kang *et al.*, 1995). In 1998, the world consumption of pesticides was worth $34.15 billion USD, of which North America accounted for $9 billion USD, and Latin America (**LA**) represented 10% of the total, equivalent to about $3 billion USD (Sidhu *et al.*, 2019).

In the late 19th and early 20th century, data appeared on the benefits of using Bt cotton, the result of biotechnology, in the field of biopesticides (Meghana *et al.*, 2018). Cotton was genetically modified with the inclusion of a strain of Bacillus thuringiensis, and researchers showed the benefit of using the bacterium via four factors: i) increased yield; ii) lower cost for production; iii) lower expenditure of additional pesticide; and iv) lower number of intoxications (Fleming *et al*., 2018; Tokel *et al.*, 2021).

This research directly favored the production, transport, and application of the transgenic/pesticide binomial in Mexico (Nava *et al.*, 2019). OPPs were introduced shortly after OCPs, a group of semi-volatile pesticides, characterized by having carbon and chlorine atoms bonded in their structure, which entered the Mexican market in the 1950s (Valdez *et al.*, 2000). Their consumption was on the rise, so much so that, in 1995, 54,678 t were used; 47% were insecticides, 29% herbicides, 17% fungicides, and 7% others, with 200 brands of products, including 24 banned and 13 restricted (Sanchez *et al.*, 2011). During 2017, pesticide production in Mexico was over 106 thousand t (Leyva *et al.*, 2017a). According to the consultation of Sanitary Registrations of Pesticides, Plant Nutrients and Maximum Residue Level (**MRL**), for their use by the Federal Commission for the Protection against Sanitary Risks (2022), 2,070 a.i. were manufactured in Mexico, during 2019, across more than 230 companies. The World Health Organization (2022) classifies pesticides (Table 2), based on their toxicity, into: Extremely hazardous (I_a); Highly hazardous (I_b); Moderately hazardous (II); Slightly hazardous (III); and Unlikely to present acute hazard (IV). For example, the insecticide OPPs Dichlorvos cholinesterase inhibitor is Highly hazardous (I_b) and has LD_{50} of 5-50 mg/kg body wt. (Zhang *et al.*, 2021).

Box 2

Table 2

World Health Organization recommended classification of pesticides

Class	Toxicological bands	LD_{50} for rats mg/kg body wt. Oral	Dermal	Examples
I_a	Extremely hazardous	< 5	< 50	Parathion, Dieldrin
I_b	Highly hazardous	5 – 50	50 - 200	Aldrin, Dichlorvos
II	Moderately hazardous	50 – 2000	200 - 2000	DDT, Chlordane
III	Slightly hazardous	> 2000	> 2000	Malathion
IV	Unlikely to present acute hazard	5000 or higher	-	Carbetamide, Cycloprothrin

LD_{50}: Median Lethal Dose.

(World Health Organization, 2022)

The use of pesticides over the last 4 decades requires deep inspection. Originally, pesticide development used metal precursors of arsenic, mercury, lead, and copper in the 1970s (Pesticide Action Network, 2016). This resulted in the discovery of Dichlorodiphenyltrichloroethane (**DDT**). However, the adverse impact of DDT on the environment and human health was realized, and its domestic and agricultural use was banned, leading to the development of other synthetic pesticides, such as Pyrethroid and OPPs (International Agency for Research on Cancer, 2022b).

OPPs are esters derived from phosphoric acid and have their antecedents in the toxic gases sarin, tabun, and soman - originally used for military purposes (Dash and Osborne, 2022). After their application in war, their insecticidal effect was discovered (Rashid *et al.*, 2022). One of the first OPPs produced was parathion, marketed by Bayer^MR in 1944 (Garcia *et al.*, 2022). As an insecticide, its synthetic production expanded, and by 1998, the Environmental Protection Agency (**EPA**) of the United States of America (**USA**) had registered 20,000 products (García *et al.*, 2003; Edwards and Tchounwou, 2005; Calaf *et al.*, 2021).

Calaf *et al*. (2021) reported that 23,000 t of a.i. were consumed in Central America, of which Guatemala used 9,000 t, El Salvador 7,000 t, Nicaragua 5,800 t, and Honduras 176 t. Imports during 1974 totaled $641 million USD, and by 1980, they amounted to $2,817 million USD (Kang *et al*., 1995). In 1978, Colombia ranked 3rd in LA, with the use of insecticides OPPs and carbamates, and herbicide Paraquat dichloride (also known as Gramoxone) (Chaparro and Castañeda, 2015). The agricultural population of the country corresponded to 40% of its inhabitants, whose health was at risk due to intoxications. Consequently, Paraquat dichloride was withdrawn (due to damage to multiple organs of the body) thanks to the decision of the Constitutional Court of Colombia T-080-17 (2017).

However, at the same time that Paraquat dichloride was banned in 1984, the Colombian government authorized the use of Glyphosate, and by 1994, the "Program for the Eradication of Illicit Crops using Aerial Spraying with the Herbicide Glyphosate" was officially regulated (Olasolo, 2015). Since then, Glyphosate, composed of 480 g/L of isopropylamine salt of N-phosphonomethylglycine, and which commercial brand worldwide is RoundupMR, is frequently used in Valle del Cauca for sugarcane ripening, and as an herbicide for: i) coffee; ii) banana; iii) rice; iv) cocoa; v) African palm; and vi) citrus (Varela *et al*., 2019). Arellano *et al.* (2016) of Greenpeace compiled the data in Table 3, referencing the global use of pesticides.

