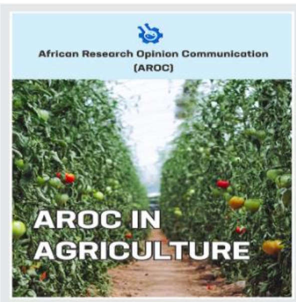
REVIEW ARTICLE

Biopesticides and Conventional Pesticides: Comparative Review of Mechanism of Action and Future Perspectives

Abdulhakeem Rotimi Agboola*, Chibuzor Onyinye Okonkwo, Eyuwa Ignatius Agwupuye, Gladys Mbeh



Department of Biochemistry, Faculty of Basic Medical Sciences, University of Calabar, PMB 1111 Eta Agbor road, Calabar, Crossriver State, Nigeria

*Corresponding author
Abdulhakeem Rotimi Agboola
https://orcid.org/0000-0003-3364-8121
Email: agboolara@unical.edu.ng

ABSTRACT

Pesticides are substances or chemicals employed in the control of pests. The rate of food losses in the world especially in third world countries continues to be on an upward scale. These losses are often caused by the damaging and destructive activities of pests during cultivation, harvest and post-harvest activities including drying and storage. To curtail the huge problems these pests, pose to farmers and other players in the agricultural food chain, researchers have over the years developed different types and forms of pesticides and more efforts are still ongoing in the quest to develop more pesticides especially of natural origin. There is a general belief that pesticides of natural origin are safer to non-target species than the synthetic pesticides. While this may be expected given the fact that many synthetic pesticides are made from unhealthy chemicals and heavy metals and are non-biodegradable resulting in accumulation of residues in food and water, it is still a subject of serious debate among researchers. Also, lack of government support, incentives and poor regulatory policies especially for biopesticides, are part of the challenges facing the development of natural pesticides. This review is aimed at unravelling the characteristics of the two major classes of pesticides: synthetic and natural pesticides with a view to advising on which is safer for human health and the environment and the way forward for farmers and other stakeholders in the agricultural sector.

Keywords: Biopesticides; biodegradable; accumulation; environment; ecosystem

Received: 15 February 2022, Revised: 05 April 2022, Published: 25 April 2022
Citation: Agboola, A.R., Okonkwo, C.O., Agwupuye, E.I., and Mbeh, G. (2022). Biopesticides and Conventional Pesticides: Comparative Review of Mechanism of Action and Future Perspectives. *AROC in Agriculture,* 01(01);14-32, https://doi.org/10.53858/arocagr01011432

1.0 Introduction

One of the major challenges faced by farmers and other players in the agricultural value chain is the destruction caused by pests during cultivation, after harvest and during storage of agricultural produces. Every year, pests destroy a marked percentage of the world's food production and in Africa alone about a couple of dozen pests' especially arthropods are responsible for the steep decline in food availability as well as agricultural productivity [1]. To curtail the deleterious effects of these pests, pesticides are utilised at various stages of the agricultural chain. In general, a pesticide is a synthetic or biological agent that deters, incapacitates, kills, or otherwise discourages the activities of pests. Apart from their use in agriculture, pesticides are used to kill or deter insect vectors of malaria, trypanosomiasis and dengue fever. In this way, they also help to prevent the transmission of these diseases from one person to another. Pesticides include all of the following: herbicides, insecticides (which may include insect growth regulators, termiticides,etc.) nematicide, molluscicide, piscicide, avicide, rodenticide, bactericide, insect repellent, animal repellent, antimicrobial, fungicide, disinfectant (antimicrobial), and sanitizers. Most pesticides are intended to serve as plant protection products, which in general protect plants from weeds, fungi, or insects [2]. Targets of pesticides include insects, plant pathogens, weeds, nematodes (roundworms), and microbes that destroy properties, cause nuisance, or spread diseases. Although conventional pesticides have benefits, some also have drawbacks, such as potential toxicity to humans and other species [3]. Most pesticides are intended to serve as plant protection products, which in general protect plants from weeds, fungi, or insects [2].

The use of pesticides in agriculture is quite old and became more pronounced with time due to increased pest population coupled with decreasing soil fertility as well as increased resistance of pests to older pesticides. The use of modern pesticides in agriculture and public health is dated back to the 19th century [4].

The first important synthetic organic pesticide was Dichlorodiphenyltrichloroethane (DDT), first synthesized by a German scientist Ziedler in 1873 [2]. Its insecticidal effect was discovered by a Swiss chemist Paul Muller in 1939. In its early days, DDT was hailed as a miracle because of its broad-spectrum activity, persistence, insolubility, affordability and ease of application [5]. *Though* the ban on the agricultural use of DDT was proposed under the Stockholm Convention on Persistent Organic Pollutants [6] its manufacture and application was however permitted for the purpose of controlling disease vectors in accordance with strict recommendations and guidelines of the World Health Organization (WHO) and only in the absence of locally safe, effective, and affordable alternatives [7]. Consequently, DDT is still used in some developing nations to prevent malaria and other tropical diseases by spraying on the interior of walls to kill or repel disease vectors. [8]. This review aims to discuss in details the new green muscle; biological pesticides, their advantages, mechanism of action, current challenges and future prospects relative to the synthetic pesticides.

2.0 Classification of pesticides

Pesticides are classified based on several parameters, including their source and the type of pests they either kill or destroy. The two major classes based on source are synthetic and natural pesticides.

2.1 Natural/biopesticides

Natural pesticides are derived from natural sources including living organisms such as animals, plants and microorganisms and have the capability to control plants damaging pests through their non-toxic and eco-friendly mode of action [9]. Because natural pesticides are wholly sourced from natural sources, they are adjudged to be generally safer and less toxic when compared to the synthetic pesticides. Natural pesticides have some distinct advantages including non-generation of harmful residues in food [9].

Farmers and gardeners do not have to worry about poisoning themselves, their families, or pets when treating their crops or plants. Biopesticides are highly specific and exhibit selective toxicity due to their ability to target specific pests and leave the beneficial ones intact [9]. Another advantage of biopesticides is that they are often effective in low quantity therefore leading to lower exposure which could prevent pollution to the environment [9].

Biopesticides do not give off dangerous vapours, accumulate in the soil, or collect in water. They can be cheaper than chemical pesticides when locally produced especially for small scale agricultural use or for domestic pest manangement and can be more effective than synthetic pesticides in the long-term [10]**.** The rationale for the development and deployment of biopesticides or pest controls for pest management is their environmental safety, specificity, and biodegradability. Commercially available microbial pathogens are target specific and have not been shown to infect vertebrates or plants. [11].

However**,** natural pesticides especially the ones sourced from plants are largely dependent on the availability of plants. Some of these plants also have other uses including food, medicinal and aesthetic uses and this may hamper the commercialisation of these pesticides [12]. Again the cultivation of plants for the production of pesticides will require vast amounts of land and this will lead to competition of arable lands for food production [12].

Another challenge that comes with the production of natural pesticides is that a single plant could have many active substances therefore leading to a challenge in the formulation of these pesticides, additionally for pesticides to be produced from a plant; there is a need to extract the active ingredient from the plant using organic solvents which may pollute the environment. Though the biodegradability of biopesticides is an advantage to the environment, it also entails a short shelf life [12]. Due to their high specificity, microbial pesticides may only have effect on a portion of pests on the field thereby excluding others. The efficacy of microbial pesticides may also be affected by environmental factors such as UV light and desiccation [12].

Natural pesticides are classified into three major groups namely, Biochemical pesticides, Microbial pesticides and Botanicals/Plant-incorporated pesticides (PIP) [13].

a) Biochemical pesticides

These are naturally occurring substances or compounds with the ability to control pests via non-toxic mechanisms, their mode of action is quite different from that of chemical pesticides which contain molecules that are synthesised in the laboratory and designed in such a way that they can kill the pests directly. Biochemical pesticides can be further divided into different biologically functional classes, including pheromones, semiochemicals, plant extracts, and natural insect growth regulators [14].

i) **Pheromones**: These are chemicals or substances produced by insects which they use to stimulate certain behavioural patterns in other organisms or individuals. These pheromones have a wide range of effects and their naming is according to the responses they elicit. For example aggregation pheromones, alarm pheromones and sex pheromones. Pheromones are important in the control and monitoring of agricultural pests, consequently more than 1600 pheromones and sex attractants have been reported [15]. At present, pests on vast hectares of farmlands can be monitored and controlled via the application of pheromones and semiochemicals and this particular mode of pest control has several advantages including lower costs, specificity, ease of use and high sensitivity [16, 17].

ii) **Insect Growth Regulators (IGRs):** This group of natural pesticides control pests through the inhibition of certain fundamental processes neccessary for the survival of the insects thereby eliminating them, these compounds are highly selective and less toxic to non-target organisms [18]. Different groups of IGRs include the chitin synthesis inhibitors (CSIs) and substances that interfere with the action of insect hormones such as; juvenile hormone analogues and ecdysteroids [19]. IGRs are useful in the control of various types of insects including fleas, cockroaches, and mosquitoes, but they also have reduced fatality against adult insects [19]. Although low in toxicity to humans, they prevent reproduction, egg-hatch, and molting from one stage to the next in young insects but can act in synergy with other insecticides to kill adult insects [19].

b) **Microbial pesticides and entomopathogens**

These consist of microorganisms, like bacteria, fungi, or virus, which attack specific pest species, or entomopathogenic nematodes. These organisms target specific pest, and prevent the mortality of beneficial insects. [14]. Specific examples of microbial pesticides include bacteria, virus and fungi.

i) **Bacteria:** The bacteria based pesticide; *Bacillus thuringiensis* has been in commercial use for over four decades [20]. Other bacteria pesticides later developed include; *Bacillus thuringiensis var israelensis* (Bti) and *Bacillus sphaericus* (Bs). These were found particularly effective against mosquito [21] and other dipteran larvae. A number of bacterial species and subspecies especially *Bacillus pseudomonas* have also been used to produce biopesticides which are effective against insects. Other bacteria-based pesticides include; *B. thuringiensis tenebrionis*, with activity against *coleopteran* adults and larvae, most notably the Colorado potato beetle (*Leptinotarsa decemlin-eata);* and *B. thuringiensis japonensis* with activity against soil-inhabiting beetles [22;23].

