Chapter

Pesticides: Chemistry, Manufacturing, Regulation, Usage and Impacts on Population in Kenya

Joseph O. Lalah, Peter O. Otieno, Zedekiah Odira and Joanne A. Ogunah

Abstract

Pesticide use in Kenya plays a critical role in socio-economic development because its economy depends heavily on agriculture, which contributes to 30% of the GDP and accounts for 60% of export earnings. For agriculture and public health vector control, the country relies on pesticides, most of which (95%) are formulated products imported from China, India and Germany as the top exporters. In this chapter, we present the chemistry, manufacturing, importation and regulatory processes regarding pesticides in Kenya as well as their usage and impacts. All the various categories, organochlorine, organophosphate, carbamate, pyrethroid, neonicotinod insectides, as well as fungicides, herbicides and biopesticides, which are used in the country, are considered. A total of 1,447 and 157, which include formulations and active ingredients, respectively, for use in agriculture and public health sectors, with sufficient information on their usages and toxicities, are listed on the Pest Control Products Board (PCPB) database that is available to the public. A significant number of studies have been conducted in major agricultural regions, which have characterized pesticides, their toxicities, the types of crops and pests, the usage and human and environmental health risk indices, since the 2000, but the reports have not made any impacts on pesticide regulation, as some of the very toxic active ingredients, belonging to the WHO Class I and II, are still reported by farmers. However, a recent call from NGO's made an impact in government and parliament, and a bill was introduced in 2020 with the aim of banning some of the toxic ones that have already been withdrawn from the EU market.

Keywords: pesticides, regulations, usage, toxicity, human, environmental, impacts, Kenya

1. Introduction

1.1 Why are pesticides important?

Human population development has been dependent on a steady increase in abundance of food supply over the years. The world population explosion began to be felt around 1600 AD; mainly as a result of two factors: (i) ability of man to

control diseases and (ii) developments made in modern agriculture to increase food supplies [1]. Prior to 1800, there was little application of scientific information in agricultural production. Mass starvations occurred, whenever there were conflicts such as political conflicts, wars and climate change, which affected agricultural production and/or food flow. By about 1983, about 5 billion people existed, compared to the current global human population of approximately 8 billion. This population explosion to 8 billion over a period of just 38 years was possible because of developments in modern agriculture [1, 2] and ability of humankind to fight various diseases [3]. The fastest growth was realized in the 20th and 21st centuries when the population increased exponentially from about 2 billion in 1930 to about 7 billion in 2000 [2].

Kenya's *population*, which is equivalent to 0.69% of the total world population, was estimated at 53,771,296 people in 2020 [2], and this is expected to grow by around 1 million per year—3000 people every day—over the next 40 years, reaching approximately 85 million by 2050 [2]. The country will, therefore, rely on agriculture to provide food for the growing population. Agriculture contributes approximately 27% of Kenya's GDP and a large part of its rural population (approximately 80%) depends on subsistence farming as a source of food, employment and income [4]. The importation and use of pesticides are, therefore, foreseen to increase [3, 5].

Pesticides were originally introduced to control insects but have also nowadays been used to eradicate problems caused by nematodes, mites, rodents, birds, mollusks, parasitic fungi and weeds [1, 3]. Approximately 33% and 30% of food crops in the world are lost annually to pests and insects alone, respectively [1]. The losses occur in the field as well as during postharvest e.g. during storage or transportation. Tropical countries in Sub-Saharan Africa, which have a myriad of insects and disease pathogens, will have to continue relying on pesticides despite their negative impacts on the environment and human health.

Significant increases in different crop yields can be realized by using insecticides to control certain pests [1, 3]. In corn, 24.4%, 38.4% and 10.7% increases in yields have been achieved by controlling corn borers, leaf hoppers and corn root worms, respectively, using insecticides; whereas in wheat, 79%, 47%, and 29.5% increases have been realized by controlling brown wheat mites, cutworms and white grubs, respectively. In Irish potatoes, 45.6% and 42.8% increases in yields have been realized by controlling Colorado potato beetles and potato leafhoppers, respectively [3]. Bollworm and thrips can destroy cotton almost completely, reducing the yields to just 21.3% and 59.7%, respectively [3], if not controlled by insecticides. The FAO has estimated that 50% of cotton production in developing countries would be destroyed if there is no use of insecticides [3]. Pesticides not only reduce losses caused by pests and weeds but also increase profits for farmers by reducing the need for labor, specifically by using herbicides.

Many human diseases such as yellow fever and malaria, which are caused by mosquitoes, were eradicated or controlled in the past in industrialized countries by using pesticides [3]. The use of insecticides such as DDT contributed to the reduction of global annual malaria mortality rates from 6 million in 1939, to 2.5 million in 1965 and 1 million in 1991 [6]. Overcoming malaria is still a very big challenge for developing countries, especially in the Sub-Saharan African countries, partly because of failure to use pesticides effectively to control mosquito larvae, as recommended by the WHO [7]. Other diseases and their respective causes (as given here in parenthesis) have been controlled by use of insecticides including sleeping

sickness (tsetse flies), anthrax (horseflies), bubonic plague (rat flea), dysentery (houseflies), filariasis, encephalitides, dengue fever, Chagas disease and West Nile virus (all these five caused by mosquitoes), hemorrhage and Q fevers (ticks and mites), bilharziasis (snails) and bronchial asthma (cockroaches) [3, 6, 8]. However, the agricultural sector consumes most of the conventional pesticides, e.g. approximately 77% in the USA [3, 5]. The situation is quite similar in Kenya, where most the conventional pesticides in form of insecticides, fungicides and herbicides are needed in the agricultural sector. Currently, some of the major classes of pesticides that have a significant stake in the global pesticide industry include organophosphate, carbamate, pyrethroid and neonicotinoid insecticides, fungicides and herbicides, respectively; and the organophosphates, carbamates, synthetic pyrethroids and neonicotinoids together account for 70% of the global insecticide sales [3, 5].

The cost of developing a pesticide active ingredient/compound is very expensive, ranging between US dollars 50 million and 100 million per active compound. These costs cover various aspects, including screening, synthesis, trials and regulation & registration; and the time period can take between 5 and 9 years before a product goes into commercial sale [3, 9, 10]. The developing countries such as Kenya, therefore, control a very small share of the pesticide industry, with Kenya importing most pesticides, which are already manufactured (95%) and only manufacturing a very small percentage (5%) of the products it needs [11].

2. Pesticide chemistry and biochemistry

Pesticides are classified in various ways, i.e. according to target pest, or according to their chemistry, chemical structures and particular functional groups on their molecules, respectively. The classification according to pests, including terminologies such as algaecides (developed to control algae), acaricides (mites), avicides (birds/avian), bactericides (bacteria), fungicides (fungi), herbicides (weeds/plants), larvicides (larvae), molluscicides (mollusks e.g. snail, slugs), nematicides (nematodes), termicides (termites), ovicides (eggs), pediculicides (lice), predicides (predators e.g. coyotes and wolves), rodenticides (rodents), slimicides (slime) and silvicides (trees and brushes or entire forest), are used and usually indicated on the labels of the products [1]. However, in the industry as well as among scientists and researchers, pesticides are grouped broadly, according to their chemistry, chemical structures and mode of action, into four main categories, i.e. insecticides, herbicides, fungicides and biological control compounds/products such as microbial pesticides, as discussed in the following section.

2.1 Insecticides

Insecticides are used to destroy insects and can be classified according to their chemical structure as well as their mode of action as (i) Stomach poisons—which are lethal only to insects, which ingest them and were tested on target organisms through oral exposure; (ii) Contact insecticides—which kill insects following external bodily contact and do not have to be ingested to impart expected toxic effects and (iii) Fumigants—which act on the insect through its respiratory system, by emitting poisonous vapors, which can be inhaled and enter into the target organism through the respiratory system [12]. An insecticide can act by one

or a combination of two or three of these modes. These classifications are taken as the tested modes of toxicity (based on trials) at the point of registration of the product and are normally given on the labels on the containers. During development, all insecticides are subjected to standard toxicity tests as described in the EU or USEPA standard methods [3, 13] and are expressed as LD_{50} or EC_{50} values. The LD_{50} is defined as the lethal dose of a compound that kills 50% of the target organism on exposure in a standard toxicity test procedure, in milligrams per kilogram weight of the test organism (mg/kg). The EC_{50} is defined as the effective concentration of the compound in water that kills 50% of the target organism in a standard toxicity test and is expressed in mg/L, and is normally conducted for aquatic organisms. The toxicity tests are done for: insects—to show effectiveness (as insecticides), rats—to show potential hazards to mammals especially humans, birds/fishes/bees etc.—to show potential hazards to the environment or non-target organisms. Pesticides are, therefore, ranked as hazards according to the WHO, where Class I, II, III and IV pesticides, respectively, where Class I are the most toxic with the least LD_{50} values [3].

Insecticides are subdivided into organochlorines, organophosphorus (or organophosphates), carbamates, pyrethroids, neonicotinoids, insect growth regulators (IGRs) and natural products (which include microbial insecticides), respectively. Brief descriptions of these seven categories, which are all popularly used in Kenya, are presented in the following sections.

2.1.1 Organochlorine insecticides (OCs)

The organochlorine insecticides are divided into three major classes, including the *DDT and its analogues*, the *benzene hexachloride (BHC) isomers* and the *cyclodiene compounds*, respectively. The DDT and its analogues include *DDT,* which is commonly known as *p,p′-DDT* (IUPAC nomenclature: 1,1,1-trichloro-2,2-bis (p-chlorophenyl) ethane). It was the first synthesized chlorinated insecticide, manufactured in 1873 but was recognized as an insecticide at the beginning of the world war in 1939 [1, 5]. After DDT, more and more organochlorine pesticides were discovered and synthesized in Europe and USA. When DDT is synthesized, the technical mixture contains a lot of impurities, with only seventy per cent (70%) of the mixture being the active ingredient p,p′-DDT, and others—21% is the ortho-isomer (o,p′-DDT), 1% the o,o′-DDT; 4% the p,p′-DDD and 0.04% the o,p′-DDD. These isomer impurities are formed during synthesis and account for 30% of weight of the technical mixture (Note: the 'o' means 'ortho' and 'p' means 'para' position on the benzene ring). These impurities potentiate the toxicity of DDT and also add to the environmental burden of DDT because they are also persistent. Other metabolites of DDT also form in the organisms or the environment, e.g. DDE, which is more potent and persistent than DDT (**Figure 1a**). The isomeric impurities have little value as toxicants, since they are just <10% as toxic as the p,p′-DDT. DDT is toxic to non-targets and has an LD_{50} (oral, rats) of 250 mg/kg [3].

The other DDT analogues that were manufactured after DDT have various functional groups on the DDT molecule changed and include *methoxychlor*, *dicofol* and *chlorobenzilate*. As shown in **Figure 1a**, the various changes on the DDT molecule by researchers resulted in different pesticides, which were designed to be less toxic than DDT, with lower mammalian toxicities, e.g. methoxychlor has an LD_{50} (oral, rat) of 600 mg/kg, while dicofol has LD_{50} (oral, rats) of 595 mg/kg, chlorobenzilate

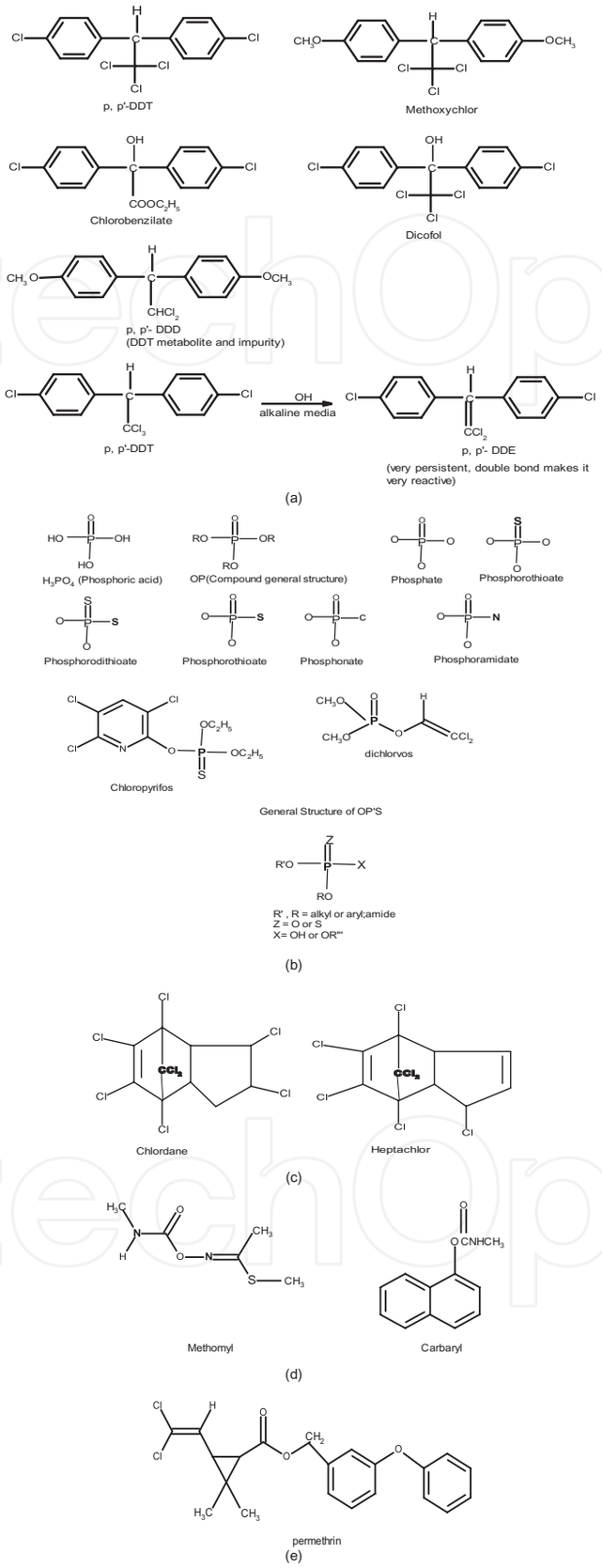

Figure 1.
(a) DDT and its analogues. (b) The general chemical structure of OPs, the starting phosphates, and two OP insecticides. (c) Chemical structures of two cyclodiene insecticides. (d) Chemical structures of two carbamate insecticides. (e) Chemical structure of permethrin, a pyrethroid insecticide.

(3888 mg/kg) and p,p′-DDD (3400 mg/kg) [3]. The DDT analogues have similar chemical and physical properties but because of the slight differences in chemical structures have differences in toxicity and specificity. Dicofol and chlorobenzilate, for example, have lower insecticidal activity, but better acaricidal activities. The DDT group are considered as persistent organic pollutants (POPs) and are environmentally persistent since they are non-polar, highly lipophilic, stable to photolysis, and have very low water solubilities and low vapor pressures [14, 15]. They cause endocrine disruptive effects because of their ability to mimic sex hormones [14, 15]. Although DDT has been banned globally, it is allowed restrictively for use in Kenya, for malaria vector control, only. *Methoxychlor* has been banned in Kenya, but *dicofol* and *chlorobenzilate* though not banned are not used in Kenya.

The second subclass of organochlorines, the *Benzene hexachloride isomers,* was first discovered in 1942 [3]. They are chlorinated saturated six-carbon cyclic alkane molecules, which can adopt a chair conformation [6]. On each C atom, there is a chlorine atom, located in axial or equatorial position, respectively, on the molecule, which gives the various five isomers (α, β, γ, δ, ε). Only the γ (gamma) isomer exhibits pronounced insecticidal activity. It is the main isomer and is known as γ-hexachlorocyclohexane (γ-HCH) or *lindane*. Lindane is odorless and is widely used even in agriculture. Other BHC isomers have unpleasant odor, and this gives an off flavor in root and tuber crops, limiting their use in agriculture. Although banned in most countries, lindane is still allowed restrictively for non-food-related use in Kenya, like seed dressing [3, 6]. Lindane is more toxic than DDT group and has an LD_{50} (oral, rats) of 125 mg/kg. It has a higher vapor pressure (9×10^{-6} mmHg) than DDT and, therefore, is slightly more water-soluble (10 ppm in pure water) [16].

The third subclass, the *cyclodiene compounds* or *cyclodiene insecticides* were discovered in the USA after the War II (around 1948). They are cyclic hydrocarbons and include *aldrin*, *dieldrin*, *chlordane* (two isomers α and β-chlordane), *heptachlor*, *endrin*, *endosulfan*, *chlordecone*, *mirex* and *toxaphene* (**Figure 1b**). Although others are synthesized, toxaphene is strictly a chlorinated terpene, produced by passing chlorine into camphene, a natural product [3, 6]. Like other OCs, all these cyclodienes are heavily chlorinated compounds. Some of the cyclodienes have higher mammalian toxicity than the DDT group but the LD_{50}s (oral, rat) vary widely, ranging from aldrin 38–67 mg/kg, dieldrin 37–87 mg/kg, chlordane 367–515 mg/kg, endrin 7–15 mg/kg, heptachlor 147–220 mg/kg, endosulfan 18–43 mg/kg, chlordecone 114–140 mg/kg, mirex 306 mg/kg and toxaphene 69 mg/kg [3, 6]. In this group, *aldrin, heptachl*or and other *cyclodienes* have long residual lives in soil, expressed in terms of 'half-life', and; therefore, cyclodienes were important agents for controlling termites and soil insects. They are very stable, lipophilic and have low vapor pressures (range of 10^{-5} to 10^{-7} mmHg). They have been banned or severely restricted because of environmental persistence and non-target toxicity in most countries, and even in Kenya some of them such as *aldrin, dieldrin, chlordane*, *heptachlor* and *endrin* have been banned [11]. The principal site of action of organochlorines is the nervous system, where they bind to the sodium channel and cause delayed Na-inactivation, resulting in a prolonged delay in Na-inactivation and subsequent interference with nerve impulse functions.

2.1.2 Organophosphorus insecticides (OPs)

After the OCs, the trend was to (i) avoid persistence (ii) build biodegradability and (iii) have a narrow spectrum of activity (more specificity). Therefore, the OCs have

OP subclass	Examples in the subclass
Phosphates	Dichlorvos, naled, dicrotophos, mevinphos, chlorfenvinphos, crotoxyphos.
Phosphorothioates	Ethyl parathion, methylparathion, chlorpyrifos, diazinon, temephos
Phosphorodithioates	Malathion, dimethoate, phorate, azinphos-methyl, methidathion, phosmet, azinphos-ethyl
Phosphorothiolates	Oxydemeton-methyl, pyraclofos
Phosphoramides	Acephate and methamidophos

Table 1.
Sub-classes of OPs and specific examples of active ingredients.

now been replaced by OPs, carbamates, neonicotinoids and pyrethroids, which have these desirable properties. The OPs are very popular in Kenya and, as insecticides, dominate the Kenyan synthetic pesticide market. In general, they are more toxic to insects and mammals than OCs but are readily biodegradable. They were discovered as by-products of chemical warfare research involving the development of nerve gases such as *sarin, soman and tabun*, in Germany during War II [1, 3, 17], and esters of *phosphoric acid*, *thiophosphoric acid* (*phosphorothioate*), *phosphorothiolate*, *phosphorodithioate* or *phosphoramidate* are given in **Table1** and their structures in **Figure 1c**.