Box 3

Table 3

Pesticides used worldwide

Compound	Type	Prohibited	Restricted	Effect	Applications
Aminophosphonates: Glyphosate	H	France, Netherlands, Sri Lanka, El Salvador, Denmark, Belgium	Colombia, United Kingdom, Germany, Switzerland, Canada, some states in the USA	Resistance to 14 weeds	Transgenics: corn, soybean, cotton, canola, rapeseed, wheat, barley, avocado, lemon, orange, tangerine, grapefruit
Substituted urea: Diuron		Belize, Sweden, New Zealand, EU	Canada, Yugoslavia	Carcinogenic	Corn, cotton, banana, sugar cane
OPPs: Metamidofos		Brazil, EU, China, Kuwait, Uruguay, Ecuador, Dominican Rep., Indonesia	Bangladesh, India, USA, Guatemala, Belize, China, Sri Lanka	IA (World Health Organization, 2022) Extremely dangerous (Rotterdam Convention, 2022)	Chia, tomato, potato, cucumber, chili, watermelon, soybean, cotton, cabbage, broccoli, cantaloupe, tobacco
OPPs: Mevinfos	I	EU, Belize, USA, India	China, Costa Rica Malaysia, Sudan	Endocrine disruptor	Garlic, onion
OPPs: Monocrotophos		EU, Australia, China, Philippines, Thailand, Nigeria, Jamaica		IB (World Health Organization, 2022) Regularly toxic (Rotterdam Convention, 2022)	Soybean, tobacco
OPPs: Parathion		Peru, Denmark		Extremely toxic (Rotterdam Convention, 2022)	Cotton, onion, beans, peanut, tomato, corn, wheat

OPPs: organophosphates; H: Herbicide, I: Insecticide.

The Food and Agriculture Organization (2013) reported the application of 4.85 t of pesticides per 1,000 ha in 2012, with 37,455 t of insecticides, 31,195 t of herbicides, and 42,223 t of fungicides worldwide. Centner and Eberhart (2014) indicated the consumption of 2.36 billion kg of pesticides/yr worldwide. Agricultural uses of such compounds in the USA alone amounted to 0.5 billion kg. Globally, about 2 million t of pesticides are being used each year (International Agency for Research on Cancer, 2022b). China is the largest pesticide-producing nation, followed by the USA and Argentina (Basílico *et al*., 2022).

The herbicide, Glyphosate, was introduced by the USA agrochemical company, Monsanto[MR] (European Food Safety Authority, 2022). It is applied in agriculture (Maggi *et al.*, 2020), forestry (Rolando *et al.*, 2017), horticulture, and in parks and streets (Connolly *et al.*, 2018). In Germany, the use of Glyphosate increased by 100% during the years between 1999 and 2010 (Villnow *et al.*, 2019). Steinmann *et al.* (2012) analyzed application patterns by surveying 896 farmers. They found that the compound was applied at pre-sowing in 20.7% of the study area, at pre-harvest in 11.2%, and to stubble in 68.1%, mainly in oilseed rape (27.5%), barley (20.1%), and wheat (15.8%). Farmers expected an increase in yield between 38.1% and 71.4% in cultivated areas.

Glyphosate management in oilseed rape and wheat crops in the UK was estimated by Cook *et al*. (2010) with benefits of 3% for wheat and 9% for oilseed rape. They analyzed the potential results of eliminating the use of this herbicide in wheat and gave a figure of 2.9 million t/yr. If they returned to natural processes in seeds, the change for the industry would mean around $55,000 USD/yr. In recent years, the herbicide, Glyphosate, has become the most widely used non-selective, broad-spectrum, systemic herbicide (Heap and Duke, 2018). However, public concern arose regarding Glyphosate in the EU because Monsanto[MR] started to sell a broad-spectrum herbicide, which contains Glyphosate as an a.i., together with genetically modified (**GM**) crops (Tosun *et al.*, 2019). Most GM crops are resistant to other herbicides produced by different agrochemical companies, so farmers who wanted to use Glyphosate became dependent on Monsanto[MR] GM crops. In 2015, the International Agency for Research on Cancer (2022a) concluded that the herbicide, Glyphosate, among other herbicides, "is probably carcinogenic to humans".

This put the herbicide in the media spotlight and sparked a scientific controversy about the potential risks to health and industrialized agriculture.

By 2020, the total use of pesticides in agriculture remained stable globally, registering at 2.7 million t of a.i. (European Food Safety Authority, 2022). This volume of pesticides is about 47.5% herbicides, 29.5% insecticides, 17.5% fungicides, and 5.5% other pesticides (European Food Safety Authority, 2022). Global pesticide application per crop area was 1.8 kg/ha (Food and Agriculture Organization/World Health Organization, 2021). Total pesticide trade reached approximately 7.2 million t of products, with a value of $41.1 billion USD (European Food Safety Authority, 2022).

Despite the stability achieved during the last few years, pesticide use during the last 4 decades increased 50%, compared to the 1990s, and pesticide use per crop area increased from 1.2 to 1.8 kg/ha (Food and Agriculture Organization/World Health Organization, 2021), with increases in the proportion of herbicides (from 41% to 52% of total pesticides), and reductions in the proportion of fungicides (from 25% to 23%) and insecticides (from 24% to 18%) (United Nations Statistics Division of the Food and Agriculture Organization, 2021). The maximum consumption per hectare of pesticides is about 25 kg, with Asia being the highest in the world (Pesticide Action Network, 2016, 2017).

During 2020, Asia was the largest exporter of pesticides globally, with 3.7 million t, equivalent to $16.1 billion USD (Food and Agriculture Organization/World Health Organization, 2021). For its part, pesticide use in European agriculture increased by only 3% between 1990 and 2020, most likely due to the strict European Common Agricultural Policy put in place, which monitors and controls the use of pesticides (European Food Safety Authority, 2022).