Bacillus thuringiensis produces crystalline proteins and kills few target insect pest species like lepidopteran species. Bti exhibits some level of toxicity through the production of endotoxins during sporulation, these endotoxins must however be ingested by the larvae for the intended toxicity to be achieved, the ingestion of these endotoxins leads to the destruction of the gut tissues which in turns lead to gut paralysis. After the gut of the larvae becomes paralyzed, the larva is unable to feed again and this leads to starvation and eventual death [24; 25:26.).

Bt can be found in markets worldwide and are useful for the control of various important plant pests including mosquito larvae and black flies. Commercial Bt -based products include powders containing a combination of dried spores and crystal toxins. They are applied on leaves or other environments where the insect larvae feed. Advances in science have allowed scientist to genetically incorporate genes from Bt into several crops [27]. Asides producing endotoxins that cause the destruction of the gut tissues of larvae, microbial pesticides also compete with pathogens at the site of infection; this is achieved by the utilisation of nutrients and better colonization than the pathogens. This particular mode of action is used by microbial agents in the prevention of spoilage or decay that occur after harvest in pome fruits [28].

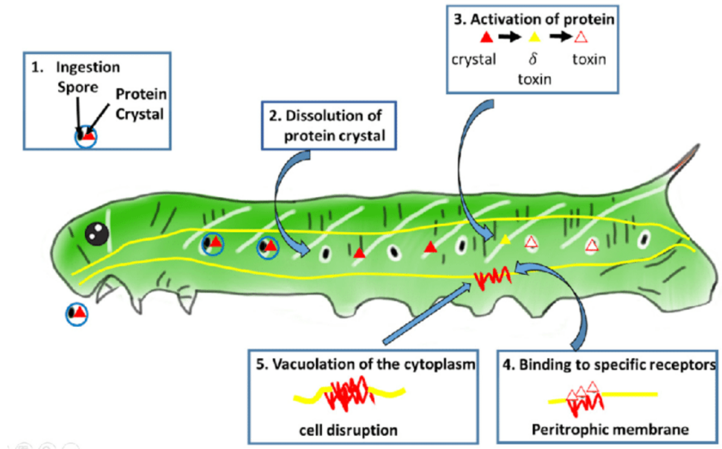


Figure 1: Mode of action of *Bacillus thuringiensis* in Lepidoptera (Modified from: 29]

ii) **Fungi:** One of the most important fungal pesticides is the *Metarhizium anisopliae* an essential entomopathogenic fungus which propagates worldwide in the soil demonstrating a wide range of insect host species. *M. anisopliae* have been reported to be extensively used in countries like Brazil for the treatment of sugarcane [30] . There are different strains and isolates of *M. anisopliae* which are of different geographical origins [31]. Under natural conditions, *Metarhizium anisopliae* are found in the soil where the moist conditions allow filamentous growth and production of infectious spores, called conidia, it is this infectious spore that the fungi uses to infect soil-dwelling insects upon contact [32]. *M.anisopliae* has been reported as safe both to the crops they are meant to protect and to the environment when compared to synthetic pesticides [33; 34].

These entomopathogenic fungi have been registered as microbial agent and many are also under consideration to be commercially developed into biological controls of several pests [35]. Asides *M..anisopliae*, other known fungal based pesticide include *Aschersonia aleyrodis* and *Lecanicillium. lecanii* which are widely used in the control and management of the Wooly Whitefly (*Aleurothrixus floccosus*), a pest of several cultivars including citrus and coffee in the Americas [36].

iii) **Virus:** The third major group of microbial pesticides is the Virus-based pesticides. Prominent members of this group are the baculoviruses, which are double-stranded DNA viruses found in arthropods especially insects. Baculoviruses have high pathogenicity and in their natural form, are highly effective against several insect pests [37]. Despite their pathogenicity, researchers have recently observed that these viruses have high specificity as they have been demonstrated to be non-infectious to both vertebrates and plants [38]. Lepidoptera is the major pest against which baculoviruses are isolated and mortality has only been observed at the larval stage [39]. For baculoviruses to cause infection in the larvae they are ingested, and enter the insects' body through the midgut from where they spread throughout the body. Although in some insects, infection can be limited to the insect midgut or the fat body [38]. Baculoviruses are of two groups; nucleopolyhedroviruses (NPVs) and granuloviruses (GVs). A common characteristic of baculoviruses is that they are occluded, i.e., the virus particles are embedded in a protein matrix. In NPVs, occlusion bodies comprise of numerous virus particles, but in GVs, occlusion bodies ordinarily contain just one

 https://doi.org/10.53858/arocagr01011432

virus particle. The occlusion of their bodies allows these viruses to survive outside the host [39]. Some baculoviruses have multispectral activities while others are known to be effective only against a particular specie hence are unlikely to pose any danger when genetically modified [40, 41]. Most newly developed baculoviruses recombinants are incorporated with insect-selective toxins. There are a number of viral formulations basically for the control of caterpillar pests. For example, Certis has recently registered Madex™, an increased-potency codling moth granulosis virus (GV) that also affects oriental fruit moth (OFM). Certis also deals Cyd-X™, which also contains the codling moth GV and which can be an efficient tool for codling moth management [42, 43]. Gemstar is registered for the control of lepidopteran pests, like the cotton bollworm and budworm, caterpillars which are majorly dangerous insect pests of corn, soybean, and other vegetables [43].

Table1: **Species of virus and the products derived from them** [30]

Species	Number of Products	Percent
Beauveria bassiana	45	37.2%
B. brongniartii	5	4.1%
Metarhizium anisopliae s l.	44	36.4%
M. acridum	3	2.5%
Isaria fumosorosea	7	5.8%
I. farinosa	1	0.8%
Lecanicillium longisporium	2	1.7%
Lecanicillium muscarium	3	2.5%
Lecanicillium sp.	10	8.3%
Hirsutella thompsonii	1	0.8%

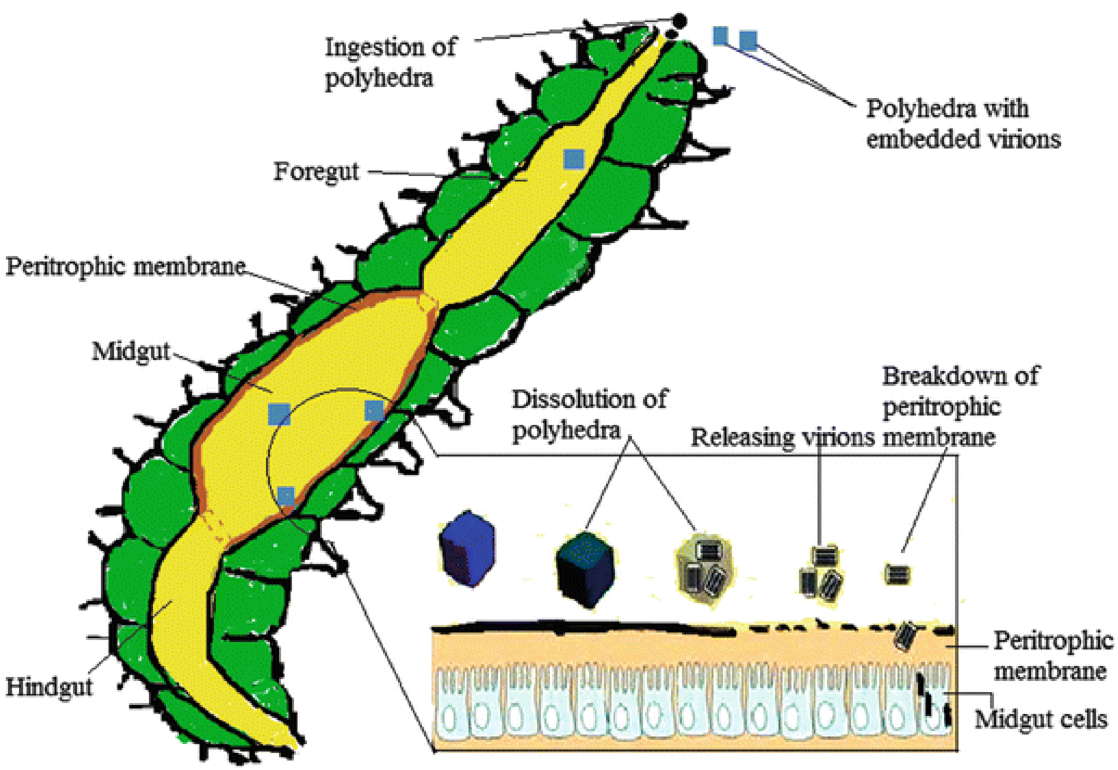


Figure 2: Mode of action of baculoviruses against lepidopteron insects [38].

