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Pesticides, Anthropogenic Activities, and the Health of Our Environment Safety

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Abstract

Mankind depends on agricultural products for food consumption. Increasing population (more than 7 billion) requires significant growth in crop yield to meet essential demand. This aim was achieved through the use of pesticides to protect crops from diseases. Pesticides are toxic by design for organisms that can threaten food products. Their mode of action is by targeting systems or enzymes in the pests that may be similar to human system and therefore pose risks to human health and the environment as well. The WHO recommended classifying pesticides according to their toxicity and chemicals according to their chronic health and environmental hazards.

Keywords: pesticides, classification of pesticides, pesticide hazards, future of pesticides

1. Introduction

Agriculture is the primary source for human food; it provides different kinds of crop production. Most common crops include wheat, rice, corn, beans, different vegetables, and season fruits.

In 2015, 7.4 billion people call earth their home. Population is projected to reach 9.7 billion by 2050 and 11.2 billion by 2100 [1]. Optimizing crop yields becomes even a more critical factor affecting the availability and affordability of food to meet increasing population demand.

Plant diseases are major factors that affect crop production. Al-Sadi [2] reported that plant diseases can affect plants by interfering with several processes such as the absorbance and translocation of water and nutrients, photosynthesis, and flower and fruit development. Infection of plants by pathogens can have serious consequences on plant health which consequently affect human health. Viruses, bacteria, and fungi that infect plants do not usually cause infection in humans [3]. The ultimate consequences of different plant diseases are reduction in crop production, reducing food availability which may lead starvation in some areas. The famous incident of plant pathology is potato disease caused by *Phytophthora infestans* fungi, which destroyed potatoes that were the main crop in Ireland during 1845–1850, where about 1 million people died and another million immigrated to other countries [4].

This disaster and other similar ones resulted from plant pathogens. Minimizing this risk requires efficient methods and practices to control pests (insects, bacteria, fungi, viruses, etc.). The term “pesticide” indicates any substance or mixture of substance used to kill, “repel,” or otherwise control a “pest,” including insects, snails, rodents, fungi, bacteria, and weeds [5].

The early methods used were simple and depended on traditional ways in specific places; however, these traditional practices were insufficient to control pests efficiently. Improvement of pest control gradually started to show satisfactory results for farmers and food manufacturing by the nineteenth century through the introduction of two natural pesticides (pyrethrum and rodent). In 1939 Muller discovered that DDT was a very effective insecticide and quickly became the most widely used pesticide in the world. Not until the 1960s when the harmful side effects of the application of DDT was discovered [6]. Despite the harmful effects of DDT, demand for pesticides continued to increase throughout the world. This is due to the many benefits attributed to pesticides; the most obvious benefits are economic, protection of commodity yield and quality, and the reduction of other costly inputs such as labor and fuel [7]. Pesticides play an essential role in farm profitability, providing reliable supplies of agricultural product, improving the quality of the product [8]. Notwithstanding pesticide benefits, there is plenty of evidence of both direct and indirect dangers involved in the use of these chemical substances both for humans and the environment [8].

For example, the contamination of pesticides may happen in several ways during manufacturing, storing, shipping, application in fields, warehouses, and wrong use by peoples. Several accidents have occurred in different parts of the world: India (1986), Italy (1976), Germany (1953), and Ethiopia (2017) [9]. Maksymiv [10] grouped the side effects of the excessive use of pesticides into diseases of ecosystems such as erosion, loss of soil fertility, pollution of water system, and biological community impact including loss of crop, animal genetic resources, elimination of natural enemies, genetic resistance to pesticides, contamination, and changes to natural control mechanisms.

Due the undesirable side effects of synthetic pesticides, search for safer analogue pesticides of natural origin is one of the most important goals. Potential alternatives to pesticides are available and include specific methods of plant cultivation, use of biological pest control, plant genetic engineering, and methods of interfering with insect breeding [11]. The most common alternative to synthetic pesticide pest control is biopesticides.

Biopesticides are a certain type of pesticides derived from natural material such as animal, plants, bacteria, and certain minerals. As of April 2016, there were 299 registered biopesticide active ingredients and 1401 active biopesticide product registration (US Environmental Protection Agency EPA).

Biopesticide offers a more sustainable solution to pest control than synthetic alternative. Botanical pesticides do not present the residue problems [12]. Microbial pesticides contain a microorganism as the active ingredient; they can control many different kinds of pest, although each separate active ingredient is relatively specific for its target pest(s). Biochemical pesticides are naturally occurring substance that interferes with growth or mating such as plant growth regulators or substances that repel or attract pests, such as pheromone [13]. Even with the satisfactory results of biopesticides on pest management, the efficacy at different geographical conditions and slow pest control makes them less desirable by farmers [14]. The science of biopesticides is still considered to be young and evolving. Some of the biopesticides are under development; this may prove to be excellent alternatives to chemical pesticides. Further research is needed in several areas such as production, formulation, delivery, and commercialization of the products [15].