During 2020, LA was the largest importer of pesticides worldwide, with 1.1 million t, equivalent to $6.9 billion USD, an increase of 160% compared to 2019 (United Nations Statistics Division of the Food and Agriculture Organization, 2021). Argentina's agricultural activity has increased in the last 30 yrs, to the point that it has become the largest producer of oil, soybean meal, and the world's 3rd largest supplier of seeds (United Nations Statistics Division of the Food and Agriculture Organization, 2021).

These economic benefits have been achieved through applications of 200 million L of different pesticide formulations, mainly of the herbicide, Glyphosate, on 19.7 million ha/yr, primarily on transgenic soybeans, followed by corn and wheat (Basílico *et al.*, 2022).

Mac Loughlin *et al*. (2017) have reported on pesticide applications in vegetable production and their effects on water bodies. They studied a peri-urban area of the city of La Plata in Argentina with application of 36 pesticides and investigated the amount of residues in stream sediments at five sampling sites. They found that the sum of fungicides, insecticides, and herbicides measured gave values of 1,080/2,329, 3,715/88, and 367/5 ng.g^{-1} respectively. Brazil is a country that is economically dependent on agriculture, with 88 million ha across a variety of products, ranging from forage grains and oilseeds to fruits and vegetables (Castro *et al*., 2020). The harvested area has expanded by 23.48% between 1930 and 2017, with an increase in productivity of 8% per decade. To meet this demand, Brazilian producers use a large amount of pesticides, estimated at 549,280 t in 2018 (Lopes *et al*., 2022). Almost half of all approved products contain a.i., listed by the Pesticide Action Network (2016, 2017).

2. Application of pesticides in Mexico

It is important to note that despite Mexico's participation in the Rotterdam Convention (2022), in the United Nations Environment Programme (2022), in the Stockholm Convention on Persistent Organic Pollutants (2022), and in the Codex Alimentarius (2022), different companies in Mexico have sanitary registrations for pesticides with undetermined production periods, which include highly toxic substances. Fifty-one active products were identified, and the presence of OPP insecticides Phosphamidon, Mevinphos, Monocrotophos, Disulfoton, and Isofenphos qualified as extremely toxic, with OPP insecticides Chloropyrifos and Oxydemeton-methyl designated as highly toxic (Valdez *et al*., 2000; Sanchez *et al*., 2011; Nava *et al*., 2019).

Leyva *et al*. (2017a) monitored pesticide residues in rivers in northwestern Mexico and detected DDT, and the insecticides OPPs Parathion, Diazinon, Ethion, Malathion, Chlorpyrifos, Carbophenothion, as well as insecticide carbamate Pirimicarb, and insecticides OCPs Endosulfan, Lindane. During the period of 2005-2017 (Table 4), sanitary actions with pesticides were carried out in the states of Nayarit, Sonora, Campeche, Chiapas, Chihuahua, Michoacan, Nayarit, Puebla, Sinaloa, Tamaulipas, Veracruz, Guanajuato, and Yucatan.

Box 4

Table 4

Estimation of pesticides used in different states of the Mexican Republic, period 2005-2017

Pesticides	Estimate (t)	State	Period (yrs)	References
Carbamate OCPs OPPs Pyrethroid	N.R.	Nayarit	2014-2015	(Benitez *et al*., 2018)
Endosulfan, 2,4-Dichlorophenoxyacetic acid, Paraquat dichloride, Glyphosate, Chlorothalonil, Mancozeb	16 to 211	Sonora	2010-2014	(Silveira *et al*., 2018)
Pesticides in general	Insecticides 37455 Herbicides 31195 Fungicides 42223	Campeche Chiapas Chihuahua Michoacan Nayarit Puebla Sinaloa Tamaulipas Veracruz	2013-2017	(Gamboa *et al*., 2018)
Chloropyrifos, 2,4-Dichlorophenoxyacetic acid, Glyphosate, Mancozeb	9878	Guanajuato	2014-2016	(Perez *et al*., 2017)
Methamidophos, Malathion, Diazinon, Carbofuran, Mancozeb, 2,4-Dichlorophenoxyacetic acid, Glyphosate	N.R.	Yucatan	2005-2007	(Gómez, 2017)

OCPs: organochlorines; OPPs: organophosphates; N.R.: No Register.

The group of Highly Hazardous Pesticides (**HHPs**) has recently been categorized. This classification responds to a modality authorized by the Strategic Approach to International Chemicals Management (**SAICM**) (Deguine *et al*., 2021). The criteria by which a pesticide is considered an HHPs are: i) high acute toxicity; ii) chronic toxicity; iii) long-term effects; iv) environmental toxicity; and v) inclusion in international conventions for which compliance is mandatory (Pesticide Action Network, 2016, 2017; Food and Agriculture Organization/World Health Organization, 2021).

The record of accredited HHPs in Mexico corresponds to the comparison that researchers of the Pesticide Action Network in Mexico (**RAPAM**) made between the Pesticide Action Network (2016) and the Federal Commission for the Protection against Sanitary Risks (2022). This agency authorizes the pesticides that are allowed to be imported, marketed, and used in the country. Among the accredited HHPs are 183 a.i., for agricultural, domestic, gardening, and industrial use. For human health, 63 of them have acute toxicity, according to IA and IB classification (World Health Organization, 2022), 19 can be lethal by inhalation, 43 are likely to cause cancer, according to the EPA, 35 are endocrine disruptors, according to the Globally Harmonized System (**GHS**), 21 are toxic in reproductive processes, and 2 are mutagenic (Pesticide Action Network in Mexico, 2022).