c) Botanicals/plant incorporated pesticides (PIP)

By far, the most commonly researched group of natural pesticides are the plant-based biopesticides. Researchers in Africa and across the world have developed massive interest in plant based extracts including essential oils and they are widely regarded as suitable alternatives to synthetic insecticides. These pesticides are naturally occurring and have a range of bioactive chemicals inherent [44]. Essential oils and other extracts from plants exhibit a wide range of actions against insects, these actions are however dependent on a number of factors including the physiological characteristics of insect species as well as the type of plant. While some of these extracts can act as repellents, attractants, or antifeedants; some others may inhibit respiration, hamper the identification of host plants by insects, inhibit oviposition and decrease adult emergence through ovicidal and larvicidal effects [45, 46, 47].

Essential oils extracted from Neem and lemon grass is very common in the global pesticides markets [48]. Studies have shown that neem oil in combination with entomopathogenic microorganisms like *Beauveria bassiana* is highly effective against vegetable sucking pests [46]. However, further studies are required in order to determine the dose of azadirachtin content in neem oil in order to avoid killing the non-target organisms [49].

The efficacy of *Moringa oleifera* seed oil and *Anona muricata* seed oil on the second and fourth larval instar of *Aedes aegypti* was investigated [50], results showed that both oils were effective against the *aedis aegypti* larvae. Studies have also shown that *C. Occidentalis* may belong to the neuromuscular cum organo-chlorine class of pesticides capable of inhibiting acetyl cholinesterase activity of target pests and also causing the disruption of ionic composition in insects. [51]. A study on the insecticidal activity of *Piper guineense* seed oil has shown that they have protectant potential against insect pest damage during storage and can serve as viable alternatives to synthetic insecticides in the control of insect pest of stored products [52]. Similarly, a study to investigate the efficacy of *Xylopia aethiopica* in the control of *sitophlius oryzae* was carried out by some researchers [53] and they concluded that the ethanolic extract of this plant was effective in the control of *Sitophlus oryzae*. *Azadiracta indica* leaf powder is another plant that has been reported to possess biopesticide potential, and recent research has shown that they can cause the mortality of adult *Periplanta americana* under laboratory conditions [54].

Currently, essential oils constitue a significant share of the pesticide market and the current market value is estimated at USD 700.00 million and a total world production of 45,000 tons, due to advanced technology. Industries in the US are able to bring essential oil-based pesticides to market in less time, as compared to the time taken in conventional pesticide launch [55]. Asides extract of plants, there are various plant-based biopesticides that are produced through genetically modified organisms [48], this is achieved through the incorporation of genetic materials into plants which are then used as a source to produce pesticidal compounds referred to as plant-incorporated protectants (PIPs) [48]. Cry proteins are the first-generation of insecticidal PIPs that were introduced into the GM crops [55].

2.2 Conventional/Synthetic pesticides

Synthetic pesticides are artificial chemicals produced specifically for the control and elimination of pests. These chemicals are mainly used in agriculture for the protection of plants from pests, weeds or diseases; they are also applied in public health protection programs to protect humans from vector-borne diseases, such as malaria, dengue fever, and schistosomiasis [56]. Asides agricultural and public health applications, these products are also used for the improvement and maintenance of non-agricultural areas like public urban green areas and sport fields [57].

The use of synthetic pesticides have helped farmers and people in the agribusiness to achieve higher crop yield and quality, as they help to eliminate or control pests that destroy these crops, for example, the use of chemical pesticides has helped in killing caterpillars known to cause massive destruction of cabbage, this in turn has led to higher yield and better quality of cabbage produced by farmers [58]. Synthetic pesticides have been employed in the process of reducing food loss caused by the damaging effects of weeds, diseases and insect pests that can markedly reduce the amount of harvestable produce [58].

Synthetic pesticides are known to eliminate beneficial species of interest. Following the application of synthetic pesticides to food crops, residues of pesticides may remain in food and may be hazardous to the body if available at elevated levels. Synthetic pesticides have also been known to eliminate natural enemies of pests such as predators and parasites, leading to increase in population of pests [54]. The use of the same synthetic pesticides for many years has led to the development of immunity to the pesticides among targeted species. Most synthetic pesticides are hazardous and poisonous and may have toxic effects on infants, children and adults if they come in contact with the body. Synthetic pesticides can easily enter the soil, rivers, and lakes and contaminate the ground water [60].

These pesticides can break out from the field where they are applied and trickle into aquatic environments or may also be carried off by wind to other fields, grazing areas, human settlements and undeveloped areas, potentially affecting other species [61]. Other problems associated with synthetic pesticides may arise from poor production, transport and storage practices. The global spread of chemical pesticide including the use of older/obsolete chemical pesticides that have been banned in some jurisdictions. However, they are still in use in some other areas, despite several laws and promulgations to control their application. [62]. There are four major classes of synthetic pesticides, they include: organochlorine pesticides, organophosphorus, carbamates and pyrethroids

a) **Organochlorines**

Organochlorine pesticides are organic compounds attached to five or more atoms of chlorine [63]. They belong to the class of chemicals known as persistent organic pollutants (POPs) due to their high persistence in the environment [64]. Organochlorines have been widely used for the control of malaria and typhus [58] and are mostly used in developing countries due to their low cost [65, 66, 67]. Available statistics shows that over 40% of all pesticides belong to the organochlorines class of chemicals [66, 65]. The most widely known organochlorine pesticide is dichlorodiphenyltrichloroethane (DDT), and they have wide application as insecticides. Asides their use as pesticides, DDT is also used as a solution in certain solvents [68]. Other common examples of organochlorine pesticides include lindane, endosulfan, aldrin, dieldrin, heptachlor, methoxychlor, toxaphene, and chlordaneother [63]. The organochlorine pesticide methoxychlor is commonly applied on fruits, vegetables, trees, home gardens, forage crops, and livestock, with the highest use occurring in the northwest and eastern seaboard states of the USA [69, 70]. Organochlorine pesticides have the ability to enter tissues of organisms through a process called bioaccumulation [71]. When assimilated, organochlorine pesticides could be found in varying concentrations in different tissues, for example higher level of Organochlorine pesticides are accumulated in tissues of the liver and kidney than they are in the muscles due to the lipophiic nature of the muscles [71]. The concentrations of the compounds become higher at elevated trophic levels. For example, concentrations of DDT, DDE, or other organochlorine pesticides may be as minute as parts per billion in water; however, upon contact with animals such as zooplanktons, these organochlorine pesticides become magnified. The zooplanktons are ingested by insects which are in turn consumed by small fish that are ingested by bigger fish, and the cycle goes on. At each step, the concentrations of OCPs increase through biomagnifications. Usually, no harmful effects are noticed initially because of the minute concentrations of OCPs at the lowest trophic level. However, the concentration peaks at the highest trophic levels at which point concentrations may be 10 million times those in water. This process of biomagnifications was quite important in the decline in population observed in many fish-eating raptors in the 1980s and 1990s [71]. The residues from OCPs are widely found in fatty foods of animal origin, such as meat, fish, eggs, and milk, and those of plant origin, such as sesame, corn, rice, oat, olives, vegetable oil, nuts, grapes and lettuce [72].

b) **Organophosphorus pesticides**

These are esters of phosphoric acid widely used as insecticides to control pests that cause damage to crops and food items [64]. They are amongst the most commonly applied pesticides in the world; with about 80 million pounds of organophosphorous pesticides applied in United States alone both for agricultural and residential use [74]. The earliest developed organophosphorous pesticides such as parathion and Tetraethyl pyrophosphate (TEPP) were highly toxic to both humans and animals leading to accidental poisoning in the process of spraying; this led to the subsequent development of less toxic organophosphorous pesticides. However, after repeated use, insects developed resistance to them and this resulted in loss of efficacy. With advanced technologies, about forty organophosphorous pesticides with moderate toxicity have been developed [74]. This group of chemicals are known to be neurotoxic to mature laboratory animals, humans and also neonates in the developmental stages of their nervous system [75].