In recent years, a new technology that provided a sustainable solution is nanotechnology through the development of nanopesticides for conventional agricultural use [16, 17]. Nanopesticides are small engineered structures that provide pesticide properties or formulation of active ingredient of pesticides in nanoform; these nanostructures show slow degradation and controlled release of nanopesticides which make them environmentally safer and less toxic compared to chemical

pesticides [14]. The nanosystems have shown great capability of controlled release pattern of active ingredient (AI) making them more efficient for long time period usability that can solve eutrophication and residual pesticide accumulation problem [18]. In spite of the excellent results of this nanotechnology in the agriculture field, further and deep studies should be conducted to ensure application safety.

2. Plant pathology and impacts of pesticide usage

A plant disease is usually defined as abnormal growth and/or dysfunction of a plant resulting from disturbance in normal life process or infections of living organisms (biotic) and nonliving environmental conditions (abiotic) [19].

Plant disease is best managed through an integrated approach, which includes a combination of:

1. Cultural management that utilize plant performance in the local climate, use of disease-resistant varieties when possible, and plant-certified seeds or seed pieces.
2. Mechanical management includes rototilling in the fall, which exposes pathogens, insect eggs, and weed seeds to cold winter temperatures. This action speeds the decomposition of crop residues, improving soil organic matter.
3. Biological control, depending on the use of compost, compost teas, and hyperparasite products that may reduce pathogens by introducing beneficial microbes. Planting flowering plants attracts beneficial insects to all stages of development.
4. Chemical control, depending on the effect of different types of pesticides to manage the problem; this will be efficient after identifying the cause of a plant problem first and applying it in the correct time using the recommended method [19].

It has been reported that field losses from pest's average 35% from the world's main food crops. Direct yield losses caused by pathogens, animals, and weeds are altogether responsible for losses ranging between 20 and 40% of global agricultural productivity [20–22].

Although weeds are the major cause of crop loss on a global scale, significant losses are suffered by agricultural crops due to insect damage and plant diseases; estimated worldwide annual production tonnage (%) age losses attributed to pests at the start of the twenty-first century are 18%, due to animal pests, 16% microbial diseases (of which 70–80% caused by fungi), and 34% weeds, totaling 68% average annual loss of crop production tonnage [22].

Oerke [23] reported that the total global potential loss due to pests are estimated at 26–30% for sugar beet, barley, soybean, wheat, and cotton and 35, 39, and 40% for maize, potatoes, and rice. Plant protection in general and protection of crops against plant diseases in particular have an obvious role to play in meeting the growing demand for food quality and quantity [24]. It involves physical, biological, and chemical methods [25].

The only way to reduce crop losses is integrated pest management. Integrated pest management (IPM) is a system approach that combines different crop protection practices with careful monitoring of pest and their natural enemies [26, 27]. The primary IPM method includes synthetic chemical pesticides that are classed by regulators as low-risk compounds and have high levels of selectivity, such as synthetic insect growth regulators.

1. Crop cultivars bred with total or partial pest resistance.
2. Cultivation practices, such as crop rotation intercropping or under sowing.
3. Physical methods, such as mechanical weeding:
 - Natural products, such as semichemical or biocidal plant extracts
 - Biological control with natural enemies, including different pathogens of plants
 - Decision support tools to inform when it is economically beneficial to apply pesticides and other controls

Ghandler et al [28] reported that although pesticides act similarly despite their chemical active group. When applied to crops or directly to the soil, for example, systemic insecticides, organophosphates, and carbamates generally persist from only a few hours to several months. However, they have been fatal to large numbers of birds on turf and in agriculture and negatively impacted breeding success in birds [29]. Nanopesticides or nanoplant protection products represent an emerging technological development that, in relation to pesticide use, could offer a range of benefits including increased efficacy, durability, and a reduction in the amount of active ingredients that need to be used [30].

Biopesticides are natural products that can be considered as sufficient alternative of synthetic pesticide in pest management.

3. Pesticides in agriculture and their benefits

The farmers around the world had used different methods and ways to fight the causes that lead to reducing crop yield, most of these methods were simple and traditional, and the result were not satisfactory until the use of pesticide application started.

Pesticides include natural and synthetic substances used to control harmful pests such as insects, plant disease organisms, and weed, as well as many other living organisms that endanger the food supply, health, or comfort [8].

The word “pesticides” is a term for all insecticides, herbicides, fungicides, rodenticides, wood preservatives, garden chemicals, and household disinfectants that may be used to kill some pests [31].

A pesticide controls any pest including vectors of human or animal diseases and unwanted species of plants or animals causing harm or interfering with the production, processing, storage, or marketing of food and agricultural commodities [32].

Pesticides are a chemical group widely used by humans, both to protect the production from harmful organisms and quality of crops and for control of vectors and pests of public health [33]. In the last decade, pesticide sales have been roughly stable worldwide with an overall budget of \$40 billion, with the US market accounting for 31.6% of the total [34]. In the last decade, the most significant increase in demand for pesticides has occurred in Central and South America (6.7% annual increase from 2004 to 2014). Followed by the Asian market (4% annual increase from 2004 to 2014); the latter is the second largest after North America. Even the small African market, accounting for 3.5% of global pesticide expenditure in 2004, has shown a sharp 6.4% annual increase during the same period. An annual increase has also been observed in Europe [35].