These starting organophosphoric acidic compounds for synthesis of OPs indicate the six subclasses of OP insecticides; e.g. when H atoms of phosphoric acid are replaced with organic radicals such as methyl, ethyl or phenyl, the compounds obtained are organophosphates. On the other hand, oxygen can be replaced with S, C, or N to yield different derivatives. *Phosphates* such as *dichlorvos* are few but many other subclasses also become *organophosphates* during metabolism by various organisms, for example by changing an S atom by an O atom through oxidation. In the subclass *phosphorothioates (*e.g. *chlorpyrifos* and *diazinon),* an S atom is double bonded to phosphorus, while in the subclass *phosphorodithioates (*e.g. *malathion* and *dimethoate)*, the molecule contains two sulfur atoms in the phosphoric acid part. In *phosphorothiolates,* there is a single bond between S and P atoms, and in p*hosphoramides (*e.g. *acephate),* there is a P atom bound to N atom (**Figure 1c**) [3, 6].

Organophosphates have different physical and chemical properties from the organochlorines. Overall, they have moderate-to-considerable water solubility, with some such as *oxydemeton-methyl*, *trichlorfon* and *phosphoramidates*, being very soluble. They also have moderate-to-considerable vapor pressures (generally ranging between 10^{-3} and 10^{-5} mmHg) and therefore are less volatile than most OCs, although some such as *naled, parathion* and *dichlorvos* are very volatile [6, 17]. The OPs are degradable in the environment, e.g. in water, soil and other compartments and are easily metabolized in the organisms, with the most common chemical reactions being hydrolysis, catalyzed by water and esterases. Insects, mammals and other organisms have esterases, which can metabolize OPs e.g. *malathion carboxylesterase,* which has been shown to *decarboxylate malathion* in rat liver [18, 19]. Another common reaction of OP compounds is oxidation of the P=S moiety on an OP molecule to P=O, which is mediated by the cytochrome P450 monoxygenases. This oxidation is referred to as oxidative desulfurization, e.g. conversion of *malathion* to *malaoxon,* which occurs in insects and mammals [3, 18]. The combination of physical (e.g. *water solubility*) and chemical (*hydrolysis and oxidation*) properties make the entire OP class of insecticides biodegradable and more easily excreted.

2.1.3 Carbamate insecticides (CBs)

Carbamates are esters of carbamic acid, $HOOCONH_2$. The 3 H atoms in the molecule can be replaced by aliphatic or aromatic radicals to become carbamate insecticides. However, the second H on the nitrogen (N) is not replaced in making CB insecticides because the monoalkyl structure (NRH) is more toxic than the N-disubstituted compound (NRR″) [20]. Carbamic acid is similar in chemical structure to the pharmaceutical agent, physostigmine (eserine), whose synthesis started the curiosity on carbamates. Physostigmine is a poison, an acetylcholinesterase (AChE) inhibitor. A typical carbamate structure is represented by *carbaryl* (1-naphthylmethyl carbamate), which was the first carbamate insecticide to be synthesized. Substituted phenyl-N-methyl carbamate insecticides can be synthesized by addition of methyl isocyanate (CH_3NCO) to various phenols, some of them with substituted alkyl or phenyl functional groups (R), as shown:

$$RC_6H_5OH + CH_3NCO \rightarrow RC_6H_5OOCNCH_3 \left(R = \text{alkyl or phenyl}\right) \quad (1)$$

During this synthetic process, all reagents and solvents are kept free from water because water reacts readily with methylisocyanate. The reaction is usually vigorous and thermic generating a lot of heat and can cause the release of methyl isocyanate, which is extremely toxic, from the reaction vessel. This is what caused the Bhopal accident in 1984, in which methyl isocyanate gas leaked from a Union Carbide factory in Bhopal, India, killing approximately 3800 people [1]. Making various changes to the carbamyl functional group ($-O-(C=O-NH_2$) by varying R (alkyl or aryl) groups researchers resulted in many different CB insecticides (**Figure 1d**). The chemical structures of two CBs, *methomyl* and *carbaryl*, are shown in **Figure 1d**. Carbamates, like OPs, act by binding to and inhibiting *acetylcholinesterase* (AChE), resulting in a buildup of acetylcholine at the synapse, which causes excessive neuroexcitation, paralysis and death. The second mode of action is by binding and interference with neuropathy target esterases (NTE) located in the nervous system in insects.

Carbamates are popular in Kenya, for example, *carbofuran*, *aldicarb*, *propoxur*, *carbaryl*, *methomyl*, *oxamyl*, *carbosulfan* and *pirimicarb* are often used in the agricultural sector [11]. Some of the carbamates are very toxic to non-target, with very low LD_{50} (oral, rats) values, e.g. *aldicarb* (LD_{50}: 1 mg/kg), *methomyl* (17–26 mg/kg), *oxamyl* (54 mg/kg) and *carbofuran* (5–13 mg/kg), while others such as *carbaryl* (500–700 mg/kg) and propoxur (95–104 mg/kg), are less toxic [3]. Carbamates are also very toxic to birds, i.e. *carbofuran* (LD_{50} 25–39 mg/kg in birds), *carbosulfan* (10 mg/kg), *propoxur* (4–120 mg.kg), *aldicarb* (1.78–5.34 mg/kg) and *methomyl* (10–42 mg/kg), except *carbaryl* (LD_{50} > 2000 mg/kg). *Carbofuran* and *carbaryl* were popularly used in field crops including rice and maize farming, from 1980's to 2000 in Kenya. Due to their high toxicity, *aldicarb, carbofuran* and *carbosulfan* have recently been misused by pastoralists and farmers against wildlife, especially predators, which has led to carbofuran withdrawal pending banning in Kenya [21, 22]. Granular forms of carbofuran and aldicarb, which are fairly soluble in water, can be picked by small organisms such as worms and grasshoppers in farm fields and through food chain transfer, larger scavenger birds and other insect-eating species get poisoned [21, 22]. Liquid formulations of carbofuran are considered safer and are still allowed in other countries despite the ban on granular formulations [21].

2.2 Herbicides

2.2.1 Herbicide chemistry and biochemistry

By definition, a herbicide is a compound that is capable of either killing or injuring plants (or weeds) and can control their growth. Herbicides are used to control weeds in farms as well as lawns, roads and other facilities, and their use has led to great reductions in agricultural production costs. Herbicides can be: (i) *selective,* killing only a particular group of plants such as the leafed plants or grasses or (ii) *non-selective*, making the ground barren of all plant life. They can be formulated either in (i) *granular form*, which is worked into the soil prior to planting the crop in a *preemergence* application or (ii) *liquid spray form,* which may be applied best at various stages after planting, *postemergence or preemergence*, the choice between (i) and (ii) depending on the particular chemical, weed, soil type and crop cultivated [3]. However, the use of herbicides is very intricate and several factors must be considered, e.g. it can destroy a lawn or the plant crops, which are meant to be protected against weeds. Therefore, there is a need to consider wind direction and proximity to wanted plants, when applying herbicides. Different species of plants in the same class may respond differently, some requiring one application and others up to 3 applications before being controlled. Herbicides can become effective either by (i) *direct contact* with plants or (ii) by movement through the entire plant following absorption (called *systemic action*) [23].

Generally, herbicides may, therefore, be classified into a number of groups, either (i) based on the *chemical structure* or (ii) based on when and how it is applied, e.g. *preplanting*—applied to soil before crop is seeded, *preemergenc*e—applied to soil before usual time of appearance of unwanted weeds/vegetation or *postemergence*—applied to soil or foliage after the germination of the crop and/or weeds; or (iii) based on mode of exposure, e.g. as *contact herbicide*—which acts by impinging on plant foliage; or *translocated/systemic herbicide* – which are absorbed via the soil or through foliage into the plant xylem and Phloem; or (v) based on *mode of toxicity* in plants e.g. as *selective herbicide*—toxic to some species only or *non-selective,* which kills all plants (**Table 2**). There are two modes of toxicity of herbicides, the first one applies to *non-selective* herbicides, which interfere with photosynthesis and thereby starve the plant to death, with loss of its green color and withering due to lack of energy to carry out the life processes. The second one applies to *selective* herbicides, which act like hormones or biochemical catalysts that control a particular chemical change in a particular type of plant organism at a particular stage/state of its growth. Most selective herbicides today are *growth hormones*, which cause abnormal growth in a plant and swelling of cells, resulting in the leaf becoming so thick that nutrients and water cannot be absorbed [23].

For example, benzoic acids act as growth hormone herbicides, and move both from leaves to the terminal meristems of leaf, shoot and root, and also move in the transpiration stream, and this permits them to also be soil-applied [24]. The majority of herbicides act by inhibiting photosynthesis I and II (**Table 2**). Various chemicals such as calcium cyanamide (CaHCN), borates, arsenates, copper sulfates, sulfuric acid, and chlorates, were used as weed killers, and some formulations such as aqueous solutions of sodium chlorate $NaClO_3$ (40%) and sodium metaborate $NaBO_2$ (50%), respectively, are still used as *non-selective* herbicides [3]. The discovery of selective herbicides started in 1935, starting with nitrophenol [3], and later, more work was directed towards auxins or hormones, as selective herbicides.

Chemical class	Mode of toxicity	Examples
Phenoxy acetic acids	Production of high levels of RNA causing abnormal fast growth and death.	2,4-D; 2,4,5-T; MCPA (4-chloro-o-toloxy acetic acid).
Triazines	Inhibition of photosynthesis I and II.	Chloro-s triazines e.g. simazine, atrazine, cyanazine; thiomethyl-s-triazines e.g. ametryn, prometryn; methoxy-s-triazines e.g. prometon.
Arylcarbamates	Inhibition of photosynthesis I and II.	Propham, chlorpropham.
Ureas (substituted ureas).	Inhibition of photosynthesis I and II	Monuron, diuron.
Dinitrophenols	Inhibition of respiration by blockage of electron transfer processes (NADH → $NAD^+ + e^-$ or ATP → ADP + Pi). Desiccants	2,4-dinitrophenol; DNOC; dinoseb, dinoterb.
Bipyridyl derivatives	Inhibition of growth of seedling	Paraquat; diquat.
Acetanilides	Inhibition of protein synthesis	Alachlor; propanil.
Dinitroanilines	Inhibition of protein synthesis and cell division	Dichlobenil; trifluralin; pendimethalin.
Amides (chloroacetamides).	Growth stimulants ('auxins', induces light absorption and causes rapid overgrowth).	Metalochlor; acetolachlor; propachlor; butachlor.
Aryl aliphatic acids (chloroaliphatic acids).	Inhibition of carotenoids synthesis (destroys chlorophyll)	Chloro-substituted benzoic acids: Dicamba; chloramben; naptalam.
Hydrazines	Inhibition of cell nucleus division.	Metribuzine; fluconazole; triadimefon; metamitron; metazachlor.
Alkyl N-aryl carbamates	Inhibition of respiration by blockage of electron transfer processes (NADH → $NAD^+ + e^-$ or ATP → ADP + Pi).	Chloropropham; propham.
Halophenols	Inhibition of protein synthesis.	2,4,5-trichlorophenol; 2,3,4.6-tetrachlorophenol.
Aliphatic chlorocarboxylic acids	Plant growth regulator (inhibit protein synthesis)	Trichloroacetic acid (TCA), dalapon.
Glycine derivatives		Glyphosate.
Non selective	Non selective; photosynthesis inhibition; desiccants etc	Inorganic agents: copper sulfate; sodium borate; organic: bentazon.

Table 2.
Herbicide classes and the corresponding modes of toxicity.

In Kenya, *2,4-D* (2,4-dichlorophenoxyacetic acid), a selective phenoxyacetic herbicide, is still one of the most widely used, while *2,4,5-T* (2,4,5-trichlorophenoxy acetic acid), was highly effective but it is no longer used because it was banned in most countries due to non-target toxicity caused by dioxins, which are inherent in the technical mixture [3, 25]. The active ingredients of the various classes of herbicides presented in **Table 2** are very popular in Kenya, including *2,4-D, atrazine, glyphosate, diuron, metribuzine, hexazinone, paraquat, alachlor, metolachlor and fluconazole*, which are commonly used in cereal (maize and wheat), coffee, tea, sugarcane and horticulture. The enhanced efficacy and popularity of *atrazine* is because corn and

certain types of crops are unaffected by it, rendering it harmless, yet killing weeds [3]. Herbicides are intensively used in certain crops in Kenya e.g. large-scale farming of maize and sugarcane, where large farm acreages are involved e.g. in Trans Nzoia maize farms and Nzoia Nucleus Estate sugarcane farms. In 2010, approximately 10,500 kg of various types of herbicides were used in a total acreage of 18,000 Ha of sugarcane farms in Nzoia [26]. Generally, in Kenya, even though herbicide use is increasing, insecticides are still being imported in higher amounts, which is different from the USA where 59% of all pesticides used are herbicides [3].

2.3 Pyrethroids

Synthetic pyrethroids entered the market in 1980s and by 1982, 30% of worldwide insecticides (in terms of sales) in the market were pyrethroids [3, 25, 27, 28]. They arose from a much older class of botanical insecticides, the pyrethrum. Pyrethrum is a mixture of five (5) insecticidal esters, *pyrethrin I, pyrethrin II, cinerin I, cinerin II and jasmins*, which are all extracted from dried pyrethrum flowers [3]. The *chrysanthemum* variety of pyrethrum grown in Kenya yields the highest proportions of active ingredients. In 1965, the world production of pyrethrum was 20,000 tons, with Kenya accounting for 10,000 tons. However, pyrethrum production dwindled around the 1990s due mainly to competition with synthetic pyrethroids. It is however currently being revived again [3, 25, 27, 28]. The increase in usage of pyrethrum extracts amidst plenty of other various types of insecticides (e.g. OPs and CBs) lies in the fact that it has rapid knockdown effect or paralytic action on flying insects. In addition, pyrethrum extracts have lower mammalian toxicity due to their more efficient enzymatic biodegradability, and good selectivity due to low toxicity in some insects. Due to high demand, chemists synthesized analogues of pyrethrum extracts, called *synthetic pyrethroids*, with better stability in air, more persistent residual effect, better selectivity to target insects, lower mammalian toxicity and cheaper costs. The term '*pyrethroids*', therefore, includes both the *pyrethrum flower extracts* and the *synthetic* analogues. The active ingredients in the *synthetic* analogues are called *Pyrethrins*. Pyrethrin consists of esters, namely *Pyrethrin I and II and Cinerins I and II*, each of which are comprised of a combination of two different alcohols, *pyrethrolone* and *cinerolone*, respectively, and two different carboxylic acids - *chrysanthemic* and *pyrethric acids*, as follows: (a) Pyrethrin I (an ester of chrysanthemic acid + pyrethrolone); (b) Pyrethrin II (an ester of pyrethric acid + pyrethrolone); (c) Cinerin I (and ester of chrysanthemic acid + cinerolone and (d) Cinerin II (an ester of pyrethric acid + cinerolone).

Pyrethrin I is the most active ingredient of the pyrethrins for lethality. Pyrethrin II possesses remarkable knockdown properties for a wide range of household, veterinary and postharvest storage pests. The esters formed from the alcohols and respective carboxylic acids are the different active ingredients used in pyrethroid insecticide formulations, whose composition includes synergists and other adjuvants [3, 25, 27, 28]. The various changes in functional groups of pyrethrins and alcohols have resulted in different chemical structures of synthetic pyrethroids (**Figure 1e**). Based on their chemical structures, there are two types of pyrethroids, Type I pyrethroids (*e.g. permethrin, resmethrin, tetramethrin, allemethrin, bifenthrin and metofluthrin*) and Type II pyrethroids (*e.g. cypermethrin, fenvalerate, esfenvalerate, deltamethrin, fenprothrin, lambda-cyhalothrin, tefluthrin, cyfluthrin, acrinathrin and imiprothrin*). The main structural difference between Type I and Type II pyrethroids lies in the fact that Type II synthetic pyrethroids contain a cyano (C=N) group, whereas Type I do not. Type I general structure can be abbreviated as $R_1(C3)C{=}O(OR_2)$ and that of Type II

as $R_1(C3)C{=}O(C(CN)R_2)$, where R_1, R_2 are alkyl or phenyl groups, C3 is a rigid cyclic propane and CN is the cyano group. Therefore, distinct chemical structures of synthetic pyrethroids convey selectivity towards certain insect species and mammals [3].

Synthetic pyrethroids have unique properties because of structural differences, which are seen in form of *stereoisomerism, i.e. geometric (cis-trans) and enantiomerism (or optical isomerism), e.g.* a technical mixture of *permethrin* contains 40% cis and 60% *trans* isomers, with the *cis* isomer being five times more toxic against tobacco budworms [3, 27, 28]; and the active isomer in the *deltamethrin* is the *dextro (+)-cis*-deltamethrin [3]. They have low water solubility, low vapor pressures (10^{-6} to 10^{-7} mmHg) and high efficacy, being very effective against most agricultural pests at low rates, especially the Type II compounds, which are more effective than organophosphorus or carbamate insecticide [3]. Apart from their application in agriculture, synthetic pyrethroids are frequent components of household sprays, flea preparations for pets, and plant sprays for green houses, among others. Currently pyrethroids are used widely in Kenya in the domestic, public health vector control, as well as agricultural sectors, where both Type II and I are widely used. Most Type I pyrethroids belong to Category WHO Class III pesticides (oral LD_{50} (rats) of 500–5000 mg/kg range), Type II pyrethroids mostly are more toxic and belong to Category WHO Class II pesticides (oral LD_{50} (rats) of 50–500 mg/kg range) and just a few belong to WHO Class I, according to the WHO rating which is based on LD_{50}'s oral rats [3]. Pyrethrum (the extract) is a safe insecticide (oral LD_{50} 1500 mg/kg in rat) and very fast-acting on insects, causing immediate paralysis. Both the natural pyrethrins and synthetic pyrethroids were more active as *contact* than *stomach* poisons, although more recently some of the synthetic pyrethroids tend to show particular potency when ingested and less susceptibility to biotransformation by insects and mammals [3, 27, 28].

2.4 Other botanical insecticides

There are six botanical insecticides currently available in the market. These are *pyrethrum, nicotine, rotenone (rotenoids), azadirachtin, sabadilla and ryania;* which are naturally occurring agents of plant origin that have been used to control insect pests. Despite many formulations of synthetic insecticides being present in the market, the botanical insecticides are still found in the market and are now becoming popular in Kenya, especially in the horticulture sector, because they are perceived to have eco-toxicological advantages compared to traditional synthetic insecticides. The advantages include less negative impacts on ecology, low human toxicity and less environmental persistence [3, 29–31]. Botanical insecticides are composed of secondary metabolites such as alkaloids, amides, chalcones, flavones, phenols, lignans, neolignans or kawapirones. They act as repellents with unpleasant odors or irritants, growth regulators and some have deterrence on oviposition and feeding, as well as biocidal activity [29, 30].

Nicotine was first used as botanical insecticide in 1763. It is highly toxic to both target and non-target species, with moderate to high toxicity in vertebrates (oral LD_{50} in rats: 55 mg/kg) and is toxic to insects such as bugs, beetles and cockroaches (LD_{50} ranging from 190 to 650 mg/kg) [31, 32]. It is an alkaloid extracted from leaves of tobacco plant by Soxhlet (with solvents such as toluene) or with alkali using steam distillation and is used in home gardens and greenhouses for controlling sucking insects such as leafhoppers, aphids, scales, thrips and white flies, and therefore is also used in horticulture e.g. in Naivasha, Kenya [11]. Its demerits include high mammalian toxicity, ready absorption by skin and, therefore, increased exposure.