They carry out their actions through inactivation of the enzyme acetylcholinesterase, which is an essential enzyme that helps in breaking down acetylcholine, a chemical released by certain insects into the intracellular space i.e synapse where nerve and muscle cells are interconnected. The primary function of the acetycholine is the stimulation of the muscle cells which causes it to contract, it is this contraction that is halted by acetylcholinesterase enzymes thereby leading to the destruction of acetylcholine signal molecules and inhibiting nerve function in humans, insects and many other animals [64].

A long term exposure to some organophosphorous insecticides could lead to extended neurological consequences as well as numbness and pain from nerve damage [75]. On exposure to light, air and soil, organophosphorous pesticides chemically deteriorate by hydrolysis at a high rate [75], and are found in surface and groundwater [76] and minute quantities could also be detected in food and drinking water [75]. The most efficient routes of absorption for organophosphates are ingestion and inhalation [74], Phosalone, an organophosphate agent is far less toxic through the dermal route than the oral route with an LD_{50} of 1500mg/kg and 120 mg/kg respectively. Organophosphates are largely believed to be safer and more environmental-friendly than the Organochlorines [77], due to their chemically reactive nature especially under alkaline conditions which makes them persist in the environment only for a short period.

Other pesticides in the organophosphate group include Malathion, parathion and dimethoate [56].

c) **Carbamates**

These are esters of carbamic acid [78] that are similar in structure and mechanisms with the organophosphate insecticides [79]. They are generally refered to as N-methylcarbamates and when properly applied, they significantly help in the control and management of pests that destroy agricultural produces and disease vectors [78]. They are well known for their broad spectrum activity, low persistence and their relatively less toxic effects to mammals when compared to organochlorine [80]. In the drug industry, carbamates have been used in certain medicines for myasthenia gravis; an autoimmune disease that affects postsynaptic elements of the neuromuscular junction, carbamate drugs like physotigmine and pyridostigmine are listed as human drugs, also it is used as a pre-exposure protection in military circles against chemical warfare nerve agents such as sarin and tabun [81]. Residues from carbamates can be found in food (legumes, fruits, contaminated meat, and dairy products), or water as a result of improper handling [81]. Like organophosphates, the mechanism of action of carbamates is also related to the acetylcholine signal molecule in insects and animals. Carbamates cause the inhibition of the enzyme acetylcholinesterase by carbamylation at the neuronal synapses and neuromuscular junctions [79].

The major difference in their mechanism and that of the organophosphates is that they reversibly bind to acetylcholinesterase while organophosphates do not [82, 79]. Animals and humans could be exposed to carbamate insecticides through dermal, inhalation or gastrointestinal routes. Cases of children being poisoned after playing on a field that has been sprayed with carbamates insecticide have been reported [79]. The least toxic route for carbamate exposure is through skin. The oral route of exposure is roughly 24 times more toxic than the dermal route. N-methyl carbamates can be broken down through enzymatic hydrolysis in the liver, and the degradation products are excreted by the kidneys and the liver [74]. In rural Asia there are about 200,000 fatalities resulting from the intentional ingestion of carbamates and organophosphate insecticides while modelling data shows that an estimated 1-2 million cases occur annually with about 20-30% of these developing respiratory failure [83]. Examples of carbamate pesticides include aldicarb, carbofuran, ziram and carbaryl [56].

d) **Pyrethroids**

These are pesticides that belong to a group of artificially synthesized chemicals that imitate the compound pyrethrins, a natural product of the plant *Chrysanthemum cinerariaefolium.* This group comprises esters of chrysanthemum acid (ethyl 2, 2-dimethyl-3-[1-isobutenyl) cyclopropane-1-carboxylate) and halogenated derivatives of their acids and alcohols [84, 85, 86]. The WHO classified Pyrethroids under group four of insecticides [7]. Pyrethroids are divided into type I and II on the basis of the structure of their compounds, the actions or effects they elicit and the kind of symptoms they cause, the use of type I Pyrethroids may cause tremors of the whole body, aggressive behaviour, ataxia and hypersensitivity which are all symptoms of a band of tremor type syndrome (T) [84,85,86]. Type II Pyrethroids on the other hand are known to cause symptoms like salivation which indicates a condition known as choreoathetosis-salivation syndrome (CS) and motor dysfunction in mammals [84, 85, 86].

Generally, pyrethroids carry out their action through interaction with sodium channels and induction of prolonged depolarization in neurons, however both type I and Type II have specific mode through which they elicit their actions, while type I Pyrethroids act by changing the conformation of the sodium channels when neuronal membranes open or close [84,85,86], type II Pyrethroids affect chloride channels including the GABA- dependent ones [84,85,86 82, 87]. Pyrethroids are generally toxic to a variety of organisms including higher animals like Man [84], insects [84] and acquatic animals [88, 89]. Their toxicity in insects is far more pronounced (up to 2250 times) than in higher animals [84] and this is because insects have more sensitive sodium channels, a smaller structure and lower body temperature [84].

Additionally, pyrethroids affect the ion channels in neuronal membranes and mitochondrial membranes of the aforementioned acquatic animals [88, 89]. Prominent members of the Pyrethroids group widely used as synthetic pesticides include permethrin (belonging to class I), deltamethrin (class II) and α-cypermethrin (class II) [90] and these three were recommended for domestic insect control as they were considered to be relatively non-toxic to humans in all stages of life. However, new details have emerged that these compounds are not completely safe to human health. Researchers have also suggested that permethrin may adversely affect fertility by causing considerable harm to the reproductive system [90]. Other metabolic systems adversely affected by permethrin include the immune system, cardiovascular and hepatic metabolism as well as enzymatic activity. Asides permethrin, deltamethrin has also been reported to induce inflammation, nephro- and hepatotoxicity and influence the activity of antioxidant enzymes in tissues while alpha-cypermethrin may impair immunity and increase glucose and

lipid levels in blood [90].

3.0 Comparative analysis of chemical and biopesticides use

The uncontrolled applications of synthetic pesticides have had serious health implications on man [56]. Studies have shown that DDT and its metabolite p,p-dichlorodiphenyldichloroethylene (DDE) may have endocrine-disrupting potential and carcinogenic effect [91]. It has also been established that exposure to both DDT and DDE caused neuro-developmental effects in children [92]. Rodríguez-Alcalá et al. [93] reported that a link exists between exposure to DDE and hepatic lipid dysfunction in rats. Organochlorine pesticides have been associated with defects related to several biochemical processes thereby leading to issues with several processes that involve endocrine system [94, 95], embryonic development [96], lipid metabolism [97], and haematological and hepatic functions [98].

Synthetic pesticides are implicated in a range of impacts on human health due to pollution. Pesticides can enter the body through inhalation of aerosols, dust, vapour and oral exposure by consuming food/water; and through skin exposure by direct contact. Synthetic pesticides secrete into soils and groundwater which can end up in water meant for domestic consumption, and into the atmosphere resulting in air pollution [91]. The effects of synthetic pesticides on human health depend on the toxicity of the chemical and the length and magnitude of exposure. Farm workers and their families experience the greatest exposure to agricultural synthetic pesticides through direct contact [99].

Children are more susceptible and sensitive to the adverse effect of these pesticides, because they are still developing and as such have a less formidable immune system when compared to adults. Also, as a result of their proximity to the ground, Children especially toddlers may be more exposed due to their tendency to put stray objects in their mouth. Children under the ages of six months are more likely to experience exposure from breast milk and inhalation of small particles. The chemicals can bioaccumulate in the body over time [100].

Exposure to synthetic pesticides may lead to several deleterious effects which may be as mild as a light skin irritation or as severe as serious birth defects, tumors, genetic changes, blood and nerve disorders, endocrine disruption, coma or death [101]. Developmental defects have also been associated with pesticide exposure. Recent increases in childhood cancers throughout North America, such as leukemia, may be a result of somatic cell mutations induced by the inhalation of synthetic pesticicdes [10]. Synthetic Insecticides targeted to disrupt insects can have harmful effects on mammalian nervous systems [10]. Both chronic and acute alterations have been observed in exposés. DDT and its breakdown product DDE disturb estrogenic activity and could possibly lead to breast cancer. Foetal DDT exposure could lead to a marked reduction in the size of the male penis in animals and can produce undecided testicles in infants. Synthetic pesticide can also affect foetuses in early stages of development; in utero and in parents exposed before conception [10] Reproductive disruption has the potential to occur by chemical reactivity and through structural changes [10].

Synthetic pesticide residues have been detected in streams, rivers, rain and groundwater. Water bodies contaminated by chemical pesticides could have harmful effects on fish and other aquatic biota sometimes leading to the extermination of all the fish in a particular stream [102]. Herbicides such as copper sulfite that are applied to water to kill plants are toxic to fishes and other water animals at concentrations similar to those used to kill the plants. Several decades back, amphibian populations had declined across the world, for unexplained reasons which are thought to be varied but of which synthetic pesticides may have played a part [102].