The use of pesticides in agriculture has led to significant improvement in crop yield per hectare of land [36]. The economy was boosted, crop yields were tremendously increased, and so were the decreases in fatalities insect-borne diseases [31]. Cooper and Dobson [37] demonstrate the three main effects of pesticides:

1. Controlling agriculture pests (including disease and weeds).
2. Controlling human and livestock disease vector nuisance organisms.
3. Preventing or controlling organisms that harm other human activities and structures.

The other strategy of protecting crops is to utilize biorational pesticides, such as biopesticides as alternative to synthetic chemicals. As synthetic pesticides are withdrawn owing to resistance problems or because they are no longer commercially viable, biopesticides are used as a replacement especially since they do not feature residue problems, which are a matter of significant concern for consumers. Currently, biopesticides comprise a small share of the total crop protection market globally, with a value of about \$ 3 billion worldwide, accounting for just 5% of the total crop protection market [38, 39].

The most important characteristics that distinguish biopesticides are (a) short RELs (most are 4 hours), (b) zero-day preharvest intervals (PHI), (c) generally safer to plants, (d) low-risk to environmental, (e) quicker to market at lower overall cost—3 years and \$5 million to develop vs. 10 years and \$200 million, (f) complex modes of action [40].

Despite synthetic pesticides' significant effectiveness on pest and crop diseases, their harmful side effects on plants, soil, and the environment require safer products. Biopesticides clearly have a potential role to play in the development of future integrated pest management strategies, and it is very likely that in the future their role will be more significant in agriculture and forestry [41].

New technology that depends on nanosize of different materials started to spread around the world, because of various and efficient application results. Among nanotechnology sections, pesticides are receiving increasing interest with the development of a range of plant protection products that termed "nanopesticides" [42, 43]. Nanopesticides involve either very small practices of a pesticide active ingredient or other small engineered structures with useful pesticide properties [44]. Dubey et al. [45] reported that there is very limited knowledge about the nanoparticle's long-term adverse effects on soil, plants, and ultimately humans; an intelligent use of nanotechnology may help to achieve food security with the qualitative and sustainable environment.

4. Classification of agrochemical pesticides

4.1 Synthetic pesticides

Synthetic pesticides are classified based on various ways depending on the needs; the three most popular ways to classifying pesticides are the mode of action, the targeted pest species, and the chemical composition of the pesticides [46]. The World Health Organization (WHO) proposed a classification of synthetic pesticides based on their health risks and estimating the median lethal dose (LD50) that produces death in 50% of exposed animals [47].

Pesticide formulation includes emulsifiable concentrates (EC) which are fine suspensions of oil droplets in water and appears milky in color. Wet table powders (WP) are suspensions of fine particles suspended in water. Granules (G) are prepared by mixing the active ingredient with clay for outdoor use. Baits are obtained by mixing the active ingredient with food base especially used for the control of rodents. Dusts (D) must be applied dry and cannot be mixed with water. Fumigants are gaseous insecticides usually packaged under pressure and stored as liquids. Some are tablets or pellets that release gas when mixed with water [31].

Pesticide's mode of action can be classified as contact (non-systemic) and systemic pesticides [31].

Garcia et al. [33] describe that pesticides are classified by target organism (e.g., insecticides, herbicides, fungicides, miticides, nematocides, molluscicides, and rodenticides) and chemical structure (organochlorines (OCs), organophosphates (OPs), carbamates, and pyrethroids).

Organochlorines are organic compounds with five or more chlorine atoms. They were the first synthetic organic pesticides to be used in agriculture and in public health; they were widely used as insecticides for the control of insects.

4.1.1 Organophosphates

Organophosphates are phosphate acid esters or thiophosphoric acid esters their original compounds were highly toxic to mammals. Organophosphates are the general name for organic derivatives of phosphorus. They are the most commonly used insecticides in the world because their unstable chemical structure leads to rapid hydrolysis and little long-term accumulation in the environment [48]. Organophosphate manufactured since then is less toxic to mammals but toxic to target organism, such as insects. Some examples of organophosphate pesticides are malathion, parathion, diazinon and dichlorvos, tribufos (DEF), vamidothion, thiometon, and oxydemeton methyl.

4.1.2 Carbamates

Carbamates are a class of insecticides structurally and mechanistically similar to organophosphate (OP) insecticides. Carbamates are N-methyl Carbamates derived from a carbamic acid and cause carbamylation of acetylcholinesterase at neuronal synapses and neuromuscular junctions, some of the carbamates are aldicarb, carbaryl, oxamyl and terbucarb [49].

4.1.3 Pyrethroids

Pyrethroids are among the most frequently used pesticides and account for more than one-third of the insecticides currently marketed in the world [50]. Pyrethroids are known for their fast knocking down effect against insect pests, low mammalian toxicity, and facile biodegradation [51]. The synthetic pyrethroids with the basic structure of cyclopropane carboxylic ester are called type I pyrethroids. The pyrethroid insecticides were enhanced further by the addition of a cyano group at the benzylic carbon to give α -cyano are called type II, e.g., cyphenothrin and cypermethrin, tefluthrin.

