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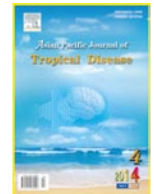

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Microbial secondary metabolites are an alternative approaches against insect vector to prevent zoonotic diseases

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PEER REVIEW

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Comments

This is a good study in which the author categorized the broad spectrum of microbial secondary metabolites as alternatives to insect vector to prevent zoonotic diseases. Broad range chemical insecticides disrupt ecosystems and affect natural balances in insect populations. Hence these data could be informative for future possibilities of recombinant DNA technology.
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ABSTRACT

Approximately 1500 naturally occurring microorganisms have been identified as potentially insecticidal agents. Metabolites from 942 microbial isolates were screened for insecticidal and properties. The isolates included 302 streptomycetes, 502 novel actinobacteria including representatives of 18 genera, 28 unidentified aerobic actinobacteria, 70 fungi and 40 bacteria other than actinobacteria showed the insecticidal activity. Most spore-forming bacteria pathogenic to insects belong to the family Bacillaceae. Only four *Bacillus* species namely *Bacillus thuringiensis*, *Bacillus popilliae*, *Bacillus lentimorbus*, *Bacillus sphaericus* have been closely examined as insect control agents. Fungi are applied directly in the form of spores, mycelia or blastospores or by their metabolites. Many viruses that belong to the family Baculoviridae are pathogenic in insects. The microbial insecticides are generally pest-specific, readily biodegradable and usually lack toxicity to higher animals. This review paper communicates the insect problem in the transmission of diseases in human, animals, plants and problem of chemical insecticides control of insects using microbial metabolites from actinobacteria, bacteria, fungi and viruses.

KEYWORDS

Bioinsecticidal agents, Chemical insecticides, Microbial metabolites, Plant insecticides, Vector control

1. Introduction

Despite significant advances in the techniques used for its control during recent decades, the mosquito continues to pose serious public health problem. In addition to the persistent irritation, they cause humans and animals simply by virtue of their bloodsucking behavior, the itching. This cause mosquitoes are also the principal vector of a variety of serious diseases[1]. Blood-feeding insects are of great medical and veterinary importance, due both to their nuisance value and as vectors of diseases[2]. Amongst insects that feed on humans, mosquitoes are of global importance[3].

Insect's transmitted disease remains a major source of illness and death worldwide. Such diseases are particularly important in the developing world. Mosquitoes are the most important single group of insects in terms of public health importance, which transmit a number of diseases such as malaria (*Anopheles*), filariasis (*Culex*), dengue (*Aedes*), *etc*., causing millions of deaths every year[4].

Culex quinquefasciatus (*Cx. quinquefasciatus*), a vector of lymphatic filariasis, is a widely distributed tropical disease

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with around 120 million people infected worldwide and 44 million people having common chronic manifestation[5]. Filariasis is a global public health problem. One hundred and twenty million people are currently infected and around 1.3 billion at risk of infection[6,7]. However, it has been estimated that the Japanese encephalitis is endemic in one hundred and thirty five districts of India. Saxena and Dhole reported the other species are *Culex vishnui* India, *Culex gelidus* and *Culex fuscocephala* India, Malaysia and Thailand[8].

The most important mosquito vector in Asia is *Culex tritaeniorhynchus* (*Cx. tritaeniorhynchus*) which breeds in stagnant waters like paddy fields or drainage ditches[9]. *Aedes aegypti* (*Ae. aegypti*), a vector of dengue that carries the arbovirus responsible for these diseases, is widely distributed in the tropical and sub-tropical zones. Recent reports of large-scale outbreaks of Chikungunya virus infection in several parts of Southern part of India[10,11].

India is endemic for six major vector-borne diseases namely Malaria, Dengue, Chikungunya, Filariasis, Japanese encephalitis and visceral leishmaniasis. Japanese encephalitis results in thousands of deaths annually. Vector borne diseases cause morbidity of millions of persons resulting in loss of man-days causing economic loss[12]. Japanese encephalitis virus is a member of the family *Flaviviridae* and the leading cause of viral encephalitis in Asia with 30 000-50 000 cases reported annually. The present review describes the insects' borne diseases in human, animals and plants and control strategies using insecticides from the microbial resources.

2. Insect-borne diseases

Insect-borne diseases cause about 1.5 million human deaths every year[13]. There are many different species of blood sucking fleas, lice, ticks and mites. Lice lives on humans or in their clothing while fleas are frequently found taking blood meals on people and domestic animals (Table 1)[14-17]. Bedbugs, which can be found in beds or furniture, feed on humans to obtain blood-meals. Some mites live in people's skin, *e.g.* the mites that cause scabies. Other mite species and ticks may take blood meals on humans[18].

In the Indian scenario, almost the entire country is endemic to the mosquito-borne diseases due to favorable ecological conditions. To prevent mosquito-borne diseases and improve public health, it is necessary to control them. In recent years, however, mosquito control programmes have failed because of the ever increasing insecticide resistance[19]. Most of the mosquito control programmes target the larval stage in their breeding sites with larvicides because the adulticides may only reduce the adult population temporarily[20]. Therefore, a more efficient way to reduce mosquito population is to target the larvae.