Again, the extensive use of synthetic pesticides in agricultural production could lead to massive degradation that would subsequently damage the community of microorganisms inhabiting the soil, particularly when these chemicals are abused either through misuse or overuse. The effect of pesticides on soil microorganisms is determined by the persistence, concentration, and toxicity of the applied pesticide, as well as several other environmental factors. Many of the chemicals used in pesticide development are persistent soil contaminants, whose effect may be felt for decades [103]. Degradation and sorption are factors which influence the persistence of synthetic pesticides in soil. Sorption affects bioaccumulation of pesticides which are dependent on organic matter in the soil. Weak organic acids have been shown to be weakly sorbed by soil. Sorbed chemicals have been shown to be less accessible to microorganisms [104]. Nitrogen fixation, which is required for the growth of higher plants, is hindered by most synthetic pesticides. The insecticides DDT, methyl parathion, and pentachlorophenol have been shown to interfere with legume-rhizobium chemical signaling. Reduction of these symbiotic chemical signaling lead to a reduction in nitrogen fixation and thus reduced crop yields [105]. Synthetic pesticides have been implicated in the decline of pollinators due to their capability to exterminate a large population of bees when they are applied to crops that are in bloom and this can have a grave effect on the environment and the conservation of the ecosystem [106]. They also have some direct harmful effects on plants including poor root hair development, shoot yellowing and reduced plant growth [107].

Chemical/synthetic pesticides can contribute to air pollution as a result of pesticide drift which could occur when pesticides suspended in the air as particles are carried by wind to other areas, thereby potentially contaminating them. Pesticides that are applied to crops can volatilize and may be blown by winds into nearby areas, potentially posing a threat to wildlife. Weather conditions at the time of application as well as temperature and relative humidity could affect the spread of pesticide in the air [106].

Reduction in bird populations has been found to be associated with times and areas in which chemical pesticides were used. DDE-induced egg shell thinning has especially affected European and North American bird populations. In another report, some types of fungicides used in peanut farming were slightly toxic to birds and mammals, this is however far better that the deleterious consequences of synthetic pesticides [91].

Some researchers carried out a study comparing the efficacy of some synthetic pesticides; Bifinthrine, abamectine and Lambda cahaloyhrine with a botanical oil and neem seed oil on cabbage white butterfly under field conditions, they concluded in their study that the Neem oil extract provided a better protection to the cabbage both when applied alone and when used as an insecticide-botanical combination regimen [108].

Fishes are common bio-indicators of pollution and they are usually affected by pesticides which pollute water bodies through accidental run off. In a study carried out to compare the toxicity of a synthetic pesticide, dichlorvos and a neem based pesticide on fishes, it was observed that fishes exposed to the synthetic pesticides showed more severe changes in behavioural patterns which include irregular erratic and darting swimming movements and loss of equilibrium and they gradually became lethargic, hyper excited, restless and secreted excess mucus all over their bodies prior to their mortality, Neem based pesticides were less toxic while dichlorvos were very dangerous to aquatic animals [109].

In another study carried out by another researcher, the comparative efficacies of some botanicals (neem seed crude extract and *eucalyptus* leaves extract) and a synthetic pesticide; cypermethrin were evaluated against major insect pests of cabbage. The result showed that both the synthetic and botanical pesticides under study were effective against the cabbage insect pests but cypermethrin had higher efficacy than neem and eucalyptus extracts [110]. It must however be emphasized that this study only considered the efficacy of the pesticides and not the safety., According to a research by Kumar [111].

Ugandan farmers believed that synthetic pesticides showed a greater efficacy in comparison with botanical pesticides. In a study to compare the efficacy of plant derived and synthetic insecticides against cabbage aphid, Brevicoryne brassicae (L.) (Homoptera: Aphididae), it was concluded that the plant derived pesticides reduced the aphid populations equally to conventional insecticides and could be used as an alternative component for the integrated pest management (IPM) of cabbage aphid, *Brevicoryne brassicae* [112].

Biswas [113] compared the effectiveness of neem extracts and synthetic organic insecticide against mustard aphid, he observed that Both the Neem and sytnthetic pesticides under study reduced the population of aphid, though the synthetic pesticide achived a greater reduction in aphid population [94%) when compared to the neem extracts [81%), he however concluded that the use of neem extract is an eco-friendly management tactics of aphid which is cheaper and safer for pollinators and natural enemies, especially coccinellid predators attacking aphids and also safe for the environment.

3.1 Future perspective

The population of the world is growing at an unprecedented rate and this has continued to pose a great challenge to people in the agricultural value chain as they continue to devise several methods to ensure food production meets up with ever growing population. At the heart of attaining increase in food production are efforts that ensure that wastages in food production are brought to the barest minimum, and this is where pest management comes in [106].

The current review has taken an extensive look at the different classes of pesticides, including the pros and cons of each class. Going forward, the usage of biopesticides is highly recommended to farmers as studies adjudge them to be safer to the crops, environment and even the health of the farmers. Also future strategies in curbing the menace of crop pests should involve integrated pest management which involves series of techniques that can subdue the menace of pests while at the same time causing minimum disturbance to the agro-ecosystem. The end goal of integrated pest management is to ensure that chemicals which may be potential pollutants and farming practices like tillage operations which could cause soil erosion, are used in such a way that does not impact soil and water negatively [105].

Nanotechnology is an emerging and promising field which has found immense application in the science and technology sector including the agriculture sector, this technology is poised to revolutionize the way biopesticides are employed in the nearest future. Currently, it is used in the development of nonporous zeolites which are used to deliver doses of water and fertiliser in a slow but efficient manner. Nanotechnology is also very useful in the development of nanocapsules for delivery of herbicides as well as nanosensors for pest detetction. One of the challenges associated with biopesticides is that they quickly degrade after being applied (partly due to environmental factors) sometimes before even reaching the target, however with the development of nanoparticles in the form of pesticides, biopesticides can be properly absorbed into target plants unlike in the case with larger particles. It is important that future studies on nanoparticles and insect control, concentrate on formulation and production of more rapid and eco-friendly pesticides that could be delivered into the target host tissue using encapsulation.

Though a number of studies have been carried out on the formulation, efficacy and safety of different classes of biopesticides, there are still not enough comparative studies x-raying side by side the effects and safety of biopesticides to that of synthetic pesticides hence a need for more studies in that direction. There is a growing need to support (by way of funding and enactment of laws) the development, formulation and commercialization of biopesticides by government through research agencies and educational institutions, it is also important to have a public-private collaboration geared towards the improvement, manufacturing and commercialization of environmentally friendly alternatives to chemical pesticides [109]. Another challenge that must be addressed is the difficulty in getting needed raw materials thereby hampering commercialization efforts and leading to high cost of production. There is a need to develop strict regulatory mechanisms that will lead to marked reduction in prices of biopesticides, to make them affordable to rural farmers in developing countries [109]. There is also need to incorporate studies related to pesticides development, safety and formulation into academic curriculum of tertiary institutions across the globe with the aim of deepening the knowledge and research about biopesticide.

4.0 Conclusion

Food stands out as one of the greatest need of man; however, there is a potential threat of food insecurity occasioned by the damaging effects of pests on crops. To combat this, researchers across the world have developed various kinds of pesticides from natural and synthetic sources. Synthetic pesticides are the most ubiquitous commercially as well as the most employed in the field of agriculture, perhaps due to the fact that they had an already established market prior to the introduction of biopesticides, also some available comparative studies on the efficacy of natural and synthetic pesticides have shown that synthetic pesticides have better efficacy within a shorter time when compared with natural pesticides.

These synthetic pesticides however, have grave consequences on the environment as revealed by several studies reviewed in the present review due to their persistence in the atmosphere, which can cause long lasting negative effects. Some of the deleterious effects of chemical pesticides are their ability to cause serious metabolic disorders in man, pollution of aquatic life which leads to contamination of water, indiscriminate elimination of useful organisms of plant, microbial and animal origin as a result of poor precision in targeting of pest, and loss of effectiveness over time due to pest resistance. Biopesticides on the other hand, are safe, effective and less damaging to the environment. They work effectively against dangerous pests and remain effective long after they have been introduced to the environment. Despite the growing interest in the development and use of biopesticides, its application is still limited when compared with synthetic pesticides, and this is because there are still various issues *inter alia* relating to high cost of production when manufactured on an industrial scale, regulatory deficiencies, poor storage stability and susceptibility to environmental factors. The good news is that these setbacks are being surmounted by improved and advanced technologies. Hopefully in the near future, more advanced and effective biopesticide will be developed and used as much as the synthetic pesticides.

Authors' contributions: This work was carried out as a collaboration between all authors. All authors read and approved the final manuscript.

Funding source: No funding

Ethical approval: Not Applicable

Competing interests: Authors have declared that no competing interests exist

References

1) Abate, T., Van-Huis, A and Ampofo, J.K.O (2000). Pest Management Strategies in Traditional Agriculture: An African Perspective, Annual Review of Entomology, 45(1):631-59

2) Othmer, K. (1996). Encyclopedia of Chemical Technology, John Wiley and Sons Inc. New York, USA

3) Dzugan, S. A.; Rozakis, G. W.; Dzugan, K. S.; Emhof, L; Dzugan, S. S.; Xydas, C; Michaelides, C; Chene, J; Medvedovsky, M (2011). "Correction of steroidopenia as a new method of hypercholesterolemia treatment". Neuro endocrinology letters. 32 (1): 77–81.