The other major practice to pest management is biopesticides that are also a type of integrated pest management (IPM): biopesticides generally perform particularly well in IPM systems. With their lower toxicity profile, they are

compatible with the use of classical biological control agents. Because they often are most effective at low pest pressures, they are well suited to be used in combination with scouting and monitoring activities, which detect pest problems before they are out of control. As well, IPM programs which include the rotation of biopesticides with conventional chemical pesticides can reduce reliance on single chemistries and delay the development of resistance within pest populations [52].

4.2 Biopesticides fall into three major classes

1. Biochemicals are naturally occurring substances (semichemical, plant extracts, minerals, PGRs, and organic acids) that control pests by nontoxic mechanism. Biochemical pesticides include substances that interfere with mating, such as insect sex pheromones. For example, neem (*Azadirachta indica*), garlic (*Allium sativum*), eucalyptus (*Eucalyptus globulus*), turmeric (*Curcuma longa*), tobacco (*Nicotiana tabacum*), and ginger (*Zingiber officinale*) have been successfully used for the management of several plant diseases [53].
2. Microbial pesticides consist of microorganism (e.g., a bacterium, fungus, protozoan). Microbial pesticides can control many different kinds of pests. The most widely used microbial pesticides are subspecies and strain of *Bacillus thuringiensis* (Bt). Almost 90% of the microbial biopesticides currently available on the market are derived from only onetime pathogenic bacterium, *Bacillus thuringiensis* (Bt) [54].
3. Plant-incorporated protectants (PIPs) are pesticide substances that plants produce from genetic material which has been added to the plant. A scientist can take the gene for the Bt pesticide protein and introduce the gene into the plant's own genetic material. Then, the plant manufactures the protein that destroys the pest. Pest resistance is one of the most widely targeted traits in plant genetic modification [55]; in Arizona (2010) cotton genetically modified by inserting Bt toxin from (*Bacillus thuringiensis*) to fight the pink bollworm moth (*Pectinophora gossypiella*) combined the release of sterile moth with growing genetically modified Bt cotton. This combined strategy reduced the need for insecticide spray and reduced pink bollworm abundance by 99%, with no increase in resistance to Bt cotton [55].

Tri-State Greenhouse IPM Workshop [6] reported that, recently, new substance has been reported as promising compounds for use as biopesticides. Extract of the *Saponaria officinalis* root and the nanoparticles showed a very good acaricidal efficacy [57], the fungus strains of *Talaromyces flavus* SAY-Y-94-01 [58], the fungus *Trichoderma harzianum*, fermentation products of the bacterium *Lactobacillus casei* strain LPT-111 [6], stilbenes accumulated in grape canes [50], and olive mill wastes [51].

In recent years, a new technology began to take place in IPM program; it could contribute to the development of less toxic biopesticides with favorable safety profiles and increased stability of the active agent, enhanced activity on target pest, and increased adoption by the end-users [43, 59]. Nanotechnology will contribute to making agriculture eco-friendlier and more profitable by reducing the usage of crop protection chemicals. Intelligent delivery of fertilizers, pesticides, and growth regulators, including nanosensors for real-time monitoring of soil conditions, crop growth, and pest and disease attack, is made possible through the development of nanodevices and products [60].

4.3 Nanopesticides

New practice that is increasing in the field of agriculture took the place for the potential to reduce the impact of other agrochemicals on human health and in the environment; the application sector of these nanomaterials is “nanopesticides” (ISO TC 299 “International standards for nanotechnology”). The European Commission (2011) based on the JRC report [61] defines that nanomaterials means “a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm to 100 nm. In specific cases, and where warranted by concerns for the environment, health, safety or competitiveness, the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50%.”

ISO TC229 has published six technical specifications on nanotechnology terminology so far, namely:

ISO/TS 27687: 2008 Nanoobjects—Nanoparticle, nanofiber, and nanoplate.

ISO/TS 80004-1: 2010 Core terms.

ISO/TS 80004-2: 2010 Carbon nanoobjects.

ISO/TS 8004-3: 2011 Nanostructured materials.

ISO/TS 8004-4: 2011 Nano-/biointerface.

ISO/TS 8004-7: 2011 Diagnostics and therapeutics for healthcare [62].

Nanoscale material helps to reduce degradation of pesticide and fungicide and increase the effectiveness of application with reduced amount [45].

5. Toxicology of pesticides

Widespread use of pesticides is a significant source of air, water, and soil pollution causing risk to human health as a result of misuse or accident as well as leaving lasting harmful chemicals in the environment [63]. Also, effects of agricultural pesticides on nontarget organisms continue to become a major problem. Indiscriminate and injudicious use of chemical pesticide in agriculture has resulted in several associated adverse effects as environmental pollution, ecological imbalance, and pesticide residues in food, fruit, vegetable, fodder, soil, and water pest resurgence [64].

The WHO [46] grouped pesticides according to the potential risks to humans caused by accidental contact to human being to five classes:

Class Ia. Extremely dangerous parathion, dieldrin.

Class Ib. Highly dangerous eldrin, dichlorvos.