Nicotine sulfate and other salts in the form of crystals such as nicotine benzoate, oxalate, salicylate and tartrate, as well as fixed nicotines (water-insoluble salts such as nicotine tannate and nicotine bentonite) are stable and have been used as insecticides, baits and for control of ectoparasites in livestock, respectively [32]. Nicotine is also used most commonly as a fumigant and as a contact spray in greenhouses [32]. Preparations of tobacco teas from tobacco products sold for smoking and chewing as homemade preparations for use against pests can also be used. Nicotine poisons insects and mammals by a similar mode of action, i.e. inhibition of acetylcholine esterase by mimicking acetylcholine which binds to postsynaptic receptors [3, 33], and since its breakdown is not catalyzed by acetylcholinesterase, it causes repeated stimulation of the receptor.

*Rotenone i*s present in the roots of *Derris spp* plant and similar Leguminosae family of plants found in Malaysia, the East Indies and other East Asian countries [31]. It is an alkaloid extracted by solvent extraction (e.g. Soxhlet), purified and crystallized; often added in combination with other insecticides. It is a selective insecticide with acaricidal properties used against garden insects, lice and ticks on animals; such as headlice (by topical application). It is very toxic to fish and can control unwanted fish species in lakes, streams and reservoirs, which are used for power generation [31]. The LD_{50} is 132 mg/kg oral in rats, obtained by administering crystalline rotenone. Rotenone is toxic not only to insects and fish but also to humans and animals, with oral LD_{50} in rats being approximately 60–135 mg per kg of body weight. Liquid preparations of derris or Derris dust can also be used. It acts by blocking electron transport in mitochondria, inhibiting oxidation linked to NADH, by binding to NADH dehydrogenase thereby interfering with electron transfer, and is referred to as mitochondrial complex I inhibitor [31].

Azadirachtin is a secondary metabolite belonging to the limonoid group present in neem seeds. This compound is found in the seeds (0.2–0.8 percent by weight) of the neem tree, *Azadirachta indica*. *Azadirachtin* is the main compound of the neem oil with insecticidal activity and can be found in its fruits and leaves. *Azadirachtin* is the active ingredient in many pesticidal products or formulations in the market, including TreeAzin and Terramera Cirkil [31, 34, 35], and it has been used as a biopesticide in Kenya. Azadirachtin has various modes of activity, including being a broad-spectrum insecticide, and acting as a feeding deterrent, insect growth disruptor (IGD) and sterilant, respectively, and is used to control various agricultural pest species, including Coleoptera, Hymenoptera, Diptera, Orthoptera and Isoptera [29, 30].

Sabadilla use as a pesticide dates back to 1819 when a basic substance from sabadilla seed was isolated [33]. *Sabadilla* is a plant that grows in countries such as Central America and Mexico. It is toxic and is used in farming as an insecticide since it contains alkaloid compounds including *veratran, cevadine, veratridine, sabadine and sabadiline,* which have insecticidal activity. The veratrine alkaloids comprise approximately 0.3% of the weight of aged sabadilla seeds; of these alkaloids, cevadine and veratridine are the most active insecticidally and have been tested successfully in citrus thrips [31]. Sabadilla alkaloids from the dried ripe sabadilla seeds of a member of the lily family, S*choenocaulon officinal*e, are often used and considered as generally safe and non-persistent insecticides. Veratrine, which is the term now used to describe the alkaloid mixture from sabadilla, has long been known for its toxicity to certain species of insects. The powdered seed itself or kerosene extract of it has been tested and used as an insect repellant. Sabadilla alkaloids have also been formulated as a wettable powder and then mixed with water and applied by either aerial or ground equipment on citrus, avocados and mangos. In making a commercial formulation,

the active ingredients of sabadilla are synergized by piperonyl butoxide (PBO) and N-octyl bicycloheptene dicarboximide (MGK 264) [3, 33]. The mode of action of sabadilla is similar to that of the pyrethrins, as it affects the voltage-dependent sodium channels of nerve axon [33], i.e. affect nerve cell membrane function by binding to the sodium channel causing loss of nerve function, paralysis and death.

Ryania insecticide preparations are derived from the *woody stem tissue* of the shrub *Ryania speciosa* (family *Flacourtiaceae*), a plant that is native to South America and has been used in the USA since 1940s. A mixture of components is present in extracts or powders of this plant material, and eleven compounds with insecticidal activity have been identified [31], the most abundant active constituents of these alkaloids (*ryanoids)* being *ryanodine* and *dehydroryanodine.* Most commercial formulations are crude dust (50% ryania powder), though the constituent alkaloids can be extracted in water, alcohol, acetone, ether or chloroform to produce liquid or wettable powder formulations. Ryania extracts or powders have very low mammalian toxicity (LD_{50} rats ranging from 750 to 4000 mg/kg), but the active ingredients are much more toxic to mammals [33]. Ryania's toxicity to insects can result from contact or ingestion; it is synergized by PPO and used most often for control of caterpillar pests of fruits and foliage, the codling moth and thrips in fruit trees (apples, pears, citrus), as well as European corn borer in corn, by organic farmers [33]. Like *rotenone,* ryania persists longer in the field after application than most other plant-derived insecticides, with residues giving some degree of residual control for up to 3–5 days after application on plant surfaces. The mode of action *of ryania is by Ryanodine effects on* the calcium cation (Ca^{2+}) release channel in muscle, resulting in poisoning of insects and mammals by a sustained contraction of skeletal muscle without depolarization of the muscle membrane, causing cardiac arrest and then eventual paralysis [33]. The binding of raynodine changes the structure of the Ca^{2+} channel and prevents its complete closure. This binding affects the cardiac and skeletal muscles.

2.5 Neonicotinoids

Neonicotinoids (meaning "new nicotine-like insecticides"), also known as chloronicotinyls, are synthetic analogues of nicotine, but unlike nicotine, they are relatively non-toxic to mammals. Neonicotinoids are a new class of insecticides with widespread use in veterinary and crop production, and include *imidacloprid, acetamiprid, dinotefuran, thiamethoxam, clothianidin, amitraz and chlormideform*. *Imidacloprid* (LD_{50} 450 mg/kg (oral rats)), *acetamiprid* (417 mg/kg), *thiamethoxan* (LD_{50} > 5000 mg/kg) and *thiacloprid* (LD_{50} 836 mg/kg), are all systemic insecticides, which have been used widely in agriculture against sucking insects such as aphids, leafhoppers, planthoppers, thrips, white flies [3], as well as soil insects, termites and biting insects, in Kenya.

Neonicotinoids first entered the market in the early 1990s and appeared to address the concerns associated with some earlier pesticide compounds, because they are effective, possess a high degree of selectivity to insects and have low mammalian toxicity, making them safer for human use than the organochlorines, organophosphates and carbamates [3]. Therefore, they soon became some of the most widely used insecticides in the world by 2014. Neonicotinoids are used to manage many honeydew-excreting pests, which are primary pests in most agricultural systems, including field crops, vegetables, fruit and nut production, tree plantations and urban forests, and therefore they have a strong potential to reach non-target pest species, which are essential in agriculture, such as bees [3]. They are most often applied as a seed coating and are absorbed into plant tissues, localizing the protectant and reducing contamination

to the environment. The insecticide's ability to translocate into plant tissues could keep environmental concentrations low and minimize exposure to sensitive non targets such as quail and other wildlife, but experimental data suggest that environmental concentrations are usually higher than anticipated [36, 37]. It was estimated that approximately 5% of the pesticide a.i. applied as a seed coating would be absorbed by the plant while the rest (95%) would be blown away during sowing, which has led to their deposition in the surrounding soil and water, leading to soil residue concentrations up to 1000 ppb, in some cases [36, 37]. Compared to OPs and carbamates, neonicotinoids differ in that they are more strongly attracted to acetylcholine esterase receptors in the invertebrate's nervous system than the vertebrate ones, making them more specific. As a mode of toxicity, neonicotinoids are neurotoxins, which target insect nicotinic acetylcholine receptors (nAChRs). By 2018, neonicotinoids made up ~30% of insecticide sales worldwide [36, 37]. However, due to their adverse impact on pollinators such as honey bees and bumble bees, as well as aquatic invertebrates, some neonicotinoids are being banned by the EU, and other countries may also follow suit in future [36]. Neonicotinoids have become popular in Kenya and are already widely used in the horticultural sectors [4]; as many are registered by the PCPB.

2.6 Insect growth regulators (IGRs)

IGRs are chemical substances that disrupt insect growth and development, resulting eventually in death. They are pesticides that affect insects' ability to grow and mature normally, rather than killing them outright as 'conventional' insecticides do. Currently, there are 5 IGRs, namely *juvenoids, benzoylphenylureas, diacylhydrazines, triazines and thiadiazines*, respectively. The IGRs have low mammalian toxicity, and there are many of their formulations in the market, including the Kenyan market [3, 11]. They are very useful in controlling disease vectors such as mosquitoes, specifically mosquito larvae [3, 31]. Many IGR products can also be mixed with other insecticides that kill adult insects. Several features of IGR make them attractive as alternatives to broad-spectrum insecticides; i.e. they are more selective, less harmful to the environment and more compatible with integrated pest management. Because IGRs act on systems unique to insects, they are less likely to affect other organisms. Some of the modes of action include acting as antijuvenile hormone agents by blocking juvenile hormone production, mimicking hormones and therefore interfering with stages of growth or life cycle, from eggs to larvae, to pupae, and to adults; and inhibiting chitin synthesis by preventing development of exoskeleton, respectively [31]. Examples of known juvenoid active ingredients are *methoprene, hydropene, fenoxycarb, pyriproxyfen* and *diflubenzuron (a benzoylphenylurea). Benzoylphenylureas* (e.g. *diflubenzuron*) and *diacylhydrazines* are known to prevent chitin synthesis by inhibiting chitin synthetase. Thiadiazines (e.g. *buprofezin*), diacylhydrazines (e.g. *halofenozide*, *methoxyfenozide* and *tebufenozide*) and benzoylureas (e.g. *novaluron*) disrupt or mimick insect growth hormones, inhibit chitin synthesis, prevent molting and metamorphosis, respectively [6].

Methoprene (LD_{50}: 34,600 mg/kg oral rats) is a larvicide juvenoid, which mimicks juvenile insect hormones, since it is similar in chemical structure to them. It has been used to control mosquitoes (in flood waters, effective at 2–4 instars stage), cigarette beetles and fleas. It is not toxic to the pupal or adult stages, with treated larvae able to pupate but adults do not hatch from the pupal stage [38]. The optically active juvenile hormone analogue, S-(+)-methoprene is synthesized by a chemical procedure [3, 39]. *Hydropene* is also a juvenoid, which is registered for use against cockroaches and mosquito larvae, with an LD_{50} > 34,000 mg/kg (oral, rats). It disrupts normal development

and emergence of insects by mimicking juvenile hormones [3, 6]. It may also cause adult sterility, physical abnormalities, desiccation, and premature death [6]. Its products are used in a variety of sectors, with commercial formulations including aerosols, liquids and impregnated materials (i.e. bait stations) [6]. *Fenoxycarb* is a carbamate insect growth regulator, with low toxicity to bees, birds and humans, but is toxic to fish [6]. The oral LD_{50} for rats is greater than 16,800 mg/kg and is used in fire ant flea baits, and for control of mosquitoes and cockroaches, as well as butterflies, moths, beetles, and scale and sucking insects on olives, vines, cotton and fruit, where it is often formulated as a grit or corncob bait. Fenoxycarb blocks metamorphosis into adults and larval molting. *Pyriproxyfen* affects a target if touched or eaten, but it is rarely toxic to adult insects. It disturbs egg-laying, egg-hatch and keeps young insects from growing into adult form, and has been used against fleas, cockroaches, ticks, ants and mosquitoes [6]. *Diflubenzuron* is a synthesized active compound, an acaricide/insecticide and IGR used to control many leaf-eating insect larvae in agricultural, forest and ornamental plants, as well as mosquito larvae in standing water, using various formulations such as emulsifiable and solution concentrates, flowable concentrates, wettable powders and pellets. Some of its benefits include being relatively non-toxic to avian species, small mammals, freshwater fish, marine/estuarine fish and bees on an acute oral dietary basis [3, 6].

2.7 Microbial pesticides

2.7.1 (a) Entomopathogenic bacteria

Entomopathogenic fungi are often relied on as important components of integrated pest management in tropical agriculture, either as biopesticides or as naturally occurring soil microbes conserved in the environment. As pest control products, they are becoming very significant, especially in mosquito larval control. The entomopathogenic fungi, *Metarhizium anisopliae* and *Beauveria bassiana,* have demonstrated effectiveness against *anopheline* larvae in the laboratory, but effective formulations from such fungi, which are not sensitive to UV radiation, high temperatures and water not are needed [40, 41]. They are being manufactured and used in Kenya [11]. Metarhizium *robertsii*, formerly known as M. *anisopliae*, and even earlier, as Entomophthora *anisopliae* (*basionym*) is a fungus that grows naturally in soils throughout the world and causes disease in various insects by acting as a parasitoid [42]. A parasitoid is an insect whose larvae live as parasites in a host that eventually kill its host (typically another insect). Many isolates of parasitoids, which can be injected or exposed to insect hosts, have long been recognized as new Metarhizium species, such as M. *robertsii*, M. *maju*s and M. *acridum*, respectively. Metarhizium *taii* was placed in M. var. *anisopliae*, but has now been described as M. *guizhouense*. The commercially important isolates, M.a.43 (or F52, Met52, etc.), which infect Coleoptera and other insect orders have now been assigned to Metarhizium *brunneum*. This technique, which involves using various fungi has been practiced in other countries and is being used in Kenya, as various products have been registered by the PCPB and manufactured by some local companies [11].

2.7.2 Bacillus thuringiensis

B. thuringiensis Berliner (known as Bt) is an insecticidal bacterium discovered in early 20th century. There are several dozen recognized sub-species of *B. thuringiensis*.

The sub-species commonly used as insecticides include *B. thuringiensis* (Bt) sub-species *kurstaki* (Btk), sub-species *israelensis* (Bti) and sub-species *aizawa,* respectively. During sporulation, many Bt strains produce crystal proteins, called *delta endotoxins*, that have insecticidal action. Commercial Bts are powders containing a mixture of dried spores and crystalline δ-endotoxin, though some contain only the toxin component. Both spores and the toxin crystals are produced within the bacterial vegetative cell of the Bt [3, 40, 41]. Currently, there are 6 strains of Bt, which possess specific activity against different insects species e.g. for control of insects such as lepidopterous on crops, e.g. corn, fruits, tobacco and vegetables, as well as mosquito larvae, but Bt has very low toxicity in mammals (LD_{50} in mammals is >5000 mg/kg). They are used as biopesticides, in form of sprayable products and currently take about 2% of the global pesticide market.

Bt still finds low use in many countries such as Kenya because of high costs, lower efficiency, poor control of sucking and borers insects (e.g. in maize where there is large need), limited persistence and narrow spectrum; but a significant amount of them are being imported and registered by the PCPB [11], indicating their use in agriculture and vector control in Kenya. The advantages of Bt include their environmentally friendly nature compared with other synthetic pesticides as well as their ability to be adopted in new biotechnology. Bt toxins genes have been inserted into chromosomes in some plants and therefore such plants are resistant to attack by insects as they grow. Such crops are called transgenic crops and are available in the market e.g. Bt-corn (a genetically modified crops/organisms (GMO)). Bt corn produces Cry 1Ab toxin, which is used to control European corn borers; such plants which have been genetically engineered to contain δ-endotoxin are called *plant pesticides*. The major concern with Bt (and GMOs in general) is the potential impacts on non-target insects (e.g. beneficial insects such as bees), and interference with natural processes, such as change in biodiversity, which are still not yet fully known.

The δ-endotoxin is a cytolytic pore-forming toxin with insecticidal action, e.g. Cry 1AB toxin, which is a crystal protein with helical structure. When insects ingest it, it gets activated by proteolytic cleavage and once activated it binds to the mid-gut epithelium cells of targeted pests resulting in their rupture and causing cell death. Other organisms (including humans, other animals and non-targeted insects) that lack the appropriate receptors in their gut cannot be affected by the *cry* protein, and therefore are not affected by Bt [41]. Various types of δ-endotoxin can be found in various hosts e.g. cry 1 protein, cry2 protein, cyt protein, vip 1 protein [41]. To be effective, Bt must be eaten by insects during their feeding stage of development, when they are larvae. It is ineffective against adult insects. More than 150 insects, mostly lepidopterous larvae, are known to be susceptible in some way to Bt. Different strains of Bt have specific toxicities to particular types of insects: Bt *aizawai* (Bta) is used against wax moth larvae in honeycombs; Bt *israelensis* (Bti) is effective against mosquitoes, black flies and some midges; Bt *kurstaki* (Btk) controls various types of lepidopterous insects, including the gypsy moth and cabbage looper; and a newer strain, Bt S*an Diego*, is effective against certain beetle species and the boll weevil [41]. Due to its short biological half-life and its specificity, Bt is less likely than chemical pesticides to cause field resistance in target insects. It is moderately persistent in soil, with a half-life of about 4 months in suitable moderate conditions [6, 41]. Bt spores can be released into the soil from decomposing dead insects but can get rapidly inactivated in soils that have a pH below 5.1 [41].

2.7.3 Abamectin

A microbial pesticide, is a bacterium containing a mixture of endotoxins, *avermectin B1a* (>80% by wt) and *avermectin B1b* (<20%) as active ingredients [3]. The toxins are macrocyclic lactones derived from the *Actinomycete i*.e. *Streptomyces avermitilis* (a soil microorganism). The lactones are natural fermentation products of this bacterium. Abamectin (LD_{50} 300 mg/kg oral rat) is used against insects and mites on vegetable, fruit, ornamentals and fire ants (at home) and is now being used in horticulture in Kenya. The two components, **B1a** and **B1b** have very similar biological and toxicological properties and act as insecticides by affecting the nervous system of and paralyzing insects, and on exposure to high concentrations in humans, symptoms similar to OP poisoning are shown [3, 33]. It is highly toxic to insects and fish, extremely toxic to aquatic invertebrates, but non-toxic to birds, with LD_{50} in bobwhite quail being >2000 mg/kg. Abamectin is rapidly degraded in soil, and at the soil surface, if subjected to photodegradation, with half-lives ranging from 8 hours to 1 day [3].

2.7.4 Spinosad

Spinosad is a bacterial fermentation product, a natural substance made by a soil bacterium *Saccharopolyspora spinosa* that is toxic to insects. It is a mixture of two chemicals or metabolites called spinosyn A and spinosyn D. Spinosyn A & D have the most insecticidal activity and are used to control a wide variety of pests, including thrips, armyworms, codling moths, cutworms, leafminers, spider mites, mosquitoes, ants, fruit flies and others. Spinosad has been registered for use in pesticide formulations by the US Environmental Protection Agency (EPA) since 1997 [3] and is already being used in fruit and vegetable farming in Kenya [43]. Currently, they are found in over 80 registered pesticide products, many of them being used on agricultural crops and ornamental plants, where they are important in IPM to avoid food residue problems. Other spinosad products are used in and around buildings, in aquatic settings, and as seed treatments. The products are commonly used as sprays, dust, granules, and pellets. They are neuroactive and have same mode of action such as neonicotinoids but affect different binding sites.