In relation to environmental toxicity, 44.81% present high toxicity to bees, as they can cause death at doses greater than 2 g/bee (Pesticide Action Network, 2016), 15 are included in Annex III of the Rotterdam Convention (2022), 3 in the Stockholm Convention on Persistent Organic Pollutants (2022) as persistent, organic pollutants, with methyl bromide included in the United Nations Environment Program (2022) as a substance that destroys the ozone layer. In Mexico, there are 282 companies with HHP registrations for: i) agricultural; ii) forestry; iii) livestock; iv) domestic; v) urban; and vi) industrial use. The top five manufacturers are Bayer^MR (with 202 registrations), Syngenta Agro^MR (with 133 registrations), FMC Agroquímica de Mexico^MR (with 93 registrations), Dow Agrosciences de Mexico^MR (with 92 registrations), and BASF Mexicana^MR (with 85 registrations) (Pesticide Action Network in Mexico, 2022). At the end of 2022 (Table 5), 2,322 people were reported to have been poisoned by pesticides in Mexico, of which 1,489 were men and 833 were women (National Epidemiological Surveillance System, 2022). The states of Jalisco, Chiapas, Guerrero, and Veracruz stand out for pesticide poisoning (Pesticide Action Network in Mexico, 2022).

Box 5

Table 5

Pesticide poisoning by state, year 2022

Federal State	Men	Women	Total
Aguascalientes	7	4	11
Baja California Norte	20	17	37
Baja California Sur	13	6	19
Campeche	11	4	15
Coahuila	31	9	40
Colima	19	7	26
Chiapas	137	90	227
Chihuahua	12	10	22
Mexico City	23	9	32
Durango	5	6	11
Guanajuato	43	33	76
Guerrero	112	86	198
Hidalgo	52	38	90
Jalisco	263	165	428
Mexico (State)	82	47	129
Michoacan	88	49	137
Morelos	59	25	84
Nayarit	88	21	109
Nuevo Leon	16	11	27
Oaxaca	79	30	109
Puebla	46	23	69
Queretaro	3	3	6
Quintana Roo	13	15	28
San Luis Potosi	12	5	17
Sinaloa	51	22	73
Sonora	24	18	42
Tabasco	26	11	37
Tamaulipas	21	13	34
Tlaxcala	3	1	4
Veracruz	109	43	152
Yucatan	2	3	5
Zacatecas	19	9	28
Total	1489	833	2322

(National Epidemiological Surveillance System, 2022)

About 50,000 ha of cruciferous vegetables are planted in Mexico, of which 74.42% is broccoli (*Brassica oleracea*) (Rocha and Cisneros, 2019). Guanajuato is the main producer of broccoli in Mexico, with 62% of the total harvested area, and an average yield of 12.98 t/ha (National Institute of Statistics and Geography, 2022a). However, in recent years there has been increasing concern about the consequences of pesticide use on this crop (Pesticide Action Network in Mexico, 2022). As a result, the standards established for the safety of this food, and its MRLs, have become stricter (Federal Commission for the Protection against Sanitary Risks, 2022).

Castro *et al*. (2021) analyzed 78 samples from a packing house in Irapuato, Guanajuato, Mexico, and from the Central Food Depot of Huixcolotla, Puebla, Mexico, reporting that, of the 78 samples, 42 were free of pesticides, 14 had unquantifiable concentrations (traces), and 22 had at least one residue. The pesticides found were: Boscalid (0.0061 mg/kg), Dimethoate (0.0068 mg/kg), Imidacloprid (0.0087 mg/kg), Methamidophos (0.0266 mg/kg), Omethoate (0.0111 mg/kg), Penconazole (0.0039 mg/kg), Propamocarb (0.0061 mg/kg), and Thiamethoxam (0.0045 mg/kg).

The state of Sinaloa has an arable area of 1,245,638 ha and produces corn, sorghum, tomato, chili, potato, sugarcane, watermelon, and mango (Agri-Food and Fisheries Information Service, 2022). Among the technologies used in its agriculture, 61.5% are chemical fertilizers, 67% are chemical herbicides, and 65% are chemical insecticides (National Institute of Statistics and Geography, 2022b). According to the National Epidemiological Surveillance System (2022), in the state of Sinaloa, at the end of 2022, 73 people were reported to have been poisoned by pesticides, of which 51 were men and 22 were women (Table 4). On average, there are 2.5 intoxications per week in the state (Pesticide Action Network in Mexico, 2022). Leyva *et al*. (2017a) calculated 263 commercial products applied from 97 a.i. The most abundant compounds were OPPs insecticides: Diazinon, Malathion, Parathion, Dimethoate, Chloropyrifos, and herbicide amino-phosphonate Glyphosate.

Leyva *et al*. (2017b) have reported that about 800,000 t are produced in the agricultural zone of the Culiacan valley between exported vegetables and grains. The valley is composed of eight municipalities totaling 1,243,770 inhabitants. Different researchers have identified the use of 118 pesticides, with 63 of them in the category of HHPs (Pesticide Action Network in Mexico, 2022). Total consumption was 69.92 t of 97 a.i. yr^{-1}. Malathion (3 591.80 kg a.i. yr^{-1}), and Dichlorvos (1 275.77 kg a.i. yr^{-1}) were among the most widely used OPP insecticides, but ten others of the same chemical classification were also applied during this period (Food and Agriculture Organization/World Health Organization, 2021).