4) Damalas, C. A and Eleftherohorinos, I. G. (2011). "Pesticide Exposure, Safety Issues, and Risk Assessment Indicators". International

Journal of Environmental Research and Public Health. 8 (12): 1402-19.

5) Keneth, M. (1992). The DDT Story, The British Crop Protection Council, London, UK Carson, R. L. (1962).

6) United Nations Environment Programme, 2002

7) WHO (2016). Pesticide Residues in Food. http://www.who.int/feature/9a/87/en. Accessed on 12th September, 2021.

8) Henk, V.D.B (2009). Global Status of DDT and Its Alternatives for Use in Vector Control to Prevent Disease, Environmental health perspectives, 117(11): 1656–1663.

9) EPA (2021). Ingredients Used in Pesticide Products: Pesticides. What Are Biopesticides? Available online: https://www.epa.gov/ ingredients-used-pesticide-products/what-are-biopesticides (accessed on 15 july 2021).

10) Freemark, K. (1995). "Impacts of agricultural herbicide use on terrestrial wildlife in temperate landscapes: A review with special reference to North America". Agriculture, Ecosystems & Environment. 52 (2–3): 67– 91.

11) Lacey L. A and Siegel J. P. (2000). Safety and ecotoxicology of entomopathogenic bacteria. In Entomopathogenic bacteria: from laboratory to field application (eds Charles J. F., Delecluse A., Nielsen-LeRoux C.), pp. 253–273 Dordrecht, The Netherlands: Kluwer Academic Press

12) Essiedu, J.A.; Adepoju, F.O.; Ivantsova, M.N.(2020) Benefits and limitations in using biopesticides: A review. In Proceedings of the VII International Young Researchers' Conference—Physics, Technology, Innovations (PTI-2020), Ekaterinburg, Russia, 18–22 May 2020; Volume 2313, p. 080002.

13) Mazid, S. (2011) Review on the Use of Biopesticides in Insect Pest Management. International Journal of Science and Advanced Technology, 1, 169-178.

14) Sporleder, M.and Lacey, L.A(2021). Biopesticides. In Insect Pests of Potato; Alyokhin, A., Vincent, C., Giordanengo, P., Eds.; Elsevier: Oxford, UK, 2021; pp. 463–497.El-Sayed AM. The Pherobase: database of pheromones and semiochemicals. http://www.pherobase.com. Accessed 10 September 2021.

15) El-Sayed A.M (2021)The Pherobase: Database of Pheromones and Semiochemicals. ((accessed on 19 January 2021)); Available online: https://www.pherobase.com.

16) Laurent P, and Frérot B (2007) Monitoring of European corn borer with pheromone-baited traps: review of trapping system basics and remaining problems. Journal for Economic Entomology 100:1797–1807

17) Witzgall P, Kirsch P, Cork A.(2010). Sex pheromones and their impact on pest management. Journal of Chemical Ecology. 2; 36:80- 100.

18) Gurr, G.M.; Thwaite, W.G.; Nicol, H.I (1999). Field evaluation of the effects of the insect growth regulator (tebufenozide) on entomophagous arthropods and pests of apples. Australian Journal of Entomology, 38, 135–140.

19) Gwinn, K.D (2018). Bioactive Natural Products in Plant Disease Control. In Studies in Natural Products Chemistry; Attaur, R., Ed.; Elsevier Inc.: Amsterdam, The Netherlands; 5:.229–246.

20) Gelernter W and Schwab GE (1993) Transgenic bacteria, viruses, algae and other microorganisms as Bacillus thuringiensis toxin delivery systems. In: Entwistle PF, Cory JS, Bailey MJ, Higgs S (eds) Bacillus thuringi-ensis, an environmental biopesticide: theory and prac-tice. Wiley, Chichester, pp 89–124

21) Revathi K, Chandrasekaran R, Thanigaivel A, Kirubakaran SA, Sathish-Narayanan S, and Senthil-Nathan S (2013) Effects of Bacillus subtilis metabolites on larval Aedes aegypti L. Pesticides Biochemistry and Physiology 107:369–376

22) Carlton, B.C (1993) Genetics of Bt insecticidal crystal proteins and strategies for the construction of improved strains. In: Duke SO, Menn JJ, Plimmer JR (eds), Pest control with enhanced environmental safety. ACS symposium series 524, American Chemical Society, Washington, DC. pp 326–337

23) Copping, LG and Menn, JJ (2000) Biopesticides: a review of their action, applications and efficacy. Pest Management Science 56:651–676

24) Betz, FS., Hammond BG and Fuchs, RL (2000) Safety and advantages of Bacillus thuringiensis -protected plants to control insect pests. Regulatory Toxicology and Pharmacology 32:156–173

25) Zhu Y-C, Kramer K.J, Oppert B, Dowdy A.K (2000) cDNAs of aminopeptidase-like protein genes from Plodia interpunctella strains with different suscepti-bilities to Bacillus thuringiensis toxins. Insect Biochemistry and Molecular Biology 30:215–224

26) Darboux, I., Nielsen-LeRoux C, Charles J-F, Pauron D (2001) The receptor of Bacillus phaericus binary toxin in Culex pipiens (Diptera: Culicidae) midgut: molecular cloning and expression. Biochemistry and Molecular Biology 31:981–990

27) Gray EJ, Lee KD, Souleimanov AM, Di Falco MR, Zhou X, Ly A, Charles TC, Driscoll BT, Smith DL (2006) A novel bacteriocin, thuricin 17, produced by plant growth promoting rhizobacteria strain Bacillus thuringiensis NEB17: isolation and classification. Journal of Applied Microbiology 100:545–554

28) Sharma, C., Vas, A. J., Goala, P., Gheewala, T. M., Rizvi, T. A., and Hussain, A. (2014). Ethanolic neem (Azadirachta indica) leaf extract prevents growth of MCF-7 and HeLa cells and potentiates the therapeutic index of cisplatin. Journal of Oncology. 2014:321754. doi: 10.1155/2014/321754

29) Schünemann, R., Knaak, N and Mariana F and, "Mode of Action and Specificity of Bacillus thuringiensis Toxins in the Control of Caterpillars and Stink Bugs in Soybean Culture", International Scholarly Research Notices, vol. 2014, Article ID 135675, 12 pages, 2014. https://doi.org/10.1155/2014/135675

30) Faria MR and Magalhães BP (2001) O uso de fungos entomopatogênicos no Brasil. Biotecnology Cienc Desenvolvimento 22:18–21

31) Roberts DW and St Leger RJ (2004) Metarhizium spp., cosmopolitan insect-pathogenic fungi: mycological aspects. Advanced Applied Microbiology 54:1–70

32) Mnyone, L.L., Koenraadt, C.J.M., Lyimo, I.N. et al. Anopheline and culicine mosquitoes are not repelled by surfaces treated with the entomopathogenic fungi Metarhizium anisopliae and Beauveria bassiana. Parasites and Vectors 3, 80 (2010). https://doi.org/10.1186/1756-3305-3-80

33) Domsch, KH, Gams, W and Anderson, TH (1980) Compendium of soil fungi. Academic, London, pp 413–415

34) Zimmermann G (1993) The entomopathogenic fungus Metarhizium anisopliae and its potential as a biocon-trol agent. Pesticides Management Science 37:375–379

35) Butt, TM., Jackson, CW and Magan, N (2001a) Fungi as bio-control agents: progress, problems and potential. CAB International, Wallingford Pp 390

36) Nakai, M and Lacey LA (2017) Microbial Control of Insect Pests of Tea and Coffee,,Microbial Control of Insect and Mite Pests, Chapter 15 Editor(s): Lawrence A. Lacey Academic Press, Pages 223-235,ISBN 9780128035276,https://doi.org/10.1016/B978-0-12-803527-6.00015-9.(https://www.sciencedirect.com/science/article/pii/B9780128035276000159)

37) Moscardi F (1999) Assesment of the application of Baculoviruses for control of Lepidotera, Annual review of entomology, 44(257-264)

38) Senthil-Nathan S (2015) A Review of Biopesticides and Their Mode of Action Against Insect Pest DOI:10.1007/978-81-322-2056-5_3

39) Cory, JS (2000) Assessing the risks of releasing genetically modified virus insecticides: progress to date. Crop Protection 19:779–785

40) Barber, KN, Kaupp, WJ, Holmes, SB (1993) Specificity testing of the nuclear polyhedrosis virus of the gypsy moth, Lymantria dispar (L.) (Lepidoptera: Lymantriidae). Canadian Entomology 125:1055–1066

41) Cory. JS, Hirst, ML, Sterling PH and Speight MR (2000) Native host range nucleopolyhedric virus

for control of the browntail moth (Lepidoptera: Lymantriidae). Environmental Entomology 29:661–667

42) Arthurs SP and Lacey LA (2004) Field evaluation of commercial formulations of the codling moth granulovirus: persistence of activity and success of seasonal applications against natural infestations of codling moth in Pacific Northwest apple orchards. Biological Control 31:388–397

43) Arthurs SP, Lacey LA, Fritts R Jr (2005) Optimizing use of codling moth granulovirus: effects of application rate and spraying frequency on control of codling moth larvae in Pacific Northwest apple orchards. Journal of Economical Entomology 98:1459–1468

44) Magierowicz, K.; Górska-Drabik, E.; Golan, K. (2020) Effects of plant extracts and essential oils on the Inc.behavior of Acrobasis advenella (Zinck.) caterpillars and females. J. Plant Dis. Prot., 127, 63–71

45) Ali, M.A., Doaa, S.M., El-Sayed, H.S., Asmaa, M.E (2017) Antifeedant activity and some biochemical effects of garlic and lemon essential oils on Spodoptera littoralis (Boisduval) (Lepidoptera: Noctuidae). Journal of Entomology Zoology., 5, 1476–1482.