2.7.5 Wolbachia

Wolbachia are obligate endosymbiotic bacteria that infect many insects, living in all orders of insects and other invertebrates, including some species of mosquitoes [44]. Although it is believed that *Wolbachia* does not naturally infect *Anopheles* mosquitoes, which are the species that spread malaria to humans, their prevalence, though sparsely in *Anopheles arabiensis* and *Anopheles funestus*, which are the two main malaria vectors, were reported recently in Tanzania [45]. Factors influencing *Wolbachia* transferring into new species are still being investigated, but the biocontrol technology has already been tried in Brazil [46]. It has not yet been tried in Kenya. Artificial infection with different *Wolbachia* strains can significantly reduce levels of the human malaria parasite, *Plasmodium falciparum*, in the mosquito, *Anopheles gambiae*. In addition, it was found to reduce levels of *Plasmodium falciparum* that could be transferred to humans and, therefore, suppressed malaria infections [47]. The procedure involves infecting or exposing *A. gambiae* mosquitoes, or any disease vector insect, with different *Wolbachia* strains (e.g. wMelPop, wAu, wInn, wMeICS and wAlbB). After infection, *Wolbachia* strains disseminate widely inside the mosquitoes

and infect diverse tissues and organs, affecting the host by manipulating its immune response, inhibiting its replication, reducing the parasite (*Plasmodium falciparum*) levels in the mosquito gut or killing the mosquitoes within a day (as was found in *A. gambiae* exposed to wMelPop strain) after the mosquitoes were blood-fed, including other transfers [47–49]. There is a vast diversity of *Wolbachia* strains available in natural populations of insects related to mosquitoes.

2.8 Fungicides

Fungicides are used against fungi (.e.g. mildews, rusts, smuts, mushrooms), parasitic plants and many allied forms capable of destroying wood, timber, leather, fabrics, glass, industrial products (e.g. paint and adhesives) and higher plants [50, 51]. Fungal attacks can cause problems of very significant importance not only to materials, the environment and aquatic organisms but also to humans. A good example of devastating fungal effects is normally seen in *Aspergillus ssp* fungi, which attack grains producing aflatoxins, and is a common problem in Kenya. Aflatoxins, which belong to the class of mycotoxins, cause acute lethal toxicity problems and, in the long term, carcinogenicity in humans. Fungicides for plant protection act by direct contact and often injure the host as well as the fungus. They can be described as *protective*, *curative* or *eradicative*; where p*rotective fungicides* are applied before appearance of infestation to prevent it, c*urative fungicides are* applied when infestation has already begun to invade the plant, thus they penetrate the plant cuticle, and destroy young fungal mycelium growing in the epidermis of the plant to prevent further development, and e*radicative fungicides* kill and also prevent sporulation, *i.e.* control fungal development following appearance of symptoms usually after sporulation, killing both new spores and the mycelium by penetrating the cuticle of the plant to the subdermal level [50, 51]. These modes of activity are established during product development and are often indicated on the labels. In agriculture, fungicides are used as foliar, soil or seed dressing, respectively.

2.8.1 Inorganic fungicides

Inorganic fungicides include elemental sulfur and alkyl/aryl compounds of heavy metals e.g. copper (Cu), mercury (Hg), tin (Sn) (e.g. organo mercury $Hg(CH_3)_2$ and organotin tin $Sn(CH_3)_4$). Heavy metal fungicides are not popular anymore due to their environmental persistence, ability to biomagnify in food chain and toxicity, and have been banned in the EU, where organotin compounds additives are no longer allowed in paints used in ships, where they were widely used [52, 53]. Methyl mercury fungicides were used in storage of cereal grain storage but were banned following two accidents of severe poisoning reported in Iraq and Minamata in Japan, respectively [53]. These heavy metal fungicides are not used in Kenya. Three inorganic fungicides, *Bordeaux mixture, lime sulfur and copper oxychloride*, respectively, are registered by the PCPB and are used to control molds and mildews in fruit and vegetable farms in Kenya [54].

2.8.2 Organic fungicides

Organic fungicides are commercially produced by chemical synthesis and are commonly used for control of vegetable blights, especially in potatoes and tomatoes, as wood preservatives. Examples of organic fungicides include *dithiocarbamates*, *chlorinated phenols* (e.g. *pentachlorophenol* 5%), *formalin* (40% formaldehyde) and *coal-tar creosote* (which is used to preserve fencing posts and wooden rail truck ties).

Fungicides are also used widely in large quantities in agriculture and domestic sectors in Kenya due to frequent damp weather conditions which encourage microbial growth. Maize, fruits and vegetable farmers in Kenya, use a number of fungicides, with main active ingredients including *carbendazim, tebuconazole, metalaxyl, mancozeb, azoxystrobin, difenoconazole, fludioxonil, epoxiconazole, trifloxystrobin and mefenoxam* [50, 51, 55, 56].

2.9 Other pesticides available in Kenya for specific uses

2.9.1 Petroleum products

The use of emulsions of certain petroleum oils with water for use as fruit tree sprays against insects such as scale insects, red spider mites, aphids and mosquito larvae has been known [57], and kerosene products are still being imported and are registered for by the PCPB [11].

2.9.2 Rodenticides

Rodenticides are used to control certain pest animals e.g. mice, rats, groundhogs, bats, squirrels and field rodents, which can cause extensive damage to crops property or spread disease [58, 59]. In food storage, cereal farming, food handling and distribution and rodenticides are important e.g. *thallium sulfate, zinc phosphide (Zn_2PH_3), strychnine, and red squill*, *fluoroacetate* ($CH_2FCOONa$), *fluoracetamide* (CH_2FCONH_2) and *ANTU* (Alpha-naphthylthiourea) are used in Kenya. Other rodenticides include *fluoroacetate* ($CH_2FCOONa$), *warfarin*, *fluoracetamide* (CH_2FCONH_2) and *ANTU* (Alpha-naphthylthiourea). Organic rodenticides, such as *difenacoum, brodifacoum, difethialone, flocoumafen and bromadiolone*, are toxic to mammals and extremely toxic to birds (e.g. *brodifacoum* LD_{50} values of 0.31, 0.72, and 19 mg kg^{-1} in ducks, gull and quails, respectively) are not registered in the PCPB database.

2.9.3 Fumigants

Fumigants act on insects through respiratory system by emitting vapors, but also kill nematodes, weed seeds, fungi, in soil, silos for stored grains, and fruits and vegetables. Often treatment is carried out in enclosures since they are volatile. Fumigants, such as carbon tetrachloride, ethylene dichloride (CH_2ClCH_2Cl), ethylene dibromide ($CH_3CH_2CH_2Br$), methyl bromide and carbon disulfide, have been used as liquid fumigants in commodities e.g. grain storage but have been banned due to human toxicity and ozone depletion properties. They have been replaced with others such as CO_2, phosphine (PH_3; a liquid, storage of grains) and sulfuryl fluoride (SO_2F_2, termite control), which are not listed by the PCPB. However, *malathion* dust (2%) and *pirimiphos-methyl* (actellic) dust formulations, respectively, are registered and are used in bulk grain storage in silos [60, 61].

2.9.4 Avicides

Avicides are used against certain birds when they become pests, such as quail birds on rice farms. The red-billed quelea (*Quelea quelea* Linnaeus) is the most important avian pest of small grain crops in Africa, causing damage up to the equivalent of US$ 88.6 million per annum [62]. It is controlled by *fenitrothion*, *fenthion* (Queletox) and

cyanophos, which are both highly toxic to non-target and costly [62] and have been used in Kenya by aerial or ground spraying. An avicide can be used as a repellant e.g. Avitrol (4-aminopyridine) or reproductive control e.g. Ornitrol, a derivative of cholesterol, which produces temporary sterility in pigeons but has no effect on mammals. *Fenitrothion* and *fenthion* are listed in the database confirming their use in Kenya.

2.9.5 Nematicides

Nematicides are used against nematodes, which can infest plant root systems and damage roots and/or encourage other microorganisms e.g. fungus to attack plants. Fumigation with *1,3-dichloropropene* can control these, although conventional pesticides such as some OPs have both insecticidal and nematicidal properties.

2.9.6 Molluscicides

Molluscicides also known as snail baits, snail pellets or slug pellets, are pesticides against gastropods such as mollusks, which are usually used in agriculture or gardening. These organisms can damage crops or other valued plants by feeding on them or exposing disease pathogens, which they carry on their bodies to humans (e.g. in vegetables, or *bilharzia* in freshwater) [63]. Synthetic *niclosamide* is mostly used although others such as *metaldehyde* have also been used against mollusks [63].

2.10 Metabolism, detoxification and excretion of pesticides

Insecticides are toxic to target insects as well as humans. However, like other xenobiotics, there are mechanisms of degradation and metabolism in both species, which are mediated by various enzymes and are responsible for reducing their toxicity and excreting them. Apart from killing the target pests such as insects, pesticides are just like any other chemical, which the human is inevitably exposed to through air, food and water, and exposure to them can lead to acute toxicity, long term-diseases or excretion. The ability of pesticides and other xenobiotics to cause long-term diseases or endocrine disruption is statistical and dependent on many factors, but the human body has inherent mechanisms to detoxify them or reduce their toxicity. Studies on pesticide metabolism, detoxification and excretion by insects and mammals, with reference to OCs, OPs and carbamates, which have been most studied, have made us understand how organisms naturally deal with toxic pesticides [3].

2.10.1 Metabolism, detoxification and excretion of pesticides: OCs, OPs, CBs

In insects and mammals, hydrophobic compounds such as OCs undergo various metabolic reactions, which make them more water-soluble and ready for excretion through urine or other matter. These reactions include hydrolysis, oxidation and reduction, followed by conjugation to more polar metabolites or biomolecules, such as sugars, amino acids, glutathione, phosphates and sulfates, which make them even more hydrophilic and, therefore, excretable. The reactions are mediated by various enzymes. *Cytochrome P450 monoxygenases* (a group of enzymes) located in the microsomes in the mitochondria are responsible for oxidation reactions in mammals, birds, fish, mollusks and insects and can transform various functional groups or moieties of the pesticide molecules, through various chemical changes such as *epoxidation, demethylation, hydroxylation, oxidation and reduction*. All other pesticides including

OPs, carbamates and other xenobiotics also undergo similar biochemical changes that make them more water-soluble for excretion. From the onset, the chemical structures of various pesticides, as shown by examples in **Figure 1a-e**, determine the kind of biochemical reactions, which are expected to occur in the environment and organisms. The metabolic pathways for these biochemical reactions have been elucidated and can be found in Hodgson and Levi [64], Usmani et al. [65], Yu [3] and Jing et al. [66]. The OPs, carbamates, neonicotinoids, pyrethroids, herbicides and fungicides are not as bioaccumulative as the OCs in the organisms and in the environment because of the nature of their chemical structures [3]. They undergo more rapid metabolism and get excreted more [3]. These descriptions of metabolic pathways can be understood by making references to the specific chemical structures (**Figure 1a-e**).

2.10.1.1 Epoxidation

Epoxides are formed by oxidation of double bonds, which can occur on phenyl rings, or alkene part of the organic molecules, and are mediated by microsomal Cyt P450 monoxygenases. Epoxides can be environmentally persistent and highly reactive and can form adducts with cellular macromolecules e.g. proteins, RNA and DNA, often resulting in chemical carcinogenesis and, therefore, not directly advantageous for the organism. However, they are more water-soluble for excretion and can also be further hydrated by *epoxide hydrolases*, which catalyze addition of H_2O molecules into the epoxide ring to yield trans-diols [3].

2.10.1.2 Hydroxylation

Hydroxylation can occur on H attached to an aliphatic or aromatic carbon atom (represented as: $-C-H \rightarrow C-OH$), and is mediated by Cyt P450's, usually resulting in a more polar and water-soluble product, and is considered a detoxification process in insects and mammals.

2.10.1.3 N-dealkylation

Microsomal N-dealkylation is a commonly observed metabolic reaction for xenobiotics containing secondary and tertiary amines, including OPs insecticides, releasing an aldehyde/ketone and alcohol. It is catalyzed by certain cytochrome P450 monooxygenases and peroxidases.

2.10.1.4 O-dealkylation

O-dealkylation of alkyl groups of the ester or ether structures on pesticide molecules occurs frequently in insects and mammals, e.g. in OP insecticides and other pesticides, mediated by cytochrome P450s, results in formation of an alcohol and acetaldehyde and detoxification.

2.10.1.5 Desulfurization

Desulfurization is also known as phosphorothioate oxidation, e.g. the OP insecticides with P=S get oxidatively desulfurized by Cyt P450 monoxygenases to give P=O analogues, resulting in activation because it gives a metabolite, which binds more strongly to AChE and, therefore, a potent inhibitor of the enzyme AChE. Examples

include parathion and malathion, giving paraoxon and malaoxon, respectively, which are more toxic than the sulfur analogues.

2.10.1.6 Sulfoxidation

Sulfoxidation of many thioether ($R_1C-S-CR_2$)-containing insecticides, such as OPs, are oxidized by Cyt P450 monoxygenases to their corresponding sulfoxides (S=O). Usually, it is an oxidative activation leading to increased anti-AChE activity (i.e. it is an inhibitor), as demonstrated in phorate. Sulfoxides are compounds containing a sulfoxide functional group, with the structure RS(=O)R′ (R,R′ = alkyl/aryl; S is joined to O (i.e. −SO)). Oxidation of certain sulfur and nitrogen-containing insecticides is also performed by another group of microsomal enzymes known as flavin-containing-monoxygenases (FMOs), e.g. sulfoxidation of phorate by FMO was demonstrated in mammalian liver [3]. Like Cyt P450's FMOs also require NADPH and oxygen for their activity, but FMOs are only involved in catalysis of oxygenation reactions.

2.10.1.7 Hydrolysis

OPs and carbamates and others containing ester linkages are susceptible to hydrolysis. *Esterases* (e.g. carboxylesterases) are *hydrolases* that split ester compounds by addition of water to yield an acid and alcohol (i.e. R′COOR + H_2O → R′COOH + ROH; R, R′ = alkyl, phenyl). Carboxyl-esterases have been classified into three categories (A, B and C) on the basis of differential patterns of inhibition by organophosphates, as discussed in detail in other texts [3]. **A-esterases** are typical aromatic esterases, which hydrolyze phenyl acetate and phenyl butyl acetate groups but not aliphatic esters. A-esterase levels of activity in plasma and liver of birds are much lower than those of mammals, the reason why birds are much more susceptible than mammals to OPs such as *pirimiphos-methyl and diazinon*. **B - esterases** are aliphatic and aromatic esterases e.g. *carboxyl esterases and lipases (in lipids)* as well as *acetylcholine esterases (AChE).* B - esterases e.g. *AChE* are *sensitive to OP and carbamate compounds* and hydrolyze both aliphatic and aromatic esters but not choline esters. B esterases are used as non-destructive biomarkers for exposure to anticholinesterase insecticides. Two types of esterases, *carboxylesterases and phosphatases* (or phosphorotriester hydrolases), are involved in metabolism of insecticides, e.g. hydrolysis of *malathion* to yield α and β- monoacids and ethanol by *carboxylesterases*. Carboxylesterase-mediated metabolism is one of the major mechanisms involved in *insecticide resistance*, and *multiple carboxylesterase* genes have been identified which are involved in pyrethroid insecticide resistance in housefly, just like glutathione s-transferase [3]. **C -esterases** preferentially *hydrolyze acetyl esters* and are, therefore, also called *acetyl esterases,* and split *acetylcholine esters* at higher rates than both *aliphatic and aromatic esters*, the latter at lower rate than aliphatic or not at all, typical substrates being 4-nitrophenyl acetate, propyl chloroacetate and fluorescein diacetate. *Phosphatases*, use water to cleave a phosphoric acid monoester into a phosphate ion and alcohol, and detoxify many OP insecticides especially the *phosphate* group, in insects and mammals, e.g. *paraoxon c*an be hydrolyzed to diethyl phosphoric acid and p-nitrophenol in houseflies [3].

2.10.1.8 Reduction

Insects contain *reductases* that catalyze reduction of xenobiotics. Reduction is less common than oxidation, and there are three types of reduction:

Nitro reduction ($RNO_2 \rightarrow RNH_2$), i.e. nitro group reduction to ammine group on the pesticide molecule.

Azo reduction—reductive cleavage of azo linkages on a pesticide molecule ($R-N=N-R_1$), resulting in formation of an ammine, e.g. for aromatic ammine ($Ar-N=N-Ar' \rightarrow ArNH_2 + Ar'NH_2$). The *Azo* group (RN=NR) *reduction* is similar to nitro *reduction* in many ways, i.e. it, too, is mediated both by *cytochrome P450* and by *NADPH-cytochrome P450 reductase.*

Aldehyde or ketone reduction—Reduction of aldehydes and ketones (hydrogenation) forms various metabolites, including primary alcohols (for aldehydes) and secondary alcohols (for ketones) mainly. Cytosolic a*ldehyde dehydrogenases,* as well as the *NADPH-dependent aldehyde reductases* widely distributed in insects and animals and their role in detoxification and insecticide resistance, have been discussed by Jing et al. [66]. Nitro group reduction, azo group reduction and aldehyde/ketonic group reduction, have all been found in insects; e.g. reduction of *parathion* to *amino parathion* and *trifluralin* reduction to *amino trifluralin*, in housefly cytosol, NADPH–cytochrome P450 reductase has mediated the resistance of *Aphis* (*Toxoptera*) *citricidus* (Kircaldy) to Abamectin by Jing et al. [66]. OPs and carbamates have various functional groups, which can be attacked, e.g. malathion can be attacked by two types of enzymes the *carboxylesterases* and the *Cyt P450 monoxygenases* for example demethylation (removal of methyl group from CH_3O-P moiety) by *Cyt P450 monoxygenases* to give other polar metabolites, and all carbamates have at least three sites that enzymes can attack; i.e. N-alkyl (methyl) group, the *ester linkage* and the *alcohol* or *pheno*l group, respectively, the most important reaction in all carbamates being *hydrolysis,* which occurs in insects and mammals. Other important reactions in carbamate insecticide metabolism would be *hydroxylation* of both ring and N-methyl and *epoxidation* to give *diols* ultimately, followed by conjugation and excretion. The oxidation, reduction, hydrolysis, epoxidation, hydroxylation, dealkylations, desulfuration, and sulfoxidation, which are involved in changing pesticide molecules to become more polar for excretion, as discussed above, are primary reactions called **Phase I** reactions or Phase I metabolism. Products of Phase I metabolism, if not excreted, can then be subjected to **Phase II** reactions or Phase II metabolism. In Phase II reactions, the phase I products are further metabolized by getting them conjugated to various endogenous molecules, e.g. Phase II conjugation with glucose (sugars), amino acids (AAs), glutathione (GSH), phosphate and sulfate. The metabolism of insecticides involving Glutathione (GSH) binding or conjugation, which is mediated by glutathione-s-transferases (GSTs) is well known as a mechanism for detoxification of pesticides in various insects, demonstrated first in housefly [3].