Class II. Moderately hazardous DDT, chlordane.

Class III. Slightly hazardous malathion.

Class IV. Products unlikely to present acute hazard in normal use.

The majority of pesticides are not specifically targeting the pest, during the application nontarget plants and animals are also affected, only about 0.1% pesticides reach the target organism, and the remaining applied pesticides contaminate the surrounding environment [63, 65].

Toxicity can be either acute or chronic:

- a. Acute toxicity is the capability of a substance to cause harmful effects rapidly following exposure (few hours to a day).
- b. Chronic toxicity is the capability of a substance to cause undesirable health effects resulting from long-term exposure [66].

5.1 Effects on humans

The main purpose of IPM is to reduce the effects of pests on crop product and help meet the increasing demand of larger population around the world. Although the application of pesticides achieves the goals of its usage, but at the same time, side effects also appear because of this practice.

Application of pesticides is a major threat to human health. It can taint food, water, soil, and air, causing headaches, drowsiness, fertility issues, and life-threatening illness; hundreds of thousands of known deaths occur each year due to pesticide poisoning [67]. Pesticide use has contributed toward improving agricultural production, in both yield and quality. Pesticides are also widely used in a variety of other settings, some of which most of the general public are not aware of [68]. It is evident that workers who are involved in mixing, loading, transport, and application of pesticide are at the highest risk of pesticide injury [69]. Pesticides can enter into the human body in three ways: (a) through the mouth (oral administration), (b) by adsorption through the skin or eyes (dermal adsorption), and (c) by breathing (inhalation) [70].

Also, atmospheric pesticides can cause hazards to humans. Atmospheric movement may cause transportation of pesticides from application sites to sensitive areas and accumulation of pesticides in the environment [71].

Risk related to pesticide poisoning can be defined as the extent of getting exposed to pesticide with a certain degree of toxicity. These can be expressed as $\text{Risk} = \text{Toxicity} \times \text{Exposure}$ [70].

5.1.1 Organochlorine pesticides (OCPs)

Organochlorine pesticides (OCPs) show multiple effects on the major physiological systems of the body including nervous, circulatory, and reproductive system and, also at some critical growth periods, may generate severe health disturbances [72].

Organophosphorus compounds are commonly used as insecticides. Organophosphate inhibits AChE, an enzyme located in the postsynaptic membrane that degrades AChE into choline and acetic acid [73]. The enzyme is classified as a B esterase whose function is the hydrolysis of acetylcholine which is a major neurotransmitter in the peripheral and central nervous system. The inhibition disturbs the capability of the enzyme to bind to its normal substrate with the subsequent accumulation of AChE at the nerve ending [74, 75]. The systematic investigation of the relationship between chemical structure and inhibition of AChE is the single most important feature required in an organophosphate for anticholinesterase activity and chemical reactivity; it has revealed a direct relationship between anticholinesterase activity and reactivity of the phosphorus atom [76]. Also, OPs can cause a type of toxicity called organophosphate-induced delayed polyneuropathy (OPIDP). It is characterized by deterioration of the long axons in the central and peripheral nervous system and ends with ataxia and paralysis which appear about 2–3 weeks after exposure [74]. Another side effect of Ops is oxidative stress and apoptosis. The damage is generated by the imbalance between reactive oxygen species (ROS) production and elimination [77]. Another side effect of Ops on human health is the disruption of estrogen function by acting as a ligand for receptor, converting other steroids to active estrogen or increasing the expression of estrogen-responsive genes [78]. Other Ops are capable of interfering with the endocrine function by inhibiting the binding of thyroid hormones to their corresponding receptors [78, 79]. Reiss [80] found out that the critical exposure period to PO insecticides for human neurological development is, by definition, the only relevant exposure for birth outcomes. Naksen et al. [81] reported that the birth outcomes as a result of OP exposure suggest a decrease in birth weight and head circumference in newborns born from mothers with low PON1 activity.

5.1.2 Carbamates

Carbamates are hepatically metabolized via hydrolysis, hydroxylation, and conjugation, and 90% is renally excreted in a matter of days. The data of carbamates on central nervous system (CNS) and cerebrospinal fluid penetration, adults tend to have less CNS toxicity, whereas, in pediatric exposures, CNS depression is often a predominant symptom. Carbamates do not undergo aging that occurs during the phosphorylation of organophosphate to acetylcholinesterase and the carbamate-cholinesterase hydrolysis spontaneously within hours [82]. Fukuto [76] found out that insecticide carbamate causes AChE inhibition by identical mechanism to that of Ops. Unlike Ops poisoning, carbamate poisoning tends to be of shorter duration because the inhibition of nervous tissue acetylcholinesterase is reversible, and carbamates are more rapidly metabolism [83]. Forde [84] studied the effects of pregnant women exposure to carbamate; the results appear to show that carbamate when associated with other pesticides is typically used as OPs and pyrethroids. The result obtained is often related to OPs and pyrethroids. Carbamates are usually considered to be of limited acute toxicity.