Malathion was applied to bean, sorghum, safflower, and mango crops to suppress pests, such as leafhoppers, bugs, thrips, scales, weevils, and ants; it is highly toxic to bees and is banned in two countries. Dichlorvos was applied on tomato and cucumber crops to control spider mite, whitefly, leafminer, and pinworm. It is considered acutely toxic and very toxic to bees; it is banned in 32 countries (Leyva *et al*., 2017a).

Arellano *et al*. (2016) reported that Greenpeace, during 2015, monitored ten water bodies in Sinaloa and reported elevated contents of insecticides OPPs Diazinon and Parathion in the Culiacan River, as well as insecticides OPPs Parathion, Chloropyrifos, and Mevinphos in the El Fuerte River. They also found Glyphosate residues at concentrations between 3.62 and 4.3 ng/L in 100% of the water samples in Yucatan.

In two valleys in northwestern Mexico (the Culiacan Valley in Sinaloa and the Yaqui Valley in Sonora), approximately 250,000 kg a.i. yr^{-1} of 54 products are used each year, 43 of which are classified as HHPs because they are persistent, bio-accumulative, or very toxic (Pesticide Action Network, 2016). García *et al*. (2021) reported that the most frequently detected pesticides (mean, µg g^{-1}) in the Culiacan Valley were OCPs (0.1967), OPPs (0.0928), Pyrethroid (0.2565), organonitrogen (0.0552), and miscellaneous pesticides (0.1851). In the Yaqui Valley, the most frequently detected pesticides were OCPs (0.8607), OPPs (0.0001), Pyrethroid (0.0124), and miscellaneous pesticides (0.0009). The OPP insecticides used are Dimethoate, Parathion, and Methamidophos for control of the bud aphid and wheat ear aphid. For safflower, chickpea, corn, citrus, and cotton crops, along with the above OPPs, they also apply OCPs and Pyrethroid (Garcia *et al*., 2017).

Similar realities are present in other regions of the country. The reproductive health problems of flower growers in the State of Mexico are highly relevant; in the case of Coatepec Harinas and Villa Guerrero, 80% and 70% of the respective populations are dedicated to flower growing. The applications of pesticide mixtures in flower production are qualitatively and quantitatively severe, since 75% of their a.i., are classified as HHPs (Pesticide Action Network in Mexico, 2022). In that list, OPPs are abundant, and their prohibition is established in 10 (and up to 90) countries (Castillo *et al.*, 2017).

In Campeche and Yucatan, similar conditions are present in corn, horticultural, floristic, and beekeeping agri-food systems, due to the high consumption of HHPs, which cause environmental imbalances, contamination of abiotic and biotic resources, and massive death of bees, which consequently results in economic damage due to rejection of contaminated exported honey and, to a larger extent, abundant and severe damage to the health of workers (Gómez, 2017; Rendon von Osten and Hinojosa, 2017).

In Chiapas, 55 a.i. yr^{-1} are used. OPPs insecticides dominate - Parathion leads, followed by Monocrotophos; 18 of them are applied to maize, in addition to the herbicide, Glyphosate, (available in five presentations). In floriculture, 46 a.i. yr^{-1} are applied; 32 of them are on the list of HHPs, and 27 ingredients are banned worldwide (Hernandez *et al.*, 2017).

Recent studies in southern Yucatan reported that 55% of farmers use the herbicide, Glyphosate, for GM soybean production (Ponce *et al.*, 2022), and in the cattle zone of eastern Yucatan, 72% of farmers use Glyphosate for their crops (Polanco *et al.*, 2018). In the Yucatan Peninsula, Campeche is the main producer of GM soybeans (National Institute of Statistics and Geography, 2022c).

In 2012, producers requested permission to cultivate 60,000 ha, with extensive use of the herbicide, Glyphosate (Ponce *et al.*, 2022). Soy (Glycine max L. cv.A5403) Faena Solution (or **RR**) (MON-04032-6) has been introduced in its experimental phase in Campeche beginning in 2001, being incorporated in Yucatan since 2003, and in Quintana Roo since 2005 (Polanco *et al.*, 2018).

Soybean cultivation in Yucatan exceeded 25,000 t in 2017, 25% more than in 2016, covering the peninsular area since then (National Institute of Statistics and Geography, 2022c); the products used in greater proportion are six commercial herbicides which a.i., is Glyphosate; they also employ the OPPs insecticides Methamidophos and Chloropyrifos, in addition to Pyrethroid, Carbamate, and OCPs (Rendón von Osten and Hinojosa, 2017).

Other observations that Gómez (2017) refers to are related to industrial agriculture in the Yucatan peninsula and are the following: (i) the handling of pesticides with spray pumps and backpacks near the population; (ii) aerial spraying disperses most of the pesticide via wind to distant sites; (iii) the handling of agrochemicals by workers is virtually experimental, sometimes mixing up to eight compounds without respecting the indicated doses; iv) they do not follow safety standards, and there is no adequate protection; v) there is no care in the handling of containers, and they contaminate water bodies; vi) this type of corporate agriculture does not protect human resources, soil, or water it is only oriented towards economic benefit; and vii) it does not protect the environment overall.

3. Harmful effects of pesticides on human health

In the national territory, there is extensive evidence of the consequences of pesticide use (Sierra *et al.*, 2019). Their presence was identified in the blood serum of agricultural workers (Valencia *et al.*, 2021) and in pasteurized milk consumed in Mexico City (Schopf *et al.*, 2022).