Conjugations are Phase II reactions and are mediated by various enzymes, leading to products which are more polar, less toxic and more readily excreted, therefore, Phase II metabolism leads to detoxification. There are three types of Phase II metabolism, known as **Type I**, **Type II and Type III**, respectively, depending on the types of functional groups of the metabolites which are involved. The chemical functional groups required for Type I (of Phase II reactions) include $-OH$, $-NH_2$, $-COOH$, $-SH$ conjugation with *glucose*, *sulfates* and *phosphates*. Type II (of Phase II reactions) involves $-COOH$ groups binding with *amino acids*, i.e. amino acid conjugations; and Type III of Phase II conjugation involves halogens, alkene, $-NO_2$, epoxides, ethers functional groups and their conjugation with *Glutathione*, i.e. glutathione conjugation. Glucose conjugation is found in insects and plants but is rare in mammals. Mammals use glucuronic acid instead of glucose for excretion of xenobiotics. Glucose conjugation involves binding of Phase I metabolites to α, D-glucose, mediated by glucosyl transferase:

α, D-glucose + ROH → (*glucosyl transferase)* → RO. β-D-glucose (in insects/plants), where R = alkyl or phenyl group and ROH is a metabolite. Glucuronic acid conjugation, which occurs in mammals, involves Phase I metabolite conjugation to UDP-α-D-glucuronic acid (UDPGA); whereby D-glucose is first activated with *uridyl triphosphate* (UTP), mediated by *uridyl diphosphate glucose (UDPG) pyrophosphorylase*, to form *uridyl diphosphate-α-D-glucose (*UDPG), which is then oxidized to *uridyl diphosphate-α-D-glucuronic acid* (UDPGA). It is the UDPGA that binds to the Phase I metabolite, mediated by *UDP-Glucuronyl transferase*, for excretion, summarized as:

$$\text{D-glucose-Pi} + \text{UTP} \xrightarrow{\text{(UDPG pyrophosphorylase)}} \text{UDP-}\alpha\text{-D-glucose(UDPG)} + \text{PPi} \quad (2)$$

$$\text{UDPG)} + 2\text{NAD} + \text{H}_2\text{O} \xrightarrow{\text{(oxidation)}} \text{UDP-}\alpha\text{-D-glucuronic acid(UDPGA)} + 2\text{NADH}_2 \quad (3)$$

$$\text{UDPGA)} + \text{ROH} \xrightarrow{\text{(UDP-Glucuronyl transferase)}} \text{RO-}\beta\text{-glucuronic acid} + \text{UDP} + \text{H}_2\text{O} \quad (4)$$

In Phase II metabolism, sulfate conjugation requires ATP and *sulfotransferase* and phosphate conjugation, which occurs in insects but is rare in mammals, requires *phosphotransferase*. In amino acid conjugation, *glycine* is most frequently used, and Glutathione conjugation is mediated by a group of enzymes, the *glutathione-s-transferases* (GSTs). GSTs are involved in conjugation of various metabolites, e.g. binding *to epoxide, unsaturated compounds, aldehydes, ketones, lactones, nitriles, nitro compounds, phosphorothioates and phosphates* [3]. Phase I metabolism is responsible for decreasing biological activity and toxicity of toxicants and Phase II metabolism is responsible for detoxification or excretion.

3. Pesticide importation, regulation and manufacturing in Kenya

3.1 Pesticide regulation and importation in Kenya

3.1.1 The role of PCPB

The Pest Control Products Board (PCPB) was established in 1984 under Cap 346 Laws of Kenya, to regulate the use of pest control products (PCPs) and safeguard human and environmental health from the undesirable risks associated with PCPs. Pesticide regulation includes policy making and changing (with involvement of the PCPB, government agencies, non-governmental organizations (NGOs) and Parliament), adherence to International Conventions that Kenya is a signatory to (such as UNEP), and prosecution, respectively. The importation, registration, distribution and sale, as well as law enforcement against misuse, are implemented by the PCPB. The role of PCPB, i.e. the Board, in pesticide regulation and its mandate are prescribed in PCPB Act Cap 346 Laws of Kenya of 1984 [67, 68] and include issuance of import/export permits, assessment of safety, efficacy and quality of PCPs, assessment of suitability of premises, advising the Cabinet Secretary/Minister, monitoring and adherence to standards in the entire pesticide industry/trade, supervision of

disposal of obsolete PCPs, keeping records of importation and information on specific uses, creating awareness and investigation and prosecution of contravenors of the Act. Since its establishment, the Board has registered many pest control products for use in public health, livestock and agriculture, and provided important information for labeling, and this is all available to the public on the PCPB website. It is an offense under the Pest Control Products Act to import or sell in Kenya any PCP unless it has been registered by the Board.

In undertaking the regulation of PCPs, the PCPB undertakes evaluation and registration of imported pesticide products and those manufactured in the country for safety, efficacy and quality, before registration. In addition, it regulates trade of pest control products through inspection, licensing and product certification. Any other uses of the products outside those specified in the registration are not authorized unless the product is reviewed and given a label extension [67, 68]. The PCPB registration numbers of products are given and continue to be amended as prescribed in the Pest Control Products Act under the labeling, advertising and packaging Amendment Regulations L.N. 127/2006. To carry out its mandate, the PCPB, is thus, composed of three technical departments namely registration, compliance and enforcement and Analytical Departments, respectively, with clearly defined roles available on their website [67–69].

3.1.2 Laws and regulation of pesticides

The regulation of pesticides is governed by the Pest Control Products Act Chapter 346 laws of Kenya, which was enacted in 1984 and became operational in 1985 [67]. There are other pieces of legislation in the Pest Control Products Act (Revised Edition 2012) and the Pest Control Products Act (Subsidiary Legislation), available freely on internet. The Pest Control Products Board (PCPB) was established under the Act to oversee its implementation. The Act regulates importation, exportation, manufacture, repackaging, warehousing and distribution. Some important Clauses in the Act include all aspects of manufacturing, storage, distribution, packaging, labeling, sale, importation and exportation, as stated therein, and each piece of legislation is given a number L.N. (L.N. meaning legal notice), e.g. L.N. 45/1984: licensing of premises regulations, L.N. 46 and 109/1984: registration regulations, L.N. 125/2006: the pest control products (importation and exportation) (Amendment) Regulations, etc. The Acts and these pieces of legislation can be retrieved freely from the internet or bought from the Government Printer in Nairobi. The Minister/Cabinet Secretary in charge of the Ministry of Agriculture in consultation with the Board is empowered to make subsidiary legislations (Regulations), which are then printed by the government printer as legal notices (L.N) in the Kenya Gazette.

3.1.3 Pesticide importation

Kenya is among the largest consumers of pesticides in Africa besides South Africa, Nigeria and Ethiopia [70]. It is an agricultural economy, and therefore farmers use a significant amount of pesticides every year in different parts of the country in order to enhance agricultural productivity. Pesticide imports have increased steadily from about 9.52 thousand metric tons in 2009 to about 14.6 thousand metric tons in 2019. Currently, the PCPB has listed about 1447 formulations and active ingredients registered for use [11]. Most of the products have been insecticides (43%), followed by fungicides (22%) and herbicides (18%), but this changed in 2021, when the volume

of total imports further rose to 20.5 thousand metric tons, with a significant increase in fungicides to 6.9 thousand metric tons (34%), herbicides to 7 thousand metric tons (3.14%) and a decline in volume of insecticides to 4.8 thousand metric tons (23.4%). The insecticides include those used in public health and in mosquito nets. The consumption of biopesticides is still very low, with just about 311 metric tons imported in 2020/2021 financial year. In the 2021/2022 financial year, approximately 267 active ingredients of pest control products were imported into the country, either as formulated products or technical grade material (a.i.) for formulation locally, respectively. In some instances, the active ingredients were of mixed form containing more than one active ingredients [11]. On average, 5% of the volume of pesticide imports is technical grade material, therefore, formulation locally is relatively minimal. Approximately 95% of formulated pesticides come mainly from China, India and Germany, and smaller quantities from the USA, the UK, Japan, the Netherlands, and Switzerland, among others [11].

The most recent lists of various registered PCPs have been placed on the PCPB database [11], which are available as an open-source to the public on their website, and provide comprehensive information about all products registered for use in Kenya (www.pcpb.go.ke). The first comprehensive list contains information on names of 1447 various products and active ingredients registered for *use in crops*, their trade names, types of formulations, active ingredients, names of international and local manufacturers, local distributors, specified crops, the maximum residues limits (MRLs), the postharvest intervals (PHI) and the WHO toxicity data and any restrictions (e.g. if the product is restricted), respectively. Fungicides, pyrethroids, neonicotinoids, OPs insecticides and herbicides dominating the list, and much fewer numbers of carbamates (mainly *methomyl and propoxur*), petroleum oil, biopesticides (*e.g. Bt, abamectin and azadirachtin*), biological control products in form of predatory mites (including parasitic wasps) and entomopathogenic fungal spores including *Metarhizium anisopliae,* respectively [11], are given. The list also includes adjuvants and surfactants. Natural pyrethrum extracts are manufactured, formulated and distributed by Pyrethrum Board of Kenya; and other local companies are actively involved in manufacturing and distribution of biological control products including entomopathogenic fungal products for use against thrips and mites in Flowers and French beans. Almost all active ingredients, such as glyphosate, are registered in numerous different formulations, manufactured by different companies (more than 50 international and local companies) and distributed by different local companies; making the list very long.

The second list comprises of 157 pesticidal products registered for use in *public health* [11], consisting mainly of various active ingredients of pyrethroids, OPs (*temephos, pirimiphos methyl, chlorpyrifos and fenthion*), carbamates (*propoxur and carbaryl*), rodenticides *(zinc phosphide, brodifacoum, bromadiolone and flocoumafen*), neem oil, boric acid (specified for cockroach control), plant extracts, and neonicotinoids (*imidacloprid*), respectively, in various formulations (liquids, solids, vaporizing liquids with electrical heaters, baits, sticky tapes); and sold by various companies. The registrations are for specified uses, including *pyriproxyfen* as a mosquito larvicide, *deltamethrin* for indoor residual spraying (IRS), *alpha cypermethrin* for Long Lasting Insecticide-treated Nets (LLIN) and *bifenthrin* as a grain storage dust. The third list contains products, which are registered as technical grade materials for formulation purposes only, where information on technical mixtures (a.i.), mostly >95% pure, are given and the formulations for which they are imported are stated. The active ingredients of pyrethroids, OPs, carbamates, fungicides, rodenticides and neonicotinoids, as

well as adjuvants such as PPO and plant oils, are given. The last two lists (**4th and 5th**) in the database include the 4th one containing information on *temporarily registered products* with their specified uses; and 5th one for *banned pesticides* including *monocrotophos, alachlor and endosulfan*, which the farmers in Kenya are still using illegally [4], as well as *restricted products* such as DDT for malaria vector control only.

3.2 Pesticide manufacturing in Kenya

The PCPB also regulates the manufacture, distribution and sale of PCPs. According to the information in the database, pesticide manufacturing/formulation and trade, respectively, in Kenya involve several multinational companies (e.g. Bayer, BASF, Monsanto, Syngenta and DuPont) with branches in Kenya, as well as numerous local companies. The world's six largest pesticide manufacturers including Syngenta (and ChemChina), Bayer Crop Science, BASF, Dow Agrosciences, FMC and Adama, control nearly 75% of the global pesticide market, with products ranging from insecticides such as DDT, organophosphates, carbamates, herbicides, fungicides, neonicotinoids, and biopesticides [70]. Weed killers (herbicides) account for about one-third of the global pesticide market.

Manufacturing of pesticides involves formulation, packaging and labeling of the product to make it ready for sale. A pesticide formulation is defined as a combination of active ingredients with compatible inert ingredients of chemicals, which ultimately control a pest. Formulating a pesticide involves processing it to improve its storage, handling, safety, application or effectiveness [71, 72]. A pesticide product, which is ready for use, therefore, contains two parts, the active and inert ingredients. Active ingredients (or technical mixtures >95% purity, usually) are chemicals, which actually control the pest. Inert ingredients are solvents, solids and other adjuvants that help present the active ingredients to the target pest. *Adjuvants* assist in the mixing of some formulations during formulation and dilution just before field application and include surfactants, thickeners, baits, buffers, abrasives and *synergists*, which lack any direct pesticidal activity, but they are added to pesticide formulations to optimize product performance while using the minimum amount of it. The inert ingredients serve to enhance the utility of the product by diluting and reducing costs and field effectiveness [73], because an active ingredient in a fairly pure form is not suitable for field application. The formulation process also improves pesticide safety features and enhances handling qualities.

Examples of specific inert materials include *diatomaceous earth, petrolatum, crop oil, biodiesel, surfactants*, etc. Carrier materials can allow the pesticide to be dispersed effectively, e.g. *a talc in a dust formulation*, the *water for mixing a wettable powder* before a spray application, or the *aerosol that disperses the pesticide* in an air blast application. Inert means the carrier or diluent cannot interfere in the toxicity of the active compound. However, inert does not imply that the chemical, say a surfactant, is nontoxic, as some of the inert diluents or carriers can be toxic e.g. to the plant weeds or other non-target plants, and need to be tested alongside the formulation in a performance field trial [56, 74] as well as in a non-target active ingredient toxicity test. Therefore, pest control products exist in different formulations which are manufactured bearing in mind the nature of a.i.'s (solids and liquids), their solubility, ability to control the pest, storage, ease of application and transportation. A review of materials used as carriers in the pesticide industry can be found in other texts [75–77]. The principles involved in formulation are determined by end-use and behavior of the pesticide, and important factors to consider include, chemical and physical properties

of a.i. (e.g. bp, mp, specific gravity, vapor pressure, water solubility, rate of hydrolysis, toxicity (LD_{50} or EC_{50}), biodegradability and UV-degradability) and inert materials, type of application equipment, nature of target surfaces, containers, marketing and transportation needs. For inert ingredients, there is need to know compatibility with containers, and therefore their physico-chemical properties, as well as the physical properties of the ultimate mixture. The formulation must then be tested to document various characteristics including homogeneity, particle size, storage stability, retention on target surfaces, wetting properties, penetration and translocation in plants, residual nature on target or in soil, nature of deposit, efficiency and potential hazards to users.

3.2.1 Manufacturing of synthetic pesticides

In general, there are approximately twelve (12) types of formulations, which are commonly used and these types of formulations which are discussed briefly below, are included in the manufacturing of various PCPs in Kenya and are listed in the PCPB database.

3.2.1.1 Dusts

Dusts contain 2 ingredients, i.e. an *inert diluent* and a *toxicant*, with a toxicant accounting for 1–10% by weight of the mixture. Inert diluents here must be relatively non-adsorptive material to avoid inactivating the pesticides, e.g. *talc*, *pyrophyllite* or other clay. The diluents are finely ground for ease of application and coverage. The advantages of dust formulations include simplicity to manufacture and application. However, dust is least effective and least economical since it tends to drift during application resulting in poor deposition on target surfaces. To reduce importation costs, dust can be formulated as dust concentrates, containing say 90% of a.i. by weight for further dilution with local diluents in Kenya, or by mixing or blending at the farm before application.

3.2.1.2 Wettable powders (WPs)

Wettable powders (WPs) are the most widely used in agriculture, and consist of a toxicant + inert diluent + wetting agent. Inert diluents are usually adsorptive clay, e.g. *attapulgite* (Mg, Al, Si clay), and the wetting agents may be a blend of 2 or more *surfactants*, with the *toxicant* in the range of 25–75% (wt/wt) of the mixture; therefore, highly effective due to high concentrations of the a.i.'s. WPs can be prepared by (1) (i) first spraying the *toxican*t (if liquid) onto the clay material at a controlled temperature or, (ii) mixing the clay with a solution containing the *toxicant* (if solid) and (iii) then allowing the solvent to evaporate or, (2) by direct grinding of *crystalline toxicant* mixed with diluents, to get a homogeneous mixture, which can be ground to powder. Packaged WPs are bought and diluted at the farm by mixing a specified quantity (as on the label) with water, before spraying.

3.2.1.3 Emulsifiable concentrates (ECs)

Emulsifiable concentrates (ECs) are formulations which consist of a toxicant + a solvent (e.g. water or other types such as *petroleum distillates, kerosene (C_9-C_{10} fraction), Aromax, Solvesso and biodiesel* (e.g. vegetable oil, Neem oil and xylene)) for the toxicant + emulsifier (usually a *surfactant* e.g. calcium alkyl dodecyl benzene sulfonate, or alkyl

phenolic polyexthoxylates), which are also imported. The toxicant content of ECs is expressed as weight/volume and not as wt/wt as in dust or WPs. ECs, which are very common in Kenya, typically contain approximately 25–50% by weight of a.i. On mixing at the farm (usually with water) before spraying, the product gives a stable milky emulsion, which can remain stable for up to 24 hours. ECs are more easily absorbed by the skin and plants than WPs and dust and are, therefore, more hazardous, but more effective than WPs since there is no masking effect of diluents.

3.2.1.4 Suspendable concentrates (SCs) or flowables

Suspendable Concentrates (SCs) or Flowables are used for pesticides, which are just too sparingly soluble to be made inform of ECs but can be formulated to become water-based mixtures, which are handled and applied in the same manner as ECs. SC or flowable is a liquid formulation containing a stable suspension of a *solid* pesticide active ingredient in a solvent, usually intended for dilution with water at the farm before use. They contain 50–90% by weight of toxicants and are basically WP's of much smaller particle sizes (1–5 μm), which remain in suspension for long periods. Suspendability and storage stability are improved by inclusion of adjuvants (such as *surfacta*nts, e.g. emulsifiers, penetrants etc.) which improve the physical and chemical properties and enhance the control effect. Oils such as kerosene can be added when penetration into plant parts such as leaves is desired. A *water-miscible organic liquid*, or a mixture of multiple fluids, is usually used to dissolve water-insoluble or partially soluble pesticide a.i.

3.2.1.5 Water-soluble powders (SP's)

Water-Soluble Powders (SP's) are water-soluble formulations of solids/powders, in which the a.i.'s (and solid diluents) are easily dissolved in water. The technical grade material is formulated into a finely ground solid, packed and sold, for adding to a spray tank with water, where it dissolves quickly without any binders or surfactants, and spraying without constant agitation. Some examples of common SPs include *acephate* formulations with trade names *Acephate Tur*f and *Acephate PCO Pro 97.4% a.i*.

3.2.1.6 Solutions (S)

Solutions (S), a Solution formulation is the true solution containing a toxicant in a solvent, which can be used directly without further dilution, for household insect sprays, roadside weed eradication and rangeland spraying. The toxicant is dissolved in low-cost solvents such as *kerosene or aviation fuel*. No surfactants are added because the solvents wet target readily. They are prepared by direct dissolution in the selected solvent where the pesticides are sufficiently soluble in water (subject to hydrolytic stability test); or water-miscible solvents to avoid hydrolysis for mixing with water before application, e.g. Azodrin WMC (*a monocrotophos a.i.*), which is formulated in hexylene glycol, a solvent or coupling agent, giving a water-miscible product.

3.2.1.7 Granules (G)

Granular formulations are similar to Dust formulations and contain a toxicant (1–10% by weight) and an inert diluent, the major difference being particle size, with *granules* ranging from 20 to 100 mesh and *dusts* passing through 300 mesh screens. Granules are made from active ingredients, in many ways: (i) the toxicant (which is

a liquid) may be added so as to impregnate the solid granules, which are then dried and thus completely released only when the granule breaks up after application, or (ii) the toxicant may be surface-coated on to granules using a volatile solvent; i.e. the toxicant, (liquid or solid), dissolves in volatile solvent, which evaporates from the formulation, or (iii) grinding the solid toxicant with inert diluents. The inert diluents for granular formulations can be *clays* or *organic materials* such as corncobs (e.g. Furadan - with *carbofuran* a.i. formulated with *grit material made from corncobs*), pecan shells, tobacco stems and walnut shells, respectively. Granules (mostly for soil and water surfaces) are less likely to drift unlike dust or liquid sprays and have less tendency to adhere to foliage.