5.1.3 Pyrethroids

The toxic effects of pyrethroids include neurotoxicity, skin contact, and respiratory and reproductive system toxicities [77]. Type I pyrethroid typical effects include rapid onset of aggressive behavior and increased sensitivity to external stimuli, followed by fine tremor, prostration with coarse whole-body tremor, elevated body temperature, coma, and death [85]. Type II pyrethroid effects are typically characterized by pawing and burrowing behaviors, followed by profuse salivation, increased startled response, abnormal hindlimb movement, and coarse whole-body tremors that progress to sinuous writhing. Clonic seizures may be observed prior to death; the term CS-syndrome (from choreoathetosis and salivation) has been applied to type II responses [85]. Gliga et al. [86] assessed the effects of three major herbicides, three insecticides, and three fungicides on three human cell lines (HepG2, HEK294, and JEG3); they found that fungicides were the most toxic from concentration 300–600 times lower than agricultural dilution, followed by herbicides and then insecticides, with very similar profiles in all cell types. LEG3 was the most sensitive cell line.

Nonoccupational low-dose exposure of any pesticides causes chronic disease in humans and can be considered as a silent killer; almost every crop faces a number of applications of different pesticides which results into multi-residue exposure of these pesticides that could be more in causing toxicity effects [87].

5.2 Effects on plants

Plants are the primary source of food for humans through crop production; crop safety and crop productivity are of paramount importance to ensure providing sufficient and healthy food for peoples.

Plants were the main reasons for pesticide application and practices, but in the early days of chemical pesticide applications, there were little concern about the side effects of this practice until illness started to appear on farmers and farm workers who are directly exposed to pesticides and using crop products that are treated with chemical pesticides. These effects alarmed governments, agriculture intuitions, and scientists around the world to pay a greater attention to these chemical pesticides used for crop protections.

Anonymous [88] found that absorption is the take-in of chemical substance into plants or microorganism. Most chemical pesticides break down once they are absorbed; pesticide residues may separate into simpler substances or remain inside the plant or animals and be released into the environment when the animal dies or plant decays.

A result of the study of Nishisaka et al. [89] to assess the genotoxicity effect of nanoparticles containing the paraquat herbicide indicated less chromosome damage than conventional paraquat herbicide. Saha and Gupta [90] found out that metallic nanoparticle, e.g., Ag NPs, causes significant toxic effects in animal cell culture and animal models; the impact of (Ag NPs) on plant species is related to oxidative stress-related gene expression, genotoxicity, seed germination, and root elongation; and genotoxicity studies revealed different types of chromosomal abnormalities and DNA damages which ultimately lead to cell death and disintegration of plant cell exposed to different coated and uncoated Ag NPs present in the environment. Toxicity of nanoparticles depends upon various factors like plant species, size, and concentration of nanoparticles in different stages of crops; it also depends on their composition and size. Small-sized nanoparticles are more reactive and toxic than the large-sized ones and affect the respiration or photosynthesis process [91]. For example, Al_2O_3 NPs showed phytotoxicity only on corn, reducing the root elongation by 35%. All improved root growth of grape and radish and inhibited root elongation of ryegrass and lettuce but had no effect on cucumber [92]. Boonyanitipong et al. [93] assess the effect of ZnO NPs on rice plant; the result shows adverse effect on rice from 100 mg/L and fully inhibit root growth and biomass at 500–1000 mg/L concentration. In a study of the effect of TiO_2 nanoparticle on aquatic life, the result revealed that TiO_2 reduced the light to entrap the algal cell and thus reduce the growth [94].

5.3 Effects on environment

The Environment Protection Act (EPA) (1986) defined the term environment under Section 2(a) of “to include water, air, land and inter-relationship between water, air, land and human being, other living creatures, plants, microorganisms and property.” The definition includes complex relationship between environment parts; these parts must be in balance to insure healthy and accurate relationship.

Any disturbance in these relationships may lead to undesirable result. One of the most effected factors that play great roll in this disturbance is the application of different types of pesticides.

The potential for misapplication and accidental exposure is great [64]. It is found that only a very small part of the total amount of pesticides applied for weed and pest control (<0.1%) actually reaches the sites of action [95]. The runoff from agriculture and urban land, and rain precipitation and dry disposition from the atmosphere, can transport pesticides to streams and groundwater [96]. Mahmood et al. [97] reported that excessive use of pesticides may lead to the destruction of biodiversity. Birds, aquatic organism, and animals are under the threat of harmful pesticides. The soil is an important part of the environment and plays an effective role in other parts. The application of pesticides results into two ways: positive way by destroying the specific target and negative way by transferring to another non-specific target. In a study of Cessna et al. [98], they found that pesticides enter to the atmosphere by application drift, post-application vapor losses, or wind erosion of pesticide-treated soil; also, their photodegradation may be transported in long distances before the removal processes of atmospheric wet and dry deposition return them to the earth surface. Pesticides that were detected in the atmosphere are (I) organochlorine insecticides (resistant to environmental degradation), (II) organophosphate insecticides (not long lived in the environment), (III) atrazine herbicides (heavily used herbicides, persistent in the environment), (IV) acetanilide herbicides