In the field of human health, epidemiological studies have suggested that high levels of pesticide exposure are associated with increased risk of cancer (Leonel *et al.*, 2021), cardiotoxicity (El-Nahhal and El-Nahhal, 2021), Parkinson's disease (Islam *et al.*, 2021), diabetes mellitus (Sarath *et al.*, 2021), and birth defects (Ventura *et al.*, 2022), in addition to producing various adverse health effects, such as affecting the immune system (Bartling *et al.*, 2021), nervous system (Arab and Mostafalou, 2022), endocrine system (Gea *et al.*, 2022), and reproductive system (Kaboli *et al.*, 2022).

The OPPs Diazinon, Fenthion, Malathion, Ethion, Parathion, and Phosphamidon are widely recognized to be particularly neurotoxic because they inhibit acetylcholinesterase, an enzyme that hydrolyzes the neurotransmitter, acetylcholine, at brain cholinergic synapses and neuromuscular junctions (Lopes *et al.*, 2022). During the last few years, different biomarkers have been used to detect the consequences of pesticide exposure before adverse clinical effects occur, such as modifications in blood cell composition (Neghab *et al.*, 2018) and alterations in enzymatic activities (Medithi *et al.*, 2021). In Mexico, as biomarkers of exposure, residues of OCPs and DDT have been found in human adipose tissue, breast tissue, human semen, and blood serum (Fucic *et al.*, 2021; López *et al.*, 2022).

Calderón *et al.* (2018) demonstrated that due to the lipophylic characteristic of some pesticides, residues of Lindane, α-Hexachlorocyclohexane (**α-HCH**), β-Hexachlorocyclohexane (**β-HCH**), p, p′-dichlorodiphenyl dichloroethylene (**p,p′-DDE**), and p,p'-dichlorodiphenyldichloroethane (**p,p'-DDDD**) were detected in 1,485 samples of adipose tissues of deceased people who lived in Veracruz City, Mexico.

Polanco *et al.* (2017) monitored OCPs residues in 18 Yucatan municipalities with high cervical cancer mortality rates. OCPs detected were Endosulfan I (7.35 μg/mL), Aldrin (3.69 μg/mL), and p,p'-DDDD (2.33 μg/mL), including 1.39 and 1.46 μg/mL of δ-Hexachlorocyclohexane (δ-HCH). Women from the agricultural area had high concentrations of OCPs in their blood, particularly Dieldrin (1.19 μg/mL) and of p,p′-DDE (1.26 μg/mL). In the metropolitan area, 0.080 μg/mL of γ-Hexachlorocyclohexane (**γ-HCH**) and 0.064 μg/mL of Heptachlore were detected.

Two cross-sectional studies were carried out in villages of the states of Sonora and Sinaloa in Mexico, where high levels of OPPs have been detected through environmental and human monitoring. OPPs were measured in the serum of 60 fertile-aged women. The most commonly detected OPPs in serum were: Pentachloroanisole (**PCA**) (71%), Polychlorinated biphenyl (PCB) #205 (43%), Tetrachlorobenzenes (17-33%), p,p′-DDE (21%), and residues of Lindane by-products α-HCH or β-HCH (15%). Congeners of Furans and Dioxins with the highest concentrations in milk were 2, 3, 4, 7, 8 - PeCDF (3.42 pg/g) and Octachlorodibenzo-p-dioxin (33.0 pg/g), respectively, which may reach developing embryos and infants via the placenta and lactation (Farías *et al.*, 2019).

The International Agency for Research on Cancer (2022b) classified a wide range of pesticides as carcinogenic, including 56 as carcinogenic in laboratory animals, with some associated with cancer in humans, including cervical and breast cancer. Current studies directly link the presence of xenobiotics to adverse health effects. There is evidence of these detriments in the genome with mutagenic or carcinogenic manifestations (Ramirez, 2015). Glyphosate is considered by the International Agency for Research on Cancer (2022a) as a possible carcinogen; methyl parathion, methamidophos, and methomyl are banned in numerous countries and are included in the Rotterdam Convention (2022), which Mexico has signed.

Martinez *et al.* (2017) compared the levels of OCPs in blood serum and adipose tissue, calculating their differences in concentrations for both biological matrices. 126 pairs of blood serum and adipose tissue samples were collected during autopsies and analyzed as case studies in Los Mochis, Sinaloa, Mexico. Among OCPs, higher concentrations corresponded to β-HCH and p,p′-DDE in blood serum lipids, while pp'-DDDT showed higher concentrations in adipose tissue.

Flores *et al.* (2017) evaluated 247 serum samples from children between the ages of 6 and 12 yrs old from two zones in Mexico (indigenous zones and industrial zones) to determine α-Endosulfan (178.6-306.9 ng/g lipid), β-Endosulfan (901.5 ng/g lipid), endosulfan sulfate (1,096.4 ng/g lipid), p,p′-DDE in malaria-endemic areas (1,782.2-1,358.3 ng/g lipid), and PCB #101 (1,032.7 ng/g lipid). The evidence provided by this exploratory study indicates that the evaluation of the health risks posed to children living in contaminated areas is a high-priority health issue. There are 26 HHPs used in the Campeche region; the effects on human health range from mild to severe intoxications. Estimates of pesticide residues indicate that 66% of the farmers who prepare the pesticide mixtures are the most affected by intoxication. Workers in Holpechen have registered Glyphosate in urine from 0.06 to 0.87 g. L-1, while purified water coming from groundwater has been estimated at 0.03-0.78 g. L-1 (Rendón von Osten and Dzul Caamal, 2017).

Poisonings by OPPs are numerous; the World Health Organization (2022) quantified 500,000 to 1,000,000 OPPs poisonings; deaths from pesticide accidents have been estimated at 220,000/yr; 40,000 of them have occurred in Asia and Africa, and in smaller proportion in Mediterranean countries and in the USA (Pesticide Action Network, 2016, 2017; United Nations Statistics Division of the Food and Agriculture Organization, 2021).