3.2.1.8 Water-dispersible granules (WGs)

Water-dispersible granules (WGs), known as Dry *Flowables,* contain typically a toxicant (50–95%, w/w), a dispersant (e.g. surfactant), a binder and diluents. They are granules intended for application after disintegration and dispersion in water at the farm. They have low dust properties (due to larger particles) and exhibit good flowability. WGs are manufactured by blending and agglomerating a ground solid active ingredient together, with surfactants and other ingredients, mixed with water, then drying step to reduce moisture to a 1–2% range. A binder/an anti-caking agent/carrier such as *inert clay* can be used, e.g. Greensperse® CA-N is an imported binder optimized as granules, which provide enough strength and resistance to abrasion to reduce dusting and maintain the granule's integrity until its application. When powder is agglomerated, particularly by wet granulation flowability is greatly improved. A high MW polyoxyethylene surfactant can be used in agglomeration.

3.2.1.9 Ultra-low volume (ULV)

Ultra-low volume (ULV) formulations are undiluted technical grade material or the original a.i. dissolved in a minimum amount of solvent, in case of a solid a.i. They are applied, e.g. by helicopter, without further dilution in an extremely fine spray generated by special aerial or ground spray equipment, and are useful for public health vectors and agricultural and forest pests. ULV applications offer several advantages, including high efficacy due to high directed concentrations at the target and absence of masking inert diluents/surfactants, compared with a normal formulation spray [77]. The technique is useful in treating large areas, e.g. a helicopter carrying 100 gallons of ULV-malathion, to spray 400–800 acres of rangeland before reloading. In Kenya, it is used in mosquito control programs, desert locust control and large-scale wheat farms in Narok and Laikipia.

3.2.1.10 Aerosols

Aerosols are commonly used widely in Kenya for controlling resident flying and crawling insects such as mosquitoes, ants, termites and cockroaches in the domestic sectors. The active ingredient is dissolved in a *volatile solvent*, e.g. a *petroleum solvent,* and the resulting solution is atomized through a jet by means of a propellant. The propellant can be a *gas under pressure* or a *liquid that is gaseous* at atmospheric pressure conditions. Chlorofluorocarbons propellants have now been replaced by other environmentally friendly volatile liquids such as *butane, dimethyl ether, compressed carbon dioxide or nitrogen*.

3.2.1.11 Controlled release (CR) formulations

Controlled release (CR) formulations are recent innovations, where the pesticide is incorporated into a *carrier*, generally, a *polymeric material* and are diffusion-controlled [78]. They are microencapsulated formulations consisting of a solid or liquid inert containing an active ingredient surrounded by a plastic or starch coating [79]. The resulting capsules can be sold as *dispersible granules* (dry flowables) or as *liquid* formulations. Encapsulation enhances applicator safety while providing timed release of the active ingredient. Liquid forms of microencapsulates are further diluted with water and applied as sprays, forming suspensions in the spray tank and having many similar properties as liquid flowables. The rate of release of the pesticide is determined by the properties of the polymer as well as environmental factors. Polymers, e.*g. proteins, synthesized vinyl 2, 4-dichlorophenoxyacetate and vinyl 2-(2, 4, 5-trichlorophenoxy) propionate,* respectively, can be used. An example is the *2-Acryloxyethyl ester of 2, 4-D copolymerized with triethylamine methacrylamide*. There are mainly two types of CR formulations, i.e. the *Reservoir Devices* and the *Monolithic Devices*, respectively. The reservoir devices are made when the toxicant is enclosed in the capsules of a thin polymeric material to become microcapsules of 1–100 μm in diameter; e.g. *Penn Cap-M microcapsules* (methyl parathion product). The *Monolithic Devices* are made when the toxicant is uniformly dissolved or dispersed within the polymer matrix to become microparticles of 1–100 μm diameter or strips; e.g. *Alco No-Pest Strip* (with dichlorvos is the active ingredient), which is used widely in pet flea collars [80]. The manufacturing of these devices is highly mechanized and expensive and, therefore, they are not yet popular in Kenya. There are also other disadvantages including longer-lasting residues and potential toxicity to beneficial insects such as bees.

3.2.1.12 Baits

Baits can be very useful for achieving selective toxicity of insecticides against some species of insects. Spot application, i.e. where the bait is placed in selected places, which are accessible only to target species, permits use of insecticides in a safe manner with no environmental disruption and less human exposure. A bait formulation consists of a *carrier, toxicant and feeding stimulants*. Carriers are made from *laying mash, cracked corn, wheat bran, corn cob grits and peanut hull*, while feeding stimulants include *crude cotton seed oil, refined soybean oil, sucrose, coax brewers concentrate, malt extract, glucose, maltose, honey and wheat germ*. Several types of baits are available in the market, e.g. malathion 4% w/w bait formulated from crude cotton seed oil (5%) and sucrose (10%) on a laying mash carrier, among others [81, 82].

Formulation labels-after a formulation has been manufactured, a suitable package is used and labeling is done. What goes into the labels is important for trade purposes and includes sufficient information to inform the buyer about the quality, concentrations and safety of the product as well as any notable special features of the pesticide product. The concentration of the pesticide on the label is very important because it gives guidance on further dilution with water at the site of application. For dry formulations such as WPs, dust and granules, respectively, the insecticide concentration is expressed *as percentage of active ingredient* (a.i.) by weight in the formulations e.g. Diazinon® 50 W or 50WP means it is a formulation containing 50% diazinon (by wt) as the a.i and is a wettable powder formulation. For liquid formulations such as Solutions (S) and emulsifiable concentrates (EC), the concentration of the

insecticide is expressed in pounds of a.i. /gallon or grams of a.i./Liter of formulation etc. Diazinon® 4E or Diazinon 4EC means it is an emulsifiable concentrate formulation containing 4 lb. of diazinon (or 4 g/L depending on units used in a particular country) in each gallon or liter of the formulation, respectively.

3.2.2 Manufacturing of biopesticides in Kenya

Biopesticides are derived from micro-organisms (bacteria, fungi, viruses, etc), plants (neem, pyrethrum, etc) and natural enemies of pests (parasitoids, predatory mites and pathogens). Additional substances under biopesticides are semiochemicals (e.g. insect sex pheromones), enzymes (proteins) and insect growth regulators. The biocontrol products presented in **Table 3** include twenty-seven (27) different products/formulations which are manufactured from nineteen (19) different active ingredients by nine (9) different companies in Kenya [11]. Biopesticides have become very popular in the horticultural sector, led by flowers, French beans, peas and avocadoes, which are grown mainly for export. The driving force behind this new shift

Active ingredients	Species	Number of formulations	Uses
Metarhizium anisopliae	Fungus	5	Spider mites (roses); fall army worm (maize); mealy bugs (roses).
Atoxigenic fungi	Fungus	1	Toxigenic Aspergillus falvus (maize).
Amblyseius (strains: *californicus, cucumeris, andersoni, swirski*).	Predatory mite	5	Spider mites & whiteflies (French beans, roses); thrips (in green houses).
Amphibious transcaspinus	Predatory mite	1	Aphids (French beans).
Bacillus thuringiensis (var: *aizawa, subtulis, amyloliquefaciens*).	Bacterium	3	Caterpillars (roses, chives, French beans, snow peas); mildew (roses); rice blast; coffee leaf rust; black rot (cabbages).
Paecilomyces lilacinus	Fungus	3	Nematodes (roses, French beans); aphids & white flies (tomatoes).
Lecanicillium (strains: *Verticillium, muscarium*)	Fungus	2	Aphids (roses, French beans); white flies (tomatoes, roses).
Beauveria bassiana	Fungus	3	Aphids (cabbages); bollworms; cutworms; caterpillars; thrips (French beans).
Steinernema carpocapsae	Nematode	1	Caterpillars (roses).
Trichoderma harzianum rifai	Fungus	1	Soil borne fungi (French beans, roses).
Macrocheles robustulus	Predatory mite	1	Thrips (roses).
Cryptophlebia leucotreta granulovirus	Moth isolate	1	Coddling moths (roses, avocadoes, capsicum).

Table 3.
Some biopesticides manufactured in Kenya.

towards biopesticides is mainly the need to avoid the strict residue limits imposed by the importing countries in Europe.

4. Pesticide use and impacts in Kenya

4.1 Pesticide use in agriculture and its impacts

Although developed countries consume 75% of the global pesticide in the market, it is the developing countries that will bear the heaviest burden of pesticides impact despite consuming just 22% [83–85], because of weaknesses in the regulatory mechanism and lack of education and awareness, especially among farmers. Apart from the long-term effects of pesticides, which are already known, several cases of severe impacts have been seen in Kenya including, (i) high mortalities caused by poisoning through suicides [86], (ii) high incidences of occupational exposure among farmers [4, 84, 86, 87], (iii) environmental degradation [26, 83, 84, 80–90], (iv) consumption of contaminated foods and water [26, 89, 91–95] and (v) misuse causing threats to wildlife, insects and other species [26, 83, 84, 89–90]. In Kenya, the increased amounts of pesticides being used and the reported potential human impacts, for example, cancer, which is now a major killer [83], seem to coincide, and this has raised concerns among the population. Many cases of acute pesticide poisoning, sometimes fatal, have been detected in people in the agricultural sector, where exposure to pesticides is highest [4, 84, 86, 87]. Even with low exposure, pesticides can cause serious consequences such as acute male infertility, cancers, abortions and other birth defects, and fetal malformations [84].

The rural population in Kenya constitutes approximately 80% of the total population; therefore, human and environmental health risks associated with pesticides are heavily experienced among this population since agriculture is mostly practiced in the rural areas [96]. The government has over the years put strategies to mitigate environmental impacts of pesticides, for example by the ratification of the Stockholm Convention in May 2004 and a national implementation plan in 2007 [97], which led to banning of most of the persistent OCs [11]. Banning of OCs can lead to recovery of affected species in nature [98]. However, a number of highly toxic OPs, carbamates, pyrethroids, neonicotinoids and fungicides, belonging to WHO I and II class, which have been banned in other countries such as the EU, have not been restricted or banned in Kenya [84]. There is, therefore, a dire need for risk assessment of all pesticides on the PCPB database for possible withdrawal or banning of the highly toxic ones.

Several studies on pesticide usage and impacts have been conducted following international best practices, in various agricultural regions in the country, which have revealed that the current group of pesticides used in Kenya are mostly highly toxic and pose threat to humans and the environment [84, 99–102]. Most of the pesticides are used intensively in certain regions that are traditionally agricultural zones, in the *North rift*, the *Central highlands*, the *South Rift*, *Eastern province*, as well as *Western* and *Nyanza provinces*, respectively, where specific types of crops are grown for local consumption and export; and it is in these regions where most studies have been done. In fact, several cases of pesticide misuse by farmers, occupational exposure and potential risks to human and drinking water have been documented since the year 2000. Two recent surveys were conducted in Trans-Nzoia County in Western Kenya which is the largest producer of maize in the country, producing at least 5 million bags

of the grains annually from approximately 107,000 acres of cultivated land; which highlighted the toxicities of pesticides used and their impacts on human and the environment. The first study was done in 2018 involved prioritization of the pesticide active ingredients by ranking them according to the *Quantity index* (quantity used) (QI), the Toxicity Potential (TP) and Toxicodynamic Potential (TDP) with regard to *carcinogenicity, mutagenicity, teratogenicity and endocrine disruption*, as described in Dabrowski et al. [99] and Gunier et al. [101], as well as hazard potential (HP), the groundwater ubiquity score (GUS), surface water mobility index (SWMI) to indicate their environmental hazards [99, 100, 102, 103]; and intrinsic toxic potential (ITP) for bioavailability, environmental persistence and bioaccumulation. The **Table 4** shows the criteria for scoring of toxicity potential for specific pesticides, in which a ranking of highest value (8) was given in cases where there was definitive toxic effect

No.	Pesticide	Quantity kg (a.i)	%use	ITP	HP	WHP	Mobility
1	Metalaxyl+ mancozeb	6678	19.6	3	6	1.2	Low
2	Glyphosate	5140	15.1	21	21	3.2	Low
3	Mancozeb	4443	13.0	15	15	2.0	Low
4	Terbuthylazine	4125	12.1	11	14	1.7	Medium
5	s-metolachlor + Atrazine	3561	10.4	7	14	0.1	High
6	Paraquat dichloride	1774	5.2	10	10	0.5	Low
7	Tebuconazole	1244	3.6	11	22	0.8	Medium
8	Lambda-cyhalothrin	1230	3.6	5	5	0.2	Extremely low
9	Imidacloprid	846	2.5	6	6	0.2	High
10	Atrazine	507	1.7	7	14	0.2	High
11	Carbendazim	465	1.4	11	22	0.3	Medium
12	Hexazinone	436	1.3	3	6	0.1	High
13	Carbosulfan	376	1.1	1	1	0.01	Low
14	Abamectin	367	1.1	10	10	0.1	Low
15	Deltamethrin	362	1.1	20	20	0.2	Low
16	Topramezone + dicamba	354	1.0	10	40	0.4	High
17	s-metolachlor	345	1.0	15	30	0.3	Low
18	Alpha-cypermethrin	344	1.0	14	14	0.1	Extremely low
19	Cymoxanil + propineb	344	1.0	15	23	0.2	Low
20	Chlorpyrifos	278	0.8	9	9	0.1	Low
21	Thiamethoxam	223	0.7	3	4	0.03	High
22	Cyhalothrin	221	0.3	9	9	0.1	Extremely low
23	2,4-D-Amine	181	0.5	9	36	0.2	Medium
24	Profenofos + cypermethrin	167	0.5	15	40	0.1	Extremely low
25	Diazinon	122	0.4	15	23	0.1	Low

Table 4.
Levels of pesticides (kg a.i.) used in Trans Nzoia, their Intrinsic Toxicity Potential (ITP), Hazard Potential (HP), Weighted Hazard Potential (WHP) and Mobility.

and zero was awarded to endpoints where there was no evidence of toxic effect, and the toxicity potential (TP) was obtained by adding the scores attributed to each of the five toxic effects (carcinogenicity, endocrine disrupter potential, mutagenicity, teratogenicity and neurotoxicity, respectively) for each active ingredient [101].

The GUS index was applied in a logarithmic scale where those pesticides with a GUS index below 1.8 had lower leaching potential while those with a GUS index higher than 2.8 were classified to have high leaching potential [99]. The potential of a pesticide to contaminate surface water resources was determined from surface water mobility index (SWMI), with pesticides having a SWMI tending towards 1 (one) having higher potential to be carried by surface run-off (**Table 4**) [99]. The criteria for scoring human and wildlife (bees and fish) toxicity potential and environmental impacts reported here are discussed in detail by Odira et al. [56] and Otieno et al. [55], respectively.

From this study, a total of 25 pesticides/active ingredients (**Table 4**) were considered significant in terms of their impacts on the environment and human health. The results showed that *glyphosate, mancozeb, terbuthylazine, metalaxyl-M + mancozeb, paraquat dichloride and carbendazim,* were among the most commonly used active ingredients with far-reaching environmental and health impacts. Although there were some pesticides that were not heavily used (e.g. diazinon), they still had significant toxicity from the evaluation scores and, therefore, presented substantial risk to human and environmental health in the area (**Table 4**). It was observed that the fungicide combination *metalaxy-M and mancozeb* was the most commonly used pesticide in Trans Nzoia County accounting for about 19% of all the active ingredients used (**Table 4**), while *diazinon* was the least used pesticide (0.4%) in the county. Trans Nzoia is generally damp and cold most times of the year, a condition that promotes occurrence of fungal diseases which perhaps explains the heavy usage of metalaxyl+mancozeb fungicide combination in the county. The amounts of herbicides such as *glyphosate, terbuthylazine, paraquat, metolachlor and atrazines*, were also high as expected, because of large farm sizes (5–30 acres) (**Table 4**). In addition, *topramezone + dicamba, 2,4 D-Amine, S-Metolachlor, atrazine, cymoxanil + propineb, diazinon, carbendazim, tebuconazole, glyphosphate and deltamethrin* were prioritized as active ingredients with higher potential to contaminate surface and groundwater, in the area. *Glyphosate, mancozeb, S-Metolachlor, terbuthylazine tebuconazole, paraquat dichloride and topramezone + dicamba* presented enormous risk according the weighted hazard potential (WHP) evaluation, but had low potential to contaminate surface water and groundwater due to their low GUS index, and as a result, they could present minimal risk to aquatic organisms and human through consumption of drinking water. Pesticides with high K_{oc} (as well as high water solubility and low soil half-lives) (data not presented here) have low potential to contaminate water resources and, therefore, present minimal risk to humans. *Thiamethoxam* with low WHP (**Table 4**), had very high GUS index (ranking of 4) and very high SWMI score (4), and also had the highest potential to contaminate the environment and highest potential toxicity scores (4) to birds, mammals, aquatic invertebrates and bees, respectively. Whereas there were also pesticides with high potential to present risks to humans and the environment due to the high WHP, like the top 5 in **Table 4**, including *glyphosate etc,* such risks may not be via water because of their low mobility. The environmental exposure potentials (EEP), and non-target toxicity data of commonly used pesticides in the area were compiled (full data not included here).

In a similar study done in 2019 in the same county, involving different farmers a full range of pesticides (45 a.i.'s in all) was used over 1 year (full data not shown), including

their physical-chemical properties and toxicity indices were reported. The toxicity indices, i.e. TP, EEP, GUS, and SWMI, were used to evaluate potential toxicity to humans and the environment. Most of the farmers (99.4%) involved in the survey applied pesticides, consisting of 10 different fungicides in various formulations, 5 OP's, 5 neonicotinoids, 6 pyrethroids, 2 carbamate insecticides, 4 herbicides, heptachlor (which is banned) and Abamectin, respectively; and most of them falling in the WHO Class I and II. The used pesticides in that year included *carbendazim* (32.9%), *epoxiconazole* (17.6%), *diazinon* (20.4%), *imidacloprid* (23.6%), *metolachlo*r (28.2%), *amitraz* (56.3%), *chlorpyrifos* (10.6%) and *acetochlor* (9.1%), with smaller amounts of *cypermethrin* (5.5%) and *heptachlor* (1.2%). The most applied pesticide class was the OPs (34.8%). It was found that 18.4% of the pesticides applied in the study area were persistent in soil sub-systems, 31.6% were persistent in water, and 10.5% and 13.2% had the potential of contaminating ground and surface water resources, respectively [55, 56]. The ranked order of human toxicity potential associated with the used pesticides in the area in 2019 was *teratogenicity (31.6%), neurotoxicity (29.0%), endocrine disruption (7.9%), carcinogenicity (7.9%), mutagenicity (2.6%) and multiple toxicity potentials (10.5%)*. In addition, 18.4% of the used pesticides, including *acetamiprid, heptachlor, amitraz, chlorimuron ethyl, azoxystrobin, lufenuron and copper oxychloride*, had higher potential for bioconcentration in the living tissues, while most of the pesticides, (39.5%) and (18.8%), respectively, were highly toxic to aquatic invertebrates and earthworms. All the pesticides applied in the study area in 2019 were potentially harmful to human health, if not properly handled. Round up which is restricted in the EU, as well as carbofuran, carbosulfan and heptachlor, which are restricted and banned, respectively, in Kenya, were also used.