(used heavily, but not as persistent as atrazine) [71]. Mobility may result in redistribution within the application site and sometimes off-site. After application, a pesticide may (I) attach to soil particles, vegetation, or other surfaces and remain near the site; (II) attach to soil particles and move with eroded soil in runoff or wind; (III) dissolve in water and be absorbed by plants, overflow, or leach; (IV) pass off in vapor or erode from foliage or soil with wind and become airborne [99]. Also, the mobility of pesticides can be affected by several factors of pesticide sorption, water solubility, vapor pressure, and other environmental and site characteristics including weather, topography, canopy, ground cover, soil organic matter, texture, and structure [99]. The persistence of pesticide is expressed in terms of half-life that can help estimate whether or not a pesticide tends to build up in the environment. Pesticide half-lives are classified into three groups: low (less than 16-day half-life), moderate (16–59 days), and high (over 60 days). Pesticides with shorter half-lives tend to build up less and less likely to persist in the environment, while pesticides with longer half-lives are more likely to build up after repeated application. Higher persistence increases the risk of contamination of nearby surface water, groundwater, plants, and animals. Anonymous [88] reported that some pesticides stay in the soil long enough to be absorbed by plants grown in the field years later. The behavior of pesticides in soil is governed by a variety of complex dynamic physical, chemical, and biological processes, including sorption-desorption, volatilization, chemical and biological degradation, uptake by plants, runoff, and leaching [100, 101].

Biopesticides have benefits and limitation effects on the environment, human life, or agricultural product. They are highly effective in managing pests and diseases, without creating negative impacts on the environment, and their active and inert ingredients are generally recognized as safe. Besides the microbial content, carrier media for formulating biopesticide were consisted of several organic materials, such as animal broth, organic materials, or organic waste product. The media is a biodegradable material. In addition, biopesticides support stability and sustainability of agroecosystem because they did not affect negatively on the environment [102].

The nanoagrochemical is crucial to modern agriculture, and due to their direct and intentional application in the environment, nanoagrochemical may be regarded as particularly critical in terms of possible environmental impact, as they would represent the only intentional diffuse source of engineered nanoparticles in the environment [103]. There is harmful chemical reaction and contamination by nanoparticles to soil ecosystem and change in soil structure due to their large surface area and Brownian motion [45]. Kah et al. [104] assess the environmental fate of nanopesticides; the result suggests that the photodegradation and sorption behavior of clothianidin may have a greater impact on the environmental fate of pesticide AI than commercial formulations. AI clothianidin was rapidly released from the nano-carrier systems and that the durability of three nanoformulations would be short in water as well as in soil. Nanoparticles can easily be released in the water body or air, and uptake by living organisms creates toxic effect for humans and animals [43]. Bai et al. [105] found that CU nanoparticles caused damage in the central nervous system. Gliga et al. [86] study the effects of Ag nanoparticles, and the results show that Ag particles of size 10 nm were found more cytotoxic than other sizes.

6. The future

Pesticides are essential to improve the production of crops. The quantity of pesticides will continue to increase as long as the use of pesticides increases. Despite the tremendous benefits of pesticides for human beings especially in agriculture fields, side effects and undesirable results of pest managements such as pesticide residue

crop products that are used in feed lead to several human illnesses in soil and water, microflora in soil, and ecosystem in general. Not until the year 1962 when biologist Carson published her book *Silent Spring* when dichlorodiphenyltrichloroethane (DDT) was at its high production 82 million Kg/year in the United States, it was initially used with great effect to combat malaria, typhus, and the other insect-borne human diseases among both military and civilian populations. The book inspired public concern about the toxicity in wildlife, contamination, and the increasing pest resistance. Control of regulated or quarantined pests is typically done through prevention of entry to a country or an area, eradication and containment, and use of tools such as biological control, pesticides and biopesticides, plant resistance, cultural methods, and natural enemy encouragement. In 2016 a review suggested that classical biological control has provided and should continue to provide many positive outcomes for dealing with damaging invasive alien insect pests [106].

Genetically modified (GM) food is a new type of potentially safer food without the use of pesticides; crops producing pesticides substance from genetic material that has been added to the plant. To insure safety, the EFSA Panel on Genetically Modified Organisms (GMO) require scientific risk assessment on the possible risk they might present for humans, animal health, and the environment before being authorized for market placement [107]. Also, the OECD Working Group for the Safety of Novel Foods and Feeds (WG-SNFF) addresses aspects of the safety assessment of food and feeds derived from genetically engineered crops. Their primary aim is promoting the use of consistent methods and data elements used in the risk/safety assessments among countries. The approach is to compare transgenic crops and derived products with similar conventional ones that are already known and considered safe for use, based on recognized practices, harmonized methods, and data sharing facilitated through the WG-SNFF [108].

Maximizing pesticide efficiency requires the use of radiolabeled pesticides to study pesticide metabolism, fate, residues, and formulation [109]. An increasing number of countries started to develop control strategies for the use of pesticides. The Danish National Action Plans on pesticide (2017–2021) strategy were (1) authorization of pesticides, (2) targeted inspection efforts, (3) collection of knowledge via the pesticide research program, and (4) information, advice, and guidance.