46) Halder, J.; Rai, A.B.; Kodandaram, M.H (2013) Compatibility of Neem Oil and Different Entomopathogens for the Management of Major Vegetable Sucking Pests. Natl. Acad. Sci. Lett., 36, 19–25.

47) Tripathi, A.K.; Upadhyay, S.; Bhuiyan, M.; Bhattacharya, P.R (2009). A review on prospects of essential oils as biopesticide in insect-pest management. Journal of . Pharmacognosy and Phytotherapy., 1, 52–63.

48) Kumar, J.; Ramlal, A.; Mallick, D.; Mishra, V. (2021). An Overview of Some Biopesticides and Their Importance in Plant Protection for Commercial Acceptance. Plants, 10, 1185. https://doi.org/10.3390/ plants10061185

49) Mordue, A.J.; Morgan, E.D.; Nisbet, A.J. Azadirachtin (2005) a Natural Product in Insect Control. In Comprehensive Molecular Insect Science; Gilbert, L.I., Ed.; Elsevier: Amsterdam, The Netherlands, pp. 117–135.

50) Nwanko E.N., Okonkwo, N.J., Ogbonna, C.U., Akpom C.JO., Egbuche, C.M and Ukonze, B.C (2015). Moringa Oleifera and Annona Muricata seed oilextract seed oilextracts as biopesticidesagainst the second and fourth larval instar of Aedes aegypti L. (Diptera; Culicadae). Journal of Biopesticides, 8(1):56-61

51) Okonkwo, C.O and Ohaeri, O.C (2018). Insecticidal Efficacy and Chemical Composition of Hexane Oil Extracts from the Leaves of Euphorbia milii and Cassia occidentalis. international Journal of Biochemistry Research & Review, Page 1-11

52) Chukwunonso O. N, Kingsley C. E, and Nnaemeka J. O (2020). insecticidal activity of piper guineense (schumach and thonn) seed oil against callosobruchus maculatus (f.) (coleoptera: chrysomelidae) in stored cowpea seeds. International Journal of Research - GRANTHAALAYAH, 8(8), 262-270. https://doi.org/10.29121/granthaalayah.v8.i8.2020.875

53) Ekeh, F.N., Odo, G.E., Nzei,J., Ngozi E., Ohanu, C. and Onuoha O (2018) Efficacy of Xylopia aethiopica ethanolic and aqueous extracts on the control of sitophilus oryzae in stored rice grain African Journal of Agricultural Research. 13(10):470-476,

54) Ukoroije B.R, Abowei, J.F.N and Otayoor, R.A (2018) Efficacy of Azadirachta indica Leaf Powder and Ethanol Extract on Adult Periplanata americana under Laboratory Condition. Open Access Library Journal, 5: e4458. https://doi.org/10.4236/oalib.1104458

55) Parween, T.; Jan, S. (2019) Pesticides and environmental ecology. In Ecophysiology of Pesticides; Parween, T., Jan, S., Eds.; Academic Press: Cambridge, MA, USA; pp. 1–38.

56) Nicolopoulou-Stamati, P.; Maipas, S.; Kotampasi, C.; Stamatis, P.and Hens, L (2016) Chemical Pesticides and Human Health: The Urgent Need for a New Concept in Agriculture. Front. Public Health, 4, 148.

57) Hoffman RS, Capel PD, Larson SJ (2000). Comparison of pesticides in eight U.S. urban streams. Environmental Toxicology and Chemistry (2000) 19:2249–58. doi:10.1002/etc.5620190915

58) Aktar M.W., Sengupta, D and Chowdury, A. (2009). Impact of pesticides use in agriculture: their benefits and hazards, Interdisciplinary Toxicology.; 2(1): 1–12.Published online 2009 Mar. doi: 10.2478/v10102-009-0001-7

59) Palmer, WE, Bromley, PT, and Brandenburg, RL (2007). Wildlife & pesticides - Peanuts. North Carolina Cooperative Extension Service. Retrieved on 2007-10-11.

60) WHO. Geneva: World Health Organization; (1990). Public Health Impact of Pesticides Used in Agriculture; p. 88.

61) Singh B and Mandal K (2013) Environmental impact of pesticides belonging to newer chemistry. In: Dhawan AK, Singh B, Brar-Bhullar M, Arora R (eds.). Integrated pest management. Scientific Publishers, Jodhpur, India;. p152-190.

62) Lamberth, C., Jeanmart, S., Lucksh, T and Plant, A (2013). Current challenges and trends in the discovery of agrochemicals, Science 341(6147):742-6DOI:10.1126.

63) Yusuf, A., Habibu, T., Chuckwuebuka, E., Charles, O.A., Smriti, K., Toske, L.K., Jonathan, C.I and Kingsley, C.P.I (2020). Natural remedies for pests, disease and weed control, Academic Press,pp 29-42,

64) Ravindran, J., Pankajshan, M and Puthur, S (2016). Organochlorine pesticides, their toxic effects on living organisms and their fate in the environment, interdisciplinary Toxicology ; 9(3-4): 90–100.Published online 2017 May 17.

65) FAO. (2005) Proceedings of the Asia Regional Workshop. Bangkok: Regional Office for Asia and the Pacific.

66) Gupta PK. (2004) Pesticide exposure Indian scene. Toxicology. 198:83–90.

67) Lallas P.(2001) Reproductive Effects in Birds Exposed to Pesticides and Industrial Chemicals. The Stockholm Convention on persistent organic pollutants. American Journal of International Law. 95:692–708.

68) Alewu, B and Nosiri, C (2011) Pesticides and human health. In: Stoytcheva M, editor. Pesticides in the Modern World – Effects of Pesticides Exposure. InTech (2011). p. 231–50. Available from: http://www.intechopen.com/books/pesticides-in-the-modern-world-effects-of-pesticides-exposure/pesticide-and-human-health

69) Fry DM.(1995) Reproductive effects in birds exposed to pesticides and industrial chemicals. Environmental Health Perspectives. ;103(Suppl 7):165–171.

70) Ottinger, M. A., Abdelnabi, M., Quinn, M., Golden, N., Wu, J., and Thompson, N. (2002). Reproductive consequences of EDCs in birds What do laboratory effects mean in field species? Neurotoxicol. Teratol. 24, 17–28. doi: 10.1016/S0892-0362(01)00195-7

71) Donald, W.S (2016) Organochlorine Pesticides, Ecotoxicology Essentials, Academic Press, pp 69-107, ISBN 9780128019474, https://doi.org/10.1016/B978-0-12-801947-4.000044.(https://www.sciencedirect.com/science/article/pii/B9780128019474000044)

72) Benbrook, C.M (2002). Organochlorine residues pose surprisingly high dietary risks, Journal of Epidemiology community health 56(11):822-3. doi: 10.1136/jech.56.11.822

73) Amir, M (2019) Prenatal Exposure to Industrial Chemicals and Pesticides and effects on Neurodevelopment. Encyclopedia of Environmental Health, Pages 648-658 and Beauveria bassiana . Parasite Vectors 3:80

74) Sakata M. (2005) Organophosphorus pesticides. In: Drugs and Poisons in Humans. Springer, Berlin, Heidelberg. https://doi.org/10.1007/3-540-27579-7_60

75) Lori, L and Heather, M.B (2019) Organophosphate Insecticides: Neurodevelopmental Effects Encyclopedia of Environmental Health, 2011, Pages 283-290

76) Huang, F., Li, Z.,and Zhang, C. (2019). Pesticides in the typical agricultural groundwater in Songnen plain, northeast China: occurrence, spatial distribution and health risks. Environmental Geochemistry and Health 41, 2681–2695.

77) Jaga, K and Dharmani, C (2006). Ocular toxicity from pesticide exposure: A recent review

Environmental Health and Preventive Medicine 11(3):102-7

78) Gupta R.C (2014) Carbamates Pesticides Encyclopedia of Toxicology (Third Edition), Pages 661-664 https://doi.org/10.1016/B978-0-12-386454-3.00106-8.