In horticultural farming, where farms are often smaller (1–2 acres), the amounts of insecticides and fungicides used are often higher in comparison to the amounts of herbicides [4, 90]. In a survey done in 2015 and 2016 in Meru in Central Kenya, which is famous for horticultural farming of fruits and vegetables for local consumption in major cities such as Nairobi and for export, respectively, high quantities of insecticides such as *deltamethrin, dimethoate, chlorpyrifos, carbaryl, methoxychlor, λ-cyhalothrin, endosulfan sulfate, cypermethrin, zeta-cypermethrin, malathion, diazinon and propoxur*, and even the banned pesticides including *parathion, carbofuran, heptachlor, dieldrin and endrin*, were used over the 2 year period, compared with only smaller quantities of only two herbicides, *glyphosate and paraquat*, and one fungicide a.i., *mancozeb* [4]. Fungicides such as *carbendazim* and several *neonicotinoids* were also reported in French beans, tomatoes and kales, bought during harvesting on the farms, confirming their usage on the farms [4, 104]. The farmers (26%) reported health effects after using pesticides, with most effects (>12 respondents out of 173) experienced when *dimethoate, malathion, heptachlor, endrin, dursban (chlorpyrifos), parathion and dieldrin*, were used. Nine (9) of the pesticides used in Meru county, including *parathion, methomyl, endosulfan, endrin, dieldrin, methoxychlor, heptachlor epoxide, carbofuran and endosulfan sulfate* were very toxic (WHO class I), 12 were toxic (WHO class II) and 5 were moderately toxic (WHO class III) [4].

In Muranga in Central Kenya, where small-scale farming of avocados, tea and coffee are the main cash crops, and maize, beans and bananas are the main food crops, various categories of pesticides, including neonicotinoids, acaricides, fungicides, insecticides and herbicides, were found to be used in 2021 [90], although the quantities of these products were not reported. Using honey bee pollen as an indicator of used pesticides in county, eleven (11) pesticides were confirmed to be present in the honey, including *carbendazim, carbofuran, Spinosyn A, spinosyn D, acetamiprid, chlorpyrifos, thiamethoxam, imidacloprid, acephate, trifloxystrobin and indoxacarb* [90].

A national survey done in 2020 covering 32 counties located in all agricultural regions in Kenya established that mostly subsistence farming is practiced in the counties, and the major pests affecting crops were insects and rodents, where farmers used various synthetic pesticides (80%) as well as home products (68%), with 84% of the most common pests being caterpillar-related pests such as *stalk borers, white flies, worms, army worms and cut worms, aphids, termites, weevils, rodents and fungi*. A large variety of pesticides, including mainly pyrethroids, organophosphates (*e.g. diazinon, dimethoate, pirimiphos methyl, chlorpyrifos*), fungicides (*metalaxyl-M+ mancozeb*), carbamates (*carbaryl*), neonicotinoids (*thiomethoxam*), IGRs (*pyriproxyfen*), rodenticides (*zinc phosphide*) and unspecified herbicides, were used [105]. Some of the homemade products included *lemon grass, aloe vera, ashes, cloves, marigold extracts, pepper, salt and solanum apple*; for example, *ashes and chillies* were used to control insects such as *aphids in vegetables* [105]. The large variety of pesticides used by farmers, in this study, corroborates those pesticides used in regions such as Trans Nzoia, Muranga and Meru counties [4, 55, 56], and similar types of pests reported here have also been reported and discussed extensively in a government and other reports [106, 107]. The need for pesticides sometimes is absolute because frequent unexpected attacks by pests sometimes occur, for example in 2017, 40% of farms were reported to be infested with the fall armyworm [108].

Other researchers have also reported on pesticide use and impacts in other regions of the country, including vegetable farming districts of Kiambu, Kirinyaga, Nyandarua, Muranga, Meru and Makueni [109, 110], where mostly WHO Class I and II pesticides were used and acute poisoning cases were reported; Lake Victoria basin including Nyando, Kericho and Nandi districts [54], where tea, coffee, sugarcane, maize and vegetables were cultivated, and in which 14 different active ingredients were used against maize stock borer (86% of farmers), aphids (70%), cutworms (60%), diamond black moth (50%), thrips (28%), termites (20%) and weeds (4%), and 4 of the active ingredients were known to be highly toxic to bees and birds [54]. Herbicides were used in tea, coffee and sugarcane and insecticides and fungicides, respectively, largely on vegetables [54], with frequent cases of misuse, including application of banned OCs, and declines in pollinating insects and Red-billed Oxpecker bird species being reported [54]. Mburu et al. [111] found that 141 different pesticides were used in 20 horticultural farms along the small Lake Naivasha shore catchment alone, six of them (4.3%) belonging to WHO Class I, including carbamates (*oxamyl and methomyl*), *bipyridylium, strobilurin, tetranortriterpenoids, azole* and OPs (*fenamiphos*), and 20 of them (14.3%) in the WHO Class II. The farmers also used 4 species of natural predators (*Trichoderma spp*, *Paecilomyces spp*, *phytoseiulus persimilis spp* and *Amblyseius spp*), and entomopathogenic fungi, which are registered by PCPB, as biopesticides [111]. Some of the impacts of pesticides on Lake Naivasha water have been highlighted and residues of carbamates and organophosphates have been detected in the water [92, 95]. However, much less work on pesticides and their impacts than expected in global terms is being done in Sub-Saharan Africa [112].

Recently, however, some impacts on pesticide policy in Kenya have started being felt [43]. The route for food initiative (RTFI) (an NGO) in 2019 conducted a study and found that 77% of the 230 ingredients registered in Kenya have been at least withdrawn from the EU market or are heavily restricted due to their chronic human toxicity and environmental effects (based on fish and bees), and additional 19 of them are not listed in the EU database [43]. The RTFI report further highlighted the carcinogenic, mutagenic, endocrine disruptive, neurotoxic and male infertility effects of most of them [43]. Following these concerns, the Kenya Organic Agriculture

Network (KOAN) in collaboration with Eco-Trac Consulting did a survey in 2020 and produced a comprehensive report giving detailed accounts of pesticide usage and impacts in Kirinyaga and Muranga counties in Central Kenya, where intensive horticulture is practiced for subsistence and export purposes [84]. The aim of the study was to provide the evidence needed to advocate and promote a transition from harmful pesticides, to safer alternatives such as GAPs and bio-pesticides [84]. The risk assessment was done according to the EU protocols. Apart from the information on toxicity of 64 active ingredients and 142 formulations being used to control 30 insect pests, 24 weeds and 11 plant diseases, respectively, in the two counties, they also highlighted issues such as misinformation, misuse, mishandling of pesticides and lack of education

and awareness as some of the main challenges the two counties faced [84]; a good example being *methamidophos,* which was not registered for use by the PCPB and likewise, no product containing *acephate* was registered for use on tomatoes, but these two pesticides were being used by farmers, illegally and incorrectly, resulting in residues of *acephate* and *methamidophos*, which are both very toxic [113, 114] exceeding the MRLs set by KEBS and EU in some samples of tomatoes [84]. They concluded that many of the pesticides used in Kenya are highly toxic, belonging to WHO Class I and II, and have already been banned or heavily restricted in other countries such as China, India and Europe, where most of them are imported from Kenya [43, 84]; and their risks need to be assessed with the aim of withdrawal or banning.

An Expert Taskforce [115], in 2021, was appointed by the NGOs to conduct an evaluation of selected pesticide active ingredients (from the PCPB database), including 20 insecticides, 5 fungicides and 4 herbicides, respectively, which are widely used in agriculture in Kenya [115]. The toxicity scores were obtained according to the methods of Dabrowski et al. [99]. Based on their evaluation, they recommended that seventeen (17) of the active ingredients should be withdrawn immediately, five (5) should go through phased withdrawal and only three (3), *clodinatop, flubendiamide and flufenoxuron*, should be retained [115]. The NGOs used the report and successfully pushed for a 'Pesticide Bill' to be introduced in parliament in 2020 aiming at the withdrawal/banning of pesticides considered harmful, from the Kenyan market. The PCPB is currently in the process of conducting a regulatory review of a priority list of highly active ingredients from the PCPB database, including those recommended by the expert taskforce, in support of the bill [115].

4.2 Pesticide use in malaria vector control in Kenya

Malaria remains the major cause of morbidity and mortality globally with 219 million cases reported in 2017, resulting in 435,000 estimated deaths, 61% of them being children under the age of 5 years [116–118]. The integrated malaria vector management program recommended by the WHO outlines a multipronged approach involving five methods, which include, (i) spraying with recommended insecticides against adult mosquitoes in their habitats, (ii) using insecticide-treated mosquito nets (ITNs), (iii) indoor residual spraying (IRS), whenever necessary, (iv) larval source management, and (v) early diagnosis and treatment; but only ITNs, IRS and early diagnosis and treatment, are implemented in Kenya. It is believed that lack of implementation of sustained larval control has reduced the positive gains made in combating malaria in Kenya, and it still remains a major killer accounting for 10,500 deaths annually [7].

Malaria vector control using long-lasting insecticidal nets (LLIN), has gradually increased in Western Kenya from the year 2000 [7], with about 11 million LLINs distributed freely by 2011; still far from reaching the universal coverage of all vulnerable populations. In these LLIN interventions, *permethrin*-treated LLIN has been used in various endemic zones such as Bondo, Teso, Rachuonyo and Nyando [119]. Pyrethroids such as *fenitrothion, lambda-cyhalothrin and alpha-cypermethrin*, and DDT have been used in IRS. However, with the resistance of the mosquito vectors to pyrethroids widely reported, spraying with *pirimiphos-methyl* on walls in Migori county in Nyanza [7] has been done. Although use of biopesticides such as entomopathogenic fungi has not been embraced, several small-scale trials with biolarvicides such as *B. thuringiensis israelensis (Bti)* and *Bacillus sphaericus (B.s)* in form of water-dispersible granules have reported positive results against various species of mosquito larvae along Lake Victoria shores [7]. The low residual activity makes larval control using the two interventions costly since repeated applications of the bacterial strains to the breeding sites would be necessary, and suitable formulations such as slow-release methods have to be considered. Biorational pesticides such as *Wolbachia*, *Metarhizium anisopliae, methoprene*, *hydropene, p*yriproxyfen*, B. thuringiensis and Spinosad*, which have very low human toxicity and are biodegradable, have not been significantly adopted for larval and adult mosquito control in Kenya [7].

5. Conclusions

The chemistry, manufacturing, importation and regulatory processes regarding pesticides in Kenya as well as their usage and impacts on humans and the environment have been discussed. All the various categories of pesticides, i.e. organochlorine, organophosphate, carbamate, pyrethroid and neonicotinoid insecticides, as well as fungicides, herbicides and biopesticides, which are used in the country, have been considered. Important information on a total of 1447 formulations and 157 active ingredients, respectively, for use in agriculture and public health sectors, are listed on the Pest Control Products Board database and is available freely to the public. A significant number of biopesticides are manufactured in the country and are used in horticulture. A number of studies have been conducted in major agricultural regions, which have characterized pesticides, their toxicities, types of crops and pests, usage and human and environmental health risk indices, since the 2000, but the reports have not made any impact on pesticide regulation, and very toxic active ingredients belonging to the WHO Class I and II, some of them already banned or removed from the EU, seem to dominate the market in Kenya. However, recent pressure from NGOs made an impact on government and parliament and a bill was introduced in 2020, aiming at more strict enforcement and banning of some of the very toxic pesticides, which have already been banned in the EU market. The PCPB which is the government institution charged with the responsibility of regulating pesticides in the country is currently reviewing some of the products, which can be replaced by safer alternatives, for banning.

Acknowledgements

The authors wish to thank the National Research Fund of Kenya (NRF) for their support under the Multidisciplinary Research Grants.

Pesticides: Chemistry, Manufacturing, Regulation, Usage and Impacts on Population in Kenya
DOI: http://dx.doi.org/10.5772/intechopen.105826

Author details

Joseph O. Lalah[1*], Peter O. Otieno[2], Zedekiah Odira[3] and Joanne A. Ogunah[4]

1 School of Chemistry and Material Science, Technical University of Kenya, Nairobi, Kenya

2 Pest Control Products Board, Kisumu, Kenya

3 Department of Biological Sciences, Masinde Muliro University of Science and Technology, Kakamega, Kenya

4 Department of Physical Sciences, University of Embu, Embu, Kenya

*Address all correspondence to: joseph.lalah@tukenya.ac.ke

References

[1] Jones MM, Netterville JT, Johnston DO, Wood JL, Joesten MD. Chemistry and Society. 5th ed. New York: Saunders College Publishing; 1987. pp. 491-519

[2] World bank. World Development Report 2020. 2020. Available from: Worldbank.org/en/publication/wdr.2020

[3] Yu JS. The Toxicology and Biochemistry of Pesticides. Boca Raton, USA: CRC Press; 2008. ISBN 978-1-4200-5975-5

[4] Marete GM, Lalah JO, Mputhia J, Wekesa VW. Pesticide usage practices as sources of occupational exposure and health impacts on horticultural farmers in meru county, Kenya. Heliyon. 2021;**7**:1-13. DOI: 10.1016/j.heliyon.2021.e06118

[5] Nauen R. Insecticide resistance in disease vector of public health importance. Pest Management Science. 2007;**63**:628

[6] Ware GW, Whitcare DM. The Pesticide Book. 6th ed. Willoughby, OH: Meister Pro Information Resource; 2004

[7] Ogunah JO, Lalah JO, Schramm K-W. Malaria vector control strategies: What is appropriate towards sustainable global eradication? Sustainable Chemistry and Pharmacy. 2020;**18**:100339. DOI: 10.1016/j.scp.2020.100339

[8] Helm R, Cockrell G, Stanley JS, Brenner RJ, Burks W, Bannon GA. Isolation and characterization of a clone encoding a major allergen (Bla Bd90k) involved in IgE-mediated cockroach hypersensitivity. The Journal of Allergy and Clinical Immunology. 1996;**98**:172

[9] Donaldson T, Kiely T, Grube A. Pesticide Industry Sales and Usage: 1998-1999 Market Estimates. Wahsington DC: USEPA; 1996

[10] Zilberman D, Schmitz A, Lichtenberg E, Siebert JB. The economics of pesticide use and regulation. Science. 1991;**253**:518

[11] PCPB. Pest control products board. Fully registered pest control products Version_2018. 2018. Available from: www.pcpb.go.ke

[12] Sande D, Mullen T, Wetzstein M, Houston J. Environmental Impacts from pesticide use: A case study of soil fumigants in Florida tomato production. International Journal of Environmental Research and Public Health. 2011;**8**: 4649-4661

[13] USEPA. Pesticide Assessment Guideines, Subdivision F: Hazard evaluation –Human and Domestic Animals Series. Washington DC: USEPA; 1991. p. PB-158394

[14] Lalah JO, Kaigwara PN, Getenga ZM, Mghenyi JM, Wandiga SO. The major environmental factors that influence rapid disappearance of pesticides from tropical soils in Kenya. Toxicological Environmental Chemistry. 2001;**81**:167-197

[15] Mnif W, Hassine AIH, Bounaziz A, Bartegi A, Thomas O, Roig B. Effect of endocrine disrupting pesticides: A review. International Journal of Environmental Research and Public Health. 2011;**8**(6):2265-2303

[16] Shen L, Wania F. Compilation, evaluation and selection of physical chemical property data for OCs. Journal of Chemical & Engineering Data. 2005;**50**(3):742-766

[17] Freed H, Schmedding D, Kohnert R, Haque R. Physical Chemical properties of several organophosphates: Some implication in environmental and biological behaviour. Pesticide Biochemistry and Physiology. 1979;**10**(2):203-211

[18] Keadtisuk S, Dheranetra W, Nakatsugawa T, Fukuto TR. Liver damage induced in rats by malathion impurities. Toxicology Letters. 1990;**52**:35

[19] Umetsu N, Grose FH, Allahyari R, Abu-el-Haj S, Fukuto TR. Effect of impurities on the mammalian toxicity of technical malathion and acephate. Journal of Agricultural and Food Chemistry. 1977;**25**:946

[20] Kuhr RJ, Dorough HW. Carbamate Insecticides, in: Chemistry, Biochemistry and Toxicology. Cleveland USA: CRC Press; 1976

[21] Mineau P, Tucker KR. Improving Detection of Pesticide Poisoning in Birds Part II. Journal of Wildlife Rehabilitation. Summer: Wildlfe Conservation; 2002. p. 2002

[22] Mineau P. Estimating the probability of bird mortality from pesticide sprays on the basis of the field study record. Environmental Toxicology and Chemistry. 2002;**24**(7):1497-1506

[23] Sherwani SI, Arif IA, Khan HA. In: Herbicides AP, Kelton J, Sarunaite L, editors. Modes of Action of Different Classes of Herbicides. London, UK: Intech Open; 2015. DOI: 10.5772/61779

[24] Grossman K. Mediation of herbicide effects by hormone interaction. Journal of Plant Growth Regulators. 2003;**22**:109-122

[25] Singh S, Kumar V, Chauhan A, Datta S, Wani AB, Singh N, et al. Toxicity, degradation and analysis of the herbicide atrazine. Environmental Chemistry Letters. 2018;**16**:211-237

[26] Lalah JO, Omwoma S, Osano FO, Omukunda E, Wafubwa G, Muyekho D, et al. Assessment of potential risks and effectiveness of agrochemical usage in a catchment: A case study of the Nzoia Nucleus Estate sugarcane farms in western Kenya. In: Maestroni B, Cannavan A, editors. Chapter 16 in: Integrated Analytical Approaches for Pesticide Management. Academic Press Publishers, Elsevier; 2018 eBook: 9780128161562, Paperback: ISBN: 9780128161555 (338 p)

[27] Bigley WS, Plapp FW. Metabolism of cis and trans-14C-permethrin by tobacco budworm and bollworm. Journal of Agricultural and Food Chemistry. 1978;**26**:1128

[28] Bryant R, Bite MG, Hopkins WI. Global Insecticide Directory. 2nd ed. Kent, UK: Agranova; 1999

[29] Isman MB. Botanical insecticides, deterrents, and repellants in modern agriculture and an increasingly regulated world. Annual Review of Entomology. 2006;**51**:45-66

[30] Chermenskaya TD,Stepanycheva EA, Shchenikova AV, Chakaeva AS. Insecticid acaricidal and deterrent activities of extracts of Kyrgyzstan plants against three agricultural pests. Industrial Crops and Products. 2010;**32**:157-163

[31] El-Wakeil. Botanical Pesticides and their modes of action. Gesunde Pflanzen. 2013;**65**:125-149

[32] Fusetto R, O'Hair RAJ. Nicotine as an Insecticide in Australia. J Royal Australian Institute, October: A short history; 2015. p. 2015

[33] Boomquist JR. Insecticides: Chemistries and Characteristics. 2nd ed. Radcliffe World Text book: Ipmworld. umn.edu/bloomquist-insecticides; 1996

[34] Singha A, Thareja V, Singla AK. Application of neem seed kernel extrats result in mouthpart deformites and subsequent mortality in *Nezara viricula* (L.) (hem: Pentatomidae). Journal of Applied Entomology. 2007;**131**:197-201

[35] Silva JCT, Iham GN, RDL O, Brown L. Purification of the seven tetranortriterpenoids in neem (*Azadirachta indica*) seed by counter-current chromatography sequentially followed by isocratic preparative reversed-phase high-performance liquid chromatography. Journal of Chromatography. 2007;**1151**:203-210