4. Harmful effects of pesticides on biotic and abiotic media

Pesticide formulations generally have a high concentration of solvents with low dispersion, remaining in soil for a long time, thus moving through the environment and putting biological systems at risk (Pesticide Action Network in Mexico, 2022). The main water polluting pesticides are: herbicides, insecticides, fungicides, and bactericides, including OPPs, Carbamates, Pyrethroids, OCPs, and others (many, such as DDT, are banned in most countries but are still being used illegally and persistently) (Rad *et al.*, 2022). Agricultural activities can reintroduce these pollutants into aquatic environments through wastewater (Dahshan *et al.*, 2016).

According to the Food and Agriculture Organization/World Health Organization (2021), agricultural land, which requires irrigation, has more than doubled in recent decades, which has increased the use of pesticides, eventually affecting ground/underground water quality. OPPs are soluble in water; consequently, they occur widely in water bodies (Wang *et al.*, 2021). In addition, they are toxic to aquatic microorganisms, disrupt photosynthesis and cell growth, and, therefore, cause loss of biodiversity (Rad *et al.*, 2022). The two most significant source points of pollution via OPPs into aquatic systems are sewage overflows and wastewater treatment plant effluents (Daud *et al.*, 2017; Rad *et al.*, 2022).

Rodriguez *et al*. (2019) have referenced contamination within the Ayuquila-Armeria river basin (Mexico). The most frequent pesticides were Ametryn, Dimethoate, and Diazinon. The sites with the highest number of pesticides in the four samplings were Palo Blanco, Antes Manantlan, Tuxcacuesco, and Ayuquila. Sites near the intensive agriculture zone presented higher numbers of pesticides than those located in areas with rain-fed agriculture.

Clemente *et al*. (2019) quantified the concentrations of OCPs in the water of the Laguna Negra of Puerto Marques, Acapulco. The OCPs compounds were determined by gas chromatography analysis with electron capture detector. The results obtained from the sampling sites were divided into lagoon and discharge sites and did not show a significant difference, since the total average concentrations were 5.55 and 6.02 μg/L, respectively. It was also noted that, during the dry season, a total average of 6.80 μg/L was recorded, while in the rainy season, it was 3.56 μg/L. According to the Official Mexican Standard NOM-SSA1-1994 (2022), there should be no OCPs. Although concentrations are low (μg/L), they can cause some alteration to organisms through bioaccumulation and biomagnifications, with risks to the health of both the natural ecosystem and the human being.

Pesticide residues have also been identified in water and sediments from Chacahua-Pastoria Lagoon System in the Oaxaca Coast, Mexico. The spatial distribution of insecticide OPPs Malathion and OCPs in water showed the highest values near to adjacent land with some pattern differences. DDT was the most frequent in water and sediment samples showed the highest concentrations in the Pastoria Lagoon. These results indicate the need to establish permanent monitoring programs to implement mitigation measures (Leal *et al.*, 2022).

Regarding contamination by residual pesticides in abiotic and biotic environments, accidents have unique consequences. The city of Salamanca, located in the state of Guanajuato, is characterized by its agricultural development. There is a particular case related to OCP contamination in this place: the facilities and surroundings of the former Tekchem Industrial Unit, where OCPs and OPPs were manufactured. The company ceased operations in 2007; however, to date, there is a problem of soil and groundwater contamination, due to inadequate management of processes and waste during most of the production stages (Hernandez *et al*., 2019). An on-site study showed that the soil is mostly contaminated by OCPs, which represent approximately 70% of the identified compounds, with DDT and its metabolites found in the highest concentrations (Secretariat of Environment and Natural Resources of Mexico, 2018).

Ecological costs are another set of consequences from massive application of OPPs. Several studies have analyzed air pollution (Hamsan *et al.*, 2017; Lopez *et al.*, 2017; Pozo *et al.*, 2017), water pollution (Stamatis *et al.*, 2013; Dahshan *et al.*, 2016; Daud *et al.*, 2017; Zhang *et al.*, 2017a; Di Guardo and Finizio, 2018), and soil pollution (Simon *et al.*, 2017; Zhang *et al.*, 2017b), including the interaction of the constituent elements of the biosphere, which can be synthesized into the following environmental problems: i) contamination of abiotic resources (DiGiacopo and Hua, 2020); ii) imbalance of populations (Kaur *et al.*, 2019); iii) loss of biodiversity (Kumar *et al.*, 2019); iv) contamination of food chains (Lima *et al.*, 2019); v) bioaccumulation (Rossi *et al.*, 2020); and vi) residues in food (Abbas *et al.*, 2017).

5. Legislation on the use of pesticides

Production processes and socioeconomic phenomena related to the use of pesticides, as well as their effects on biota and animal health, are regulated by conventions, institutions, treaties, and standards. Among the most relevant ones at the international level are the following:

Annex III of the Rotterdam Convention (2022), which aims to promote shared responsibility and joint efforts in the international trade of certain hazardous chemicals, in order to protect human health and the environment from potential harm, while contributing to their environmentally sound use by facilitating the exchange of information about their characteristics and establishing a national decision-making process on their import and export.

The Stockholm Convention on Persistent Organic Pollutants (2022) aims to protect human health and the environment from persistent organic pollutants by strengthening national legislation and enacting national implementation plans. Mexico signed the agreement on May 23, 2001, in Sweden, and ratified it on February 10, 2003. It was the first Latin American country to ratify the convention, which entered into force on May 17, 2004.