The Report of the OECD Workshop on Sustainable Pest Management in Practice: Anticipating and Adapting to Changes in the Pesticides Regulatory Landscape status and subsequent availability of agricultural pesticide products are necessary for sustainable pest management, including the use of registered agricultural pesticides. In general, the consequences of regulatory decision and the entailing process of adaptation of the agricultural production are not widely considered within the registration process. Regulators, pesticide manufactures, and pesticide users in OECD member countries have had to adapt their practices to ensure that sustainable and effective pest management options remain possible. These changes reduce risk to human health and the environment while promoting sustainable agriculture [110]. The Secretariat 2017 [111] in their 34 sessions includes recommendation that:

1. The international community must work on the development of a comprehensive, binding treaty to regulate hazardous pesticides throughout their life cycle. It should cover standardization among countries, policies to reduce pesticide use worldwide, and development of a framework for the banning and phasing-out of highly hazardous pesticides, as well as strict liability on pesticide producers.
2. Development of comprehensive national action plans to support alternatives to hazardous pesticides along with binding and measurable reduction targets and time frames.

While pesticides proved effective in mitigation of harmful bugs, the risk associated with their use has exceeded their beneficial effects. Nonselective pesticides can harm nontarget plants and animals along with the targeted ones; also with repeated use, some pests develop genetic resistance to pesticides [97].

To control the use of pesticides and reduce their effects, registration is an important aspect of pesticide management to ensure that the pesticide products released in the market are authorized and used only for their planned purpose. It will also enable authorities to implement controls for the price, packaging, labeling, safety, and advertisement of pesticides to ascertain protection of the user's interests [112].

To reduce pesticide impact on the environment, minimize contamination, and ensure the safety of human sources of food and water (surface and groundwater), users should be:

1. Practicing IPM
2. Using only pesticides that are labeled for their intended crop and pest
3. Considering application site characteristics and location of wells, ponds, and other water bodies
4. Maintaining application equipment, measuring, and calibrating accurately
5. Preventing back siphoning and spills, leaving buffer zone around sensitive areas, and reducing off-target drift
6. Considering the impact of weather/irrigation
7. Storing pesticides and disposing of wastes securely and safely [98–113]

Biopesticides have attracted attention in pest management in recent decades and have long promoted as prospective alternative to synthetic pesticides [68]. Although biopesticide use at a global scale is increasing by almost 10% every year [114], the global market must increase further in the future if these pesticides are to play a visible role in substituting for chemical pesticides and reducing the current over-reliance on them [115]. It is expected that biopesticides will equalize with synthetics in terms of market size, between the late 2040s and the early 2050s [116]. Also, Soesanto [101] The conclusion of biopesticides was that biopesticides are the best way to control plant pathogens because of their beneficial effects; though there are still many limitations to be reduced, biopesticides supported stability and sustainability of agroecosystem because they did affect negatively on the environment.

Nanotechnology is the new type of IPM providing a promising future in the direction of formulation that can be used to improve the stability and effectiveness of natural product [117, 118]; it provides controlled release of the molecules at the site of action, can minimize potential toxic effects on nontarget organisms, and can prevent degradation of the active agent by microorganisms [118, 119]. Nanotechnology that includes nanopesticides seems to have a promising future in IPM. The potential toxicity of these nanoparticles is not standardized and not well understood yet explored by international and national safety regulators [60, 120–122]. Athanassious et al. [60] report that safer nanopesticides as alternative methods and practice should take the following into consideration: (a) The process of nanomaterial synthesis may cause changes in dimensions and shape; therefore, risk assessment studies are essential before the use of such materials. (b) Specific guidelines explain how to use these formulations on nanomaterials. (c) The toxic nature of these compounds to plants and insects needs to be analyzed.

(d) Working on nanopesticide formulation before they become more popular in pest management by combining analytical techniques that can detect, characterize, and quantify the active ingredient and adjuvants emanating from the formulation.

Emerging pesticide nanoformulations are not only increasingly complex and biologically active but may also exhibit a potential change in the physicochemical properties and/or biological effects at a size range that is larger than the nanoscale (>100 nm) [30].

-Tool and techniques to characterize properties (particle shape, size range, surface properties) of complex formulations of nanopesticides are lacking. Nanopesticides are more complex products by design and therefore pose greater challenges to analysts [30].

7. Conclusion

Continuous growth in population around the world leads to increase the demand for higher crop production. The quality and quantity of crops provided to people must be satisfactory, which can be achieved by using specific methods to control pests that play a great role in crop losses and poor product. The main method used for this purpose is synthetic pesticides, with other methods: biopesticides and nanopesticides. Despite the harmful side effects especially of synthetic pesticide compared to the other methods with less harmful effects on humans, plants, and the environment, still the synthetic pesticides play an important part of IPM. This requires intensive work of scientists, institutions of agriculture around the world, environment studies to assess and evaluate the side effects of these different methods, and provide good training for safer application of pesticides and also continues studies for every new chemical production and methods used in the agriculture field, to decrease and minimize the harmful effects on humans, animals, plants, nontarget organisms, and the environment, including aquatic environment.

Conflict of interest

The author declares no conflict of interest.

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