[36] Ihara M, Matsuda K. Neonicotinoids: Molecular mechanisms of action, insights into resistance and impact on pollinators. Current Opinion Insect Science. 2018;**30**:86-92. DOI: 10.1016/j.cois.2018.09.009

[37] Tailebois E, Carlereau A, Jones AK, Thany SH. Neonicotinoid insecticides mode of action on insect nicotinic acetylcholine receptors using binding studies. Pesticide Biochemistry and Physiology. 2018;**151**:59-66

[38] Luetan L, Merwin I, Kovach J. Assessing the relative environmental impacts of agricultural pesticides: The quest for a holistic method. Agriculture, Ecosystem & Environment. 1995;**55**(3):153-168

[39] Odinokov VN, Ishmuranov GY, Kharisov RY, Serebreykov EP, Tostikov GA. Synthsis of s-(+)methoprene. Bulletin of the Academy of USSR, Division of Chemical Sciences. 1993;**42**(1):98-99

[40] Ravon A. In: Charles JF, Delecluse A, Nielsen-LeRoux C, editors. *Bacillus thuringiensis* Application in Agriculture, in Entomopathogenic Bacteria: From Laboratory to Field Application. London: Kluer; 2000. p. 255

[41] Bravo A, Soberon M, Gill SS. In: Gilbert LI, Iatrou K, Gill SS, editors. *Bacillus thuringiensis*: Mechanisms and use., in: Comprehensive Molecular Insect Science. Vol. 6. London: Elsevier; 2005. p. 175

[42] Mcguire AV, Northfield TD. Tropical occurrence and agricultural importance of Beauveria bassiana and Metarhizium anisopliae. Frontiers in Sustainable Food Systems. 2020;**4**:6. DOI: 10.3389/fsufs.2020.00006

[43] RTFI. Pesticides in Kenya. Why our Health, Environment and Food Security is at Stake. 2019 Available from: https://routetofood.org/pesticides-in-kenya-whats-at-stake/

[44] Werren JH, Guo L, Windsor DW. Distribution of *Wolbachia* among neotropical arthropods. Proceedings of the Royal Society B. 1995;**262**(1364):197-204. DOI: 10.1098/rspb.1995.0196

[45] Aliota MT, Walker EC, Yepes AU, Velez ID, Christensen BM, Osorio JE. The mel strain of *Wolbachia* Reduces transmission of chikungunya virus in aedes aegypti. PLOS Neglected Tropical Diseases. 2016, 2016;**10**(4):e0004677

[46] Dutra HLC, Rocha MN, Dias FBS, Mansur SB, Caragata EP, Moreira LA. Wolbachia blocks currently circulating zika virus isolates in Brazilian *Aedes aegypti* Mosquitoes. Cell Host Microbe. 2016, 2016;**19**(6):771-774

[47] Zhang D, Lees RS, Xi Z, Gilles JRL, Bourtzis K. Combining the sterile insect technique with wolbachia-based approaches: II- A safer approach to Aedes albopictus population suppression programmes, designed to minimize the consequences of inadvertent female release. PLoS One. 2015, 2015;**10**(8):e0135194

[48] Hoffmann AA, Montgomery BL, Popovici J, Iturbe-Ormaetxe I, Johnson PH, Muzzi F, et al. Successful establishment of *Wolbachia* in *Aedes* populations to suppress dengue transmission. Nature. 2011;**476**(7361):454-457

[49] Bian G, Joshi D, Dong Y, Lu P, Zhou G, Pan X, et al. Wolbachia invades Anopheles stephensi populations and induces refractoriness to Plasmodium infection. Science. 2013;**340**(6133):748-751

[50] McGrath MT. Fungicides and Other Chemical Approaches for Use in Plant Disease Control. Encyclopedia of Microbiology. 3rd ed. Amsterdam: Science Direct; 2009

[51] Zubroid JP, Brundschuh M, Arts G, Bruehl CA, et al. Fungicides: An overlooked pesticide class? Environmental Science & Technology. 2019;**53**(7):3347-3365

[52] Yang C, Hamel C, Vujanovic V, Gan Y. Fungicides: Modes of action and possible impacts on non-target organisms. International Scholarly Research Network. 2011;**2011**:1-8. DOI: 10.5402/2011/130289

[53] Sunday AO, Alafara BA, Oladel OG. Toxicity and speciation analysis of organotin. Chemistry, Speciation and Bioavailability. 2012;**24**(4):216-226

[54] Abong'o DA, Wandiga SO, Jumba IO, Madadi VO, Kylin H. Impacts of pesticides on human health and environment in the River Nyando catchment, Kenya. International Journal of Humanities, Arts, Medicine and Sciences. 2014;**2**(3):1-14

[55] Otieno PO, Lalah JO. Prioritization and Assessment of Large Scale Pesticide use in Trans Nzoia County and their Potential Impacts on Human and Environmental Health. Unpublished Report; 2022

[56] Odira Z, Lalah JO, Otieno PO, Omwoma S, Osano O, Omukunda E. Screening and Prioritization of Pesticides Application for Potential Human and Environmental Health Risk Assessment in Large Scale Farms in Trans Nzoia County. Kenya: Unpublished Report; 2022

[57] Oparaeke AM, Dike MC, Amatobi CJ. Insecticidal efficacy of Sabruka formulations as protectants of cowpeas against field pests. Journal of Entomology. 2006;**3**:130-135

[58] D'Silva C, Krishna B. Rodenticide poisoning. Indian Journal of Critical Care Medicine. 2019;**33**(4):S272-S277

[59] Rumbeiha WK, Snider DB. Veterinary Toxicology, In: Encyclopedia of Toxicology. 3rd ed. Amsterdam: Science Direct; 2014

[60] Lalah JO, Wandiga SO. Persistence and Fate of Malathion residues in stored beans (Phaseoulus Vulgaris) and maize (Zea Mays). Pesticide Science. 1996;**46**:215-220

[61] USEPA. Epa.gov/ozone-layer-protection/ozone depleting substances. 2022. [Accessed: April 26, 2022]

[62] Cheke RA, Sidatt ME. A review of alternatives to fenthion for quela bird control. Crop Protection. 2019;**116**:15-23

[63] Bustinduy AL, King CH. Schistosomiasis in Manson's Tropical Intectious Diseases. 23rd ed. Amsterdam: Science Direct; 2014

[64] Hodgson E, Levi PE. In: Krieger RI, editor. Metabolism of Pesticides, in: Handbook of Pesticide Toxicology. 2nd ed. Vol. 2. San Diego: Academic Press; 2001

[65] Usmani K, Karoly ED, Hodgson E, Ros RL. In vitro sulfoxidation of thioether compounds by cytochrome

P450 and flavin-containing monooxygenase isoforms with particular reference to the CYP2C subfamily. Drug Metabolism and Disposition: The Biological Fate of Chemicals. 2004;**32**(3):333-339

[66] Jing T-X, Tan Y, Ding B-Y, Dou W, Wei D-D, Wang J-J. NADPH–cytochrome P450 reductase mediates the resistance of *Aphis* (*Toxoptera*) citricidus (Kirkaldy) to abamectin. Frontiers in Physiology. 2018;**9**:986

[67] PCPB. The Pest Control Products Act, Chapter 346, Laws of Kenya, Revised Edition, 1985. Nairobi: Government Printer; 1985

[68] Ngaruiya. Overview of registration of pesticides in Kenya. In: Wabule MN, Ngaruiya PN, Kimmins FK, Silverside PJ, editors. Registration for Biocontrol Agents in Kenya. Proceedings of the PCPB/KARI/DFID CPP Workshop; Nakuru, Kenya; 14-16 May 2003. pp. 79-85

[69] Retkute R, Hinton RGK, Kressman K, Gilligan. Regional differences in control operations during 2019-2021 Desert locust upsurge. Agronomy. 2019;**221**(11):2529

[70] Sharma A, Kumar V, Shahzad B, et al. Worldwide pesticide usage and its impacts on ecosystem. S. N. Applied Sciences, Article number 1446, Springer. 2019. DOI: 10.1007/542452-019-1485-1

[71] Label Review Manual. US Environmental Protection Agency, Office of Pesticide Programs. Washington, DC: U.S. Government Printing Office; 1998. Available from: https://www.epa.gov/pesticide-registration/label-review-manual

[72] UNEP. Globally Harmonized System of Classification and Labelling of Chemicals (GHS): Seventh. Revised ed. New York: UN; 2017. DOI: 10.18356/e9e7b6dc-en

[73] Fishel FM. What are inert ingredients. Gainsville. University of Florida Institute of Food and Agriculture Sciences. 2010 https://edis.ifas.ufl.edu/pi231

[74] Kwiatkowska M, Huras B, Bukowska B. The effect of metabolites and impurities of glyphosate on human erythrocytes (in vitro). Pesticide Biochem Physiology. 2014;**109**:34-43

[75] Yusoff SNM, Kamari A, Aljafree NFA. A review of materials used as carrier agents in pesticide formulations. International Journal of Environmental Science and Technology. 2016;**13**:2977-2994

[76] Fishel FM. Pesticide formulations. Gainsville: University of Florida Institute of Food and Agriculture Sciences. Available from:; 2010 https://edis.ifas.ufl.edu/pi231

[77] Roberts DM, Buckley NA, Mohamed F, Eddleston M, Goldstein DA, Mehrsheikh A, et al. A prospective observational study of the clinical toxicology of glyphosate-containing herbicides in adults with acute self-poisoning. Clinical Toxicology (Phila.). 2010;**48**:129-136. DOI: 10.3109/15563650903476491

[78] Bahadir M, Pfister G. Controlled release formulations of pesticides. In: Haug G, Hoffmann H, editors. Controlled Release Biochemistry Effects of Pesticides, Inhibition of Plant Pathogenic Fungi, Chemistry of Plant Protection. Vol. 6. Berlin: Springer; 1990. DOI: 10.1007/978-3-642-46674-8_1

[79] Tsuji K. Microencapsulation of pesticides and their improved handling safety. Journal of Microencapsulation. 2001;**18**(2):137-147

[80] Nyangi M. Efficacy of Crude Onion Extracts and Yellow Sticky Trap in the Control of Leafminers Liriomyza Trifolii in Capsicum. BTech Industrial Chemistry Project, Nairobi: Technical University of Kenya; 2015

[81] Lancaster. https://lancaster.unl.edu/pest/roach.Chapter 7: Insecticide Baits. Visited 26th April 2022

[82] Jordan BW, Bayer BE, Koehler PG, Pereira RO. Bait evaluation methods for urban pest management. London, UK: Intechopen.; 2013. DOI: 10.5772/5342

[83] Oesterlund A, Thomson JF, Sekimpi DK, Maziina J, Apio R, Joers E. Pesticide knowledge, practice and attitude and how it affects the health of small scale farmers in UgandaL a cross sectional study. African Health Sciences. 2014;**14**(2):420-433

[84] KOAN. Kenya Organic Agriculture Network: Pesticide use in Kirinyaga and Muranga Counties. 2020.Available from: https://www.koan.co.ke

[85] Hayes TB, Khoury V, Narayan A, et al. Atrazine induces complete femninization and chemical castration in male African clawed frogs (Xenopus Laevis). Proceedings of National Academy of Science of USA. 2010;**107**(10):4612-4617. DOI: Doi.org/10.1073/pnas.0909519107

[86] Nyamu D, Maitai CK, Mecca LW, Mwangangi EM. Trends of acute poisoning cases occurring at the kenyatta national Hospital, Nairobi, Kenya. East and Central African Journal of Pharmaceutical Sciences. 2012;**15**(2012):29-34

[87] Pamela F, Tsimbiri PF, Moturi WN, Sawe J, Henley P, Bend JR. Health impact of pesticides on residents and horticultural workers in the lake naivasha Region Kenya. Occupational Diseases and Environmental Medicine. 2015;**2015**(3):24-34. DOI: 10.4236/odem.2015.32004

[88] Gyawali K. Pesticide uses and its effects on public health and environment. Journal of Health Promotion. 2018;**6**:28-36

[89] Otieno PO, Lalah JO, Virani M, Jondiko IO, Schramm K-W. Carbofuran and its toxic metabolites provide forensic evidence for Furadan exposure in Vultures (Gyps africanus) in Kenya. Bulletin Environmental Contamination Toxicology. 2010;**84**(5):536-544

[90] Koech SJ, Karanja RHN, Kurgat J.K, Mokaya HO, Dubois T, Lattorff MG. Pesticide Contamination and their botanical sources in pollen loads collected by honey bees in Kenya: A spatio-temporal context (in press). 2022

[91] Kenya Plant Health Inspectorate Service (KEPHIS). Annual Report and Financial Statement. Kenya: Nairobi; 2018

[92] Otieno PO, Okinda PO, Lalah JO, Pfister G, Schramm K-W. Monitoring the Occurrence and Distribution of Selected Organophosphates and Carbamate Pesticide Residues in the Ecosystem of Lake Naivasha. Kenya: Toxicological & Environmental Chemistry; 2014. DOI: 10.1080/02772248.2014.942309

[93] Getenga ZM, Keng'ara FO, Wandiga SO. Determination of organochlorine pesticides in soil and water from river Nyando Drainage System within Lake Victoria Basin, Kenya. Bulletin of Environmental Contamination. 2004;**72**(2):335-343

[94] Abong'o DA, Wandiga SO, Jumba IO, Van den Brink PJ, Nazariwo BB, Madadi VO, et al. Organochlorine pesticide residue levels in

soil from the Nyando River Catchment, Kenya. Africa Journal of Physical Sciences. 2015;**2**(1):18-32

[95] Omwenga I, Kanja L, Zomer P, Louisse J, Rietjens IMCM, Mol H. Organophosphate and carbamate pesticide residues and accompanying risks in commonly consumed vegetables in Kenya. Food Additives & Contaminants Surveillance: Part B. 2021;**14**:48-58

[96] FAO/WHO. International Code of Conduct on Pesticide Mangement. Managing pesticides in agriculture and public health: A compendium of FAO and WHO guidelines and other resources. 2nd ed. FAO/WHO 2021. 2021

[97] GoK. Government of Kenya, Ministry of Agriculture, Livestock and Fisheries report: Capacity Building Strategy for Agruclture Sector, November, 2017. 2017

[98] Chen Y, Yan C, Sun Z, Wang Y, et al. Organochlorine pesticide ban facilitated reproductive recovery of Chinese striped Hamsters. Environmental Science & Technology. 2021;**55**(9):6140-6149

[99] Dabrowski DM, Shadung JM, Wepener V. Prioritizing agricultural pesticides used in South Africa based on their environmental mobility and potential human health effects. Environment International. 2014;**62**:31-40

[100] Valcke M, Chaverri F, Monge P, Bravo V, Mergler D, Partanen T, et al. Pesticide prioritization for a case–control study on childhood leukemia in Costa Rica: A simple stepwise approach. Environmental Research. 2005;**97**(3):335-347

[101] Gunier RB, Harnly ME, Reynolds P, Hertz, Behren V. Agricultural pesticide use in california: Pesticide prioritization, use densities, and population distributions for a childhood cancer study. Environmental Health Perspectives. 2001;**109**:1071-1078. Avilable from: http://ehpnet1.niehs.nih.gov/docs/2001/109p1071-1078gunier/abstract.htm

[102] Gustafson DI. Groundwater ubiquity score: A simple method for assessing pesticide leachability. Enviromental Toxicology and Chemistry. 1989;**8**:339-357. DOI: 10.1002/etc.5620080411

[103] Chen H et al. Estrogenicity of organophosphorus and pyrethroid pesticides. Journal of Toxicology and Environmental Health Part A. 2002;**65**:1419-1435. DOI: 10.1080/00984100290071243

[104] Marete GM, Shikuku VO, Lalah JO, Mputhia J, Wekesa VW. Occurrence of pesticides residues in French beans, tomatoes, and kale in Kenya, and their human health risk indicators. Environmental Monitoring and Assessment. 2020;**192**:692. DOI: 10.1007/s10661-020-08662-y

[105] Soko JJ. Agricultural Pesticides used by small-scale farmers in Kenya: What are the experiences of the farmers? ORCiD: https://orcid.org/0000-0001-7427-9188. 2020. DOI: 10.21203/rs.3.rs-20784/v1

[106] MOA. Ministry of Agriculture, Livestock, Fisheries and Irrigation National Agricultural and Rural inclusive Growth Project (NARIGP), "Integrated Pest Management Plan,". Nairobi: Government of Kenya; 2018. p. 2018

[107] Loha KM, Lamoree M, Weiss JM, de Boer J. Import, disposal, and health impacts of pesticides in the East Africa Rift (EAR) zone: A review on management and policy analysis. Crop Protection. 2018;**112**(2018):322

[108] World Vision International. Fall armyworm invasion in Kenya. World Vision International report 2017

[109] Macharia I, Mithofer D, Waibel H. Potential environmental impacts of pesticide use in the vegetables. Africa Journal of Horticultural Science. 2009, 2009:1998-9326

[110] Macharia I. Pesticides and health in vegetable production in Kenya. BioMed Research International. 2015;**2015**(241516):10. DOI: 10.1155/2015/241516

[111] Mburu NS, Matuku T, Osano O, Gichuho CM. Pesticide Preferences and patterns of use along the shore of Lake Naivasha, Kenya. Greener Journal of Environmental Management and Public Safety. 2013;**2**(3):115-120

[112] Fuhrimann S, Wan C, Blouzard E, Veludo A, Holtman Z, Chetty-Mhlanga S, et al. Pesticide research on environmental and human exposure and risks in sub-saharan africa: A systematic literature review. International Journal of Environmental Research and Public Health. 2022;**19**:259. DOI: 10.3390/ijerph19010259

[113] Farag AT, Eweidah MH, El-Okazy AM. Reproductive toxicology of acephate in male mice. Reproductive Toxicology. 2000;**14**(5):457-462. DOI: 10.1016/S0890-6238(00)00094-0

[114] FOOTPRINT, 2006. The Footprint Pesticide Properties Database. Database collated by the University of Hertfordshire as part of the EU-funded Footprint project (FP6-SSP-022704). http://www.eu-footprint.org/ppdb.html.

[115] Expert Taskforce. Scientific Report on Pesticides in the Kenyan Market. Contributers: Biodiversity and Biosafety Association of Kenya, Kenya Organic Agricultural Network, Resources Oriented Development Initiatives and Route for Food Initiative, September 2021. 2021

[116] WHO (2018). WHO | World malaria report 2018 [Internet]. WHO. 2018 [cited 2019 Oct 14]. Available from: http://www.who.int/malaria/publications/world-malaria-report-2018/en/

[117] WHO (2003). WHO | Guidelines on the management of public health pesticides. Available from: http://www.who.int/whopes/resources/who_cds_whopes_2003.7/en/. [Accessed: October 22, 2019]

[118] WHO (2006). Guidelines for the treatment of malaria [Internet]. 2006 [cited 2019 Oct 22]. Available from: http://archives.who.int/publications/2006/9241546948_eng.pd

[119] Bayoh MN, Mathias DK, Odiere MR, Mutuku FM, Kamau L, Gimnig JE, et al. Anopheles gambiae: Historical population decline associated with regional distribution of insecticide-treated bed nets in western Nyanza province, Kenya. Malaria Journal. 2010;**9**(1):62. DOI: 10.1186/1475-2875-9-62