79) Silberman J and Taylor A. Carbamate Toxicity. (2021) . In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 29489157

80) Pogacnik L and Franko M (2003). Detection of organophosphate and carbamate pesticides in vegetable samples by a photothermal biosensor. Biosens Bioelectron.;18(1):1-9. doi: 10.1016/s0956-5663(02)00056-8. PMID: 12445439.

81) Dias, E., Costa,F.G., Morais,S and Pereira M.L (2015). A Review on the Assessment of the Potential Adverse Health Impacts of Carbamate Pesticides, Topics in Public Health, David Claborn, IntechOpen, DOI: 10.5772/59613. Available from: https://www.intechopen.com/chapters/48017

82) Goel A, and Aggarwal P.(2007) Pesticide Poisoning. The National Medical Journal of India. ;20:182–191.

83) Patel, S and Sangeeta, S (2019) Pesticides as the drivers of neuropsychotic diseases, cancers, and teratogenicity among agro-workers as well as general public Environmental Science and Pollution Research 26(1) DOI:10.1007/s11356-018-3642-2.

84) Bradberry, S.M., Cage, S.A., Proudfoot A.T and Vale, J.A. (2005). Poisoning due to pyrethroids. Toxicological. Review. 24:93–106. doi: 10.2165/00139709-200524020-0000

85) Costa L.G.(2015) The neurotoxicity of organochlorine and pyrethroid pesticides. Handbook of Clinical Neurology. 2015;131:135–148

86) Soderlund D.M (2012) Molecular mechanisms of pyrethroid insecticide neurotoxicity: Recent Advances. Archives of Toxicology. 2012;86:165–181. doi: 10.1007/s00204-011-0726-x

87) Singh A.K., Tiwari M.N., Prakash O., Singh M.P (2012) A current review of cypermethrin-induced neurotoxicity and nigrostriatal dopaminergic neurodegeneration. Current Neuropharmacology. ;10:64–71. doi: 10.2174/157015912799362779.

88) Cárcamo J.G., Aguilar M.N., Carreño C.F., Vera T., Arias-Darraz L., Figueroa J.E., Romero A.P., Alvarez M., Yañez A.J. (2017). Consecutive emamectin benzoate and deltamethrin treatments affect the expressions and activities of detoxification enzymes in the rainbow trout (Oncorhynchus mykiss) Comparative Biochemistry and. Physiology;191:129–137. doi: 10.1016/j.cbpc.2016.10.004.

89) Toynton K., Luukinen B., Buhl K., Stone D.(2009) Permethrin Technical Fact Sheet. National Pesticide Information Center, Oregon State University Extension Services; Baker City, OR, USA

90) Chrustek A, Hołyńska-Iwan I, Dziembowska I, Bogusiewicz J, Wróblewski M, Cwynar A, Olszewska-Słonina D (2018) Current Research on the Safety of Pyrethroids Used as Insecticides. Medicina (Kaunas).;54(4):61. doi: 10.3390/medicina54040061. PMID: 30344292; PMCID: PMC6174339

91) Turusov, V; Rakitsky, V; Tomatis, L (2002). "Dichlorodiphenyltrichloroethane (DDT): Ubiquity, persistence, and risks". Environmental Health Perspectives. 110 (2): 125–8.

92) Eskenazi B, Marks AR, Bradman A, Fenster L, Johnson C, Barr DB (2006). In utero exposure to dichlorodiphenyltrichloroethane (DDT) and dichlorodiphenyldichloroethylene (DDE) and neurodevelopment among young Mexican American children. Pediatrics 118:233–41. doi:10.1542/peds.2005-3117

93) Rodríguez-Alcalá LM, Sá C, Pimentel LL, Pestana D, Teixeira D, Faria A, (2015). Endocrine disruptor DDE associated with a high-fat diet enhances the impairment of liver fatty acid composition in rats. Journal of Agriculture and Food Chemistry, 63:9341–8.10.1021/acs.jafc.5b03274

94) Lemaire, G, Terouanne B, Mauvais P, Michel S, Rahman R. (2004). Effect of organochlorine pesticides on human androgen receptor activation in vitro. Toxicology and Applied

Pharmacology 196:235–46. doi:10.1016/j.taap.2003.12.011

95) Mnif W, Hassine AIH, Bouaziz A, Bartegi A, Thomas O and Roig B (2011). Effect of endocrine disruptor pesticides: a review. International Journal of Environmental Research and Public Health 8:2265–2203. doi:10.3390/ijerph8062265

96) Tiemann U. (2008) In vivo and in vitro effects of the organochlorine pesticides DDT, TCPM, methoxychlor, and lindane on the female reproductive tract of mammals: a review. Reproductive Toxicology 25:316–26. doi:10.1016/j.reprotox.2008.03.002

97) Karami-Mohajeri S, and Abdollahi M (2011). Toxic influence of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates: a systematic review. Human and Experimental Toxicology 30(9):1119–40. doi:10.1177/0960327110388959

98) Freire C, Koifman RJ, Koifman S.(2015) Hematological and hepatic alterations in Brazilian population heavily exposed to organochlorine pesticides. Journal of Toxicology and Environmental Health 78:534–48. doi:10.1080/15287394.2014.999396

99) Rattner, B. A. (2009). "History of wildlife toxicology". Ecotoxicology. 18 (7): 773–783.

100) Kohler, H.R and Triebskorn, R. (2013). Wildlife Ecotoxicology of pesticides: can we track effects to the population level and beyond? Science, 341(6147):759-765.

101) Schug, TT, Janesick, A, Blumberg, B and Heindel, JJ (2011). Endocrine disrupting chemicals and disease susceptibility. Journal of Steroid Biochemistry and Molecular Biology. 127:204–15.

102) Crain. DA, and Guillette LJ Jr (1998). Reptiles as models of contaminant-induced endocrine disruption. Animal Reproduction Science.;53(1-4):77-86. doi: 10.1016/s0378-4320(98)00128-6.

103) Cresswell, J E and Thompson, H M(2012). Comment on "A common pesticide decreases foraging success and survival in honey bees". Science 337:1453.

104) Galloway T.S, Depledge M.H (2001). Immunotoxicity in invertebrates: measurement and ecotoxicological relevance. Ecotoxicology, 10(1):5-23. doi: 10.1023/a:1008939520263.

105) Papendick, RI; Elliott, LF; Dahlgren, RB (1986). "Environmental consequences of modern production agriculture: How can alternative agriculture address these issues and concerns?". American Journal of Alternative Agriculture. 1 (1): 3–10.

106) Henry, M.; Beguin, M.; Requier, F.; Rollin, O.; Odoux, J. -F.; Aupinel, P.; Aptel, J.; Tchamitchian, S.; Decourtye, A. (2012). "A Common Pesticide Decreases Foraging Success and Survival in Honey Bees". Science. 336 (6079): 348– 350.

107) Hellar, H. (2002). The Green Revolution for Wheat in Developing Countries, US Department of Agriculture, USA.

108) Kanwal, A., Ahmad, M., Khurshid, I., Khan, M., Khan, S., Ullah, I., Khan, F., Shahid, M., Bashir, S. and Rukh, M. (2021) Comparison of Efficacy of Synthetic Pesticides with Botanical Extracts under Field Condition on Cabbage White Butterfly (Pieris brassicae). Advances in Entomology, 9, 44-48. doi: 10.4236/ae.2021.91004.

109) Bhat, B.A., Bhat, I.A., Vishwakarma,S ., Verma,A and Saxena,G (2012) A Comparative Study on the Toxicity of a Synthetic Pesticide, Dichlorvos and a Neem based Pesticide, Neem-On to Labeo rohita (Hamilton) Current World Environment Vol. 7(1), 157-161 (2012).

110) Iqbal M., Khan,A., Rafique, M., Jammu, A., Suthar, V and Khan, B (2019) Comparative Efficacy of Botanical and Synthetic Pesticides against Major Insect Pests of Cabbage European Academic Research 3(9):10038-10057.

111) Gayi, D., Ocen, D, Lubadde,G and Serunjogi,L (2016) Efficacy of bio and synthetic pesticides against the American bollworm and their natural enemies on cotton, Uganda Journal of Agricultural Sciences,, 17 (1): 67 – 81

112) Shonga, E and Getu, E (2021), Efficacy of plant derived and synthetic insecticides against cabbage aphid, Brevicoryne brassicae (L.) (Homoptera: Aphididae) and their effect on

coccinellid predators, Ethiopian Journal of Science., 44(1): 27–37

113) Biswas, G. C. (2013). Comparative effectiveness of neem extracts and synthetic organic insecticide against mustard aphid, Bangladesh Journal of Agricultural Research 38(2): 181-187,

114) Kumar, S., and Singh, A. (2015). Biopesticides: Present Status and the Future Prospects. Journal of Fertiliser and Pesticides 6:129.