The World Health Organization (2022), in collaboration with the Food and Agriculture Organization/World Health Organization (2021), is responsible for assessing the risks of pesticides to humans, either through direct exposure or residues in food, and recommending appropriate protective measures. These assessments are based on all data submitted for national pesticide registrations worldwide, as well as on all scientific studies published in peer-reviewed journals. After assessing the level of risk, safe intake limits are established to ensure that the amount of pesticide residues to which people are exposed to by eating food over a lifetime does not result in adverse health effects.

These acceptable daily intake limits are used by governments and international risk managers, such as Codex Alimentarius (2022), to establish MRLs for pesticides in food. Codex standards are the benchmark for international food trade, which means that consumers around the world can be confident that the food they buy meets agreed safety and quality standards, regardless of where it was produced.

The World Health Organization (2022) and the Food and Agriculture Organization/World Health Organization (2021) have also jointly developed the International Code of Conduct on Pesticide Management. The most recent edition of this voluntary framework was published in 2014. It provides guidance to regulators, the private sector, the general public, and other stakeholders on best practices in the management of pesticides throughout their lifecycle, from production to disposal.

The European Food Safety Authority (2022) provides scientific advice to the European Commission on potential risks related to the presence of pesticide residues in food treated with plant protection products, including the approval of a.i. for use in the EU. It is also involved in the establishment of MRLs in food. In addition, it is responsible for preparing the Annual Report on Pesticide Residues in the EU.

The International Agency for Research on Cancer (2022b) is the specialized cancer agency of the World Health Organization. It is an interdisciplinary group that brings together expertise in epidemiology, laboratory science, and biostatistics to identify the causes of cancer (e.g., by the presence of pesticide residue), so that preventive measures can be taken.

The Pesticide Action Network (2017) is a network of over 600 participating non-governmental organizations, institutions, and individuals in over 90 countries who are working to replace the use of hazardous pesticides with ecologically-sound and socially-just alternatives.

The Federal Commission for the Protection against Sanitary Risks (2022) establishes an electronic database for individual consultation of sanitary registrations of pesticides, plant nutrients, and their MRLs in food.

"http://siipris03.cofepris.gob.mx/Resoluciones/Consultas/ConWebRegPlaguicida.asp"

The Pesticide Action Network in Mexico (2022) is a Mexican, non-profit, civil association that works to progressively eliminate chemical pesticides that affect human health and the environment, promoting the necessary changes in public policies that promote agroecological pest control. It trains and supports workers, communities, producers, and consumers to strengthen the rights to healthy food and food sovereignty. They also establish collaboration agreements with professionals and specialists from the academic sector, institutions, environmental organizations, and social organizations to protect the rights to healthy food, free of pesticides and transgenics, as well as food sovereignty and an environment free of contaminants. The Official Mexican Standard NOM-SSA1-1994 (2022) provides information on the permissible limits and chemical characteristics of water for human use and consumption. According to the standard, the content of chemical constituents must conform to Aldrin and Dieldrin (separate or combined) 0.03 μg/L, Chlordane (total isomers) 0.30 μg/L, DDT (total isomers) 1.00 μg/L, γ-HCH 2.00 μg/L, Hexachlorobenzene 0.01 μg/L, and 2,4-D 50.00 μg/L. It is important to recognize that pesticide management regulations and provisions become more restrictive as both theoretical and methodological research provides greater insight into health effects and environmental alterations, as well as increases in sensitivity and resolution of analytical determinations.

Conclusions

Pesticide exposure is very common throughout the world. Farmers and people who come into contact with pesticides are often unaware of their history, classification, and hazardous effects. With knowledge of pesticide classification, proper use, exposure, toxicity, and regulation, along with effective public health programs, the burden of human disease caused by pesticide exposure should be greatly reduced, while public health and the ecosystem should be improved. In addition, the rationale for pesticide regulation should be clarified. The benefits and costs related to pesticide use on farmers or consumers are essentially private in nature, so the duality between health and sustained profit growth is unclear. Our final observation is that our review, which involves highly specialized research in different disciplines, also illustrates that interactions between disciplines are very limited. Indeed, health studies generally deal with pesticide toxicity in farmers, while economic studies generally deal with the effects of pesticides on the agricultural market, without pursuing interdisciplinary cohesion.

Declarations

Conflict of interest

The authors declare no interest conflict. They have no known competing financial interests or personal relationships that could have appeared to influence in this chapter.

Author contribution

García-Casillas, Arturo César: Writing original draft.
Prado-Rebolledo, Omar Francisco: Review and correction.
Martínez-González, Sergio: Data curation.
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Abbreviations

2,4-D	2,4-Dichlorophenoxyacetic acid
a.i.	Active Ingredient
DDT	Dichlorodiphenyltrichloroethane
EPA	Environmental Protection Agency
EU	European Union
FAO	Food and Agriculture Organization
GHS	Globally Harmonized System
GM	Genetically Modified
HHPs	Highly Hazardous Pesticides
LA	Latin America
LD_{50}	Median Lethal Dose
MRL	Maximum Residue Level
OCPs	Organochlorine Pesticides
OPPs	Organophosphates Pesticides
p,p'-DDD	p,p'-dichlorodiphenyldichloroethane
p,p′-DDE	p,p′-dichlorodiphenyl dichloroethylene
PCA	Pentachloroanisole
PCB	Polychlorinated biphenyl
RAPAM	Pesticide Action Network in Mexico
SAICM	Strategic Approach to International Chemicals Management
USA	United States of America
α-HCH	α-Hexachlorocyclohexane
β-HCH	β-Hexachlorocyclohexane
γ-HCH	γ-Hexachlorocyclohexane
δ-HCH	δ-Hexachlorocyclohexane

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