3. Chemical insecticides

Carbamates were developed in the 1950s and are still used today. These insecticides are rapidly detoxified and excreted in warm-blooded animals and in general, they are selective against targeted insect pests. Twelve insecticides from four classes (organochlorines, organophosphates, carbamates and pyrethroids) have been recommended for Internal Revenue Service but only pyrethroids have been approved for treating bed nets[21].

However the heavy use of chemical insecticides has not been without drawbacks. Let's mention contamination of water and food sources, poisoning of non-target fauna and flora, concentration in the food chain and selection of insect pest populations resistant to the chemical insecticides[22]. Increased public concern of the potential adverse environmental effects associated with the heavy use of chemical insecticides has prompted the examination of alternative methods for insect pest control. Since the mid-1950s, there have been numerous reports of reduced *Anopheles* susceptibility to malathion, fenitrotion, propoxur, bendiocarb and resistance to all four classes of insecticides has been found in *Anopheles* species in different parts of Africa. Synthetic chemical insecticides provide many benefits to food production and human health, but they also pose some hazards.

4. Plant insecticides

Mosquitoes in the larval stage are attractive targets for pesticides because mosquitoes breed in water, and thus, it is easy to deal with them in this habitat. Many researchers have reported on the effectiveness of plant extract against mosquito larvae (Table 2)[23-26].

Garlic (*Allium sativum* L.) is not only a food ingredient widely used in gastronomy; it has also been used for over 4 000 years as a medicinal plant for a variety of ailments including headaches, bites, intestinal worms and tumors. The medicinal use of garlic remains popular all over the world and its strong insecticidal activity has also been demonstrated by several studies. Extracts from many

Table 1

Insect borne diseases.

Disease	Vector	Endemic zone	Reference
Malaria	Plasmodium *Anopheles gambiae*	Global tropical and subtropical areas	[14]
Lyme disease	Ticks	Europe (Inc. UK), USA, Australia, China and Japan.	[15]
Bancroftian filariasis	*Cx. quinquefasciatus* black flies	Africa, West Asia, the Middle East and the United States.	[16]
Tick-borne encephalitis	*Ixodes ricinus and Ixodes persulcatus*	Europe (Inc. UK), USA, Australia and China	[15]
Chikungunya	*Ae. aegypti*	Swahili or Makonde (the effect of the incapacitating arthralgia)	[17]
West nile virus	Transmitted by mosquitoes (mainly of the genus *Culex*)	Greece	[18]

Table 2

Plant insecticidal agent to control the insects.

No.	Name of the Plant	Name of the extract	Target insect	Reference
1.	*Momordica charantia*	Methanol extract	*Ae. aegypti* and *Cx. quinquefasciatus*	[24]
2.	*Ocimum sanctum* and *Rhinacanthus nasutus*	Acetone crude extract	*Ae. aegypti* and *Cx. quinquefasciatus*	[25]
3	*Cassia auriculata*, *Solanum torvum* and *Vitex negundo*	Petroleum ether extracts	*Anopheles subpictus* and *Culex tritaeniorhynchus*	[26]
4.	*Eclipta prostrate*	Leaf extract	Filariasis and malaria vector	[27]
5.	*Calotropis gigantea*	Leaf extract	*Culex* sp.	[28]

medicinal plants such as *Phytolacca dodecandra* aerial part possess a potent larvicidal activity against mosquito larvae[27]. In the past few decades, synthetic insecticides were used as mosquito controlling agents but had produced a negative feedback of environment ill effect, non-target organisms being affected and most of mosquito species becoming physiologically resistant[7]. Plant extracts in general have been recognized as an important natural resource of insecticides[28].

Govindarajan reported that the leaf methanol[29], benzene, and acetone extracts of *Cassia fistula* were studied for the repellent activity against *Ae. aegypti*. The larvicidal activity of crude hexane, ethyl acetate, petroleum ether, acetone and methanol extracts were assayed for their toxicity against the early fourth instar larvae of *Cx. quinquefasciatus*[22]. These factors have created a search for eco-friendly, biodegradable and target specific insecticides against the mosquitoes. In recent years, the emphasis on controling the mosquito population has shifted steadily from the use of conventional chemicals towards more specific and environmentally friendly materials, which are generally of botanical origin.

Plant products have been used traditionally by human communities in many parts of the world against the vector and pest species of insects[30,31]. The plant derived natural products as larvicides have the advantage of being harmless to beneficial non-target organisms and environment when compared to synthetic insecticides[32]. For this purpose, a lot of phytochemicals extracted from various plant species have been tested for their larvicidal actions against mosquitoes[33,34]. Members of the plant family Asteraceae possess various types of activity against many species of mosquitoes[35].

It is commonly known as 'little ironweed' in English, 'joanbeer', 'kukshim' in Bengali, 'puvamkurunnel' in Malayalam and 'sahadevi' in Sanskrit and Hindi[36]. The roots of the plant are used traditionally for the treatment of all types of eruptive boils and the juice is used for quicker healing of accidental wounds, filariasis and toxic viral fevers[37]. Synthetic insecticides have created a number of ecological problems, such as the development of resistant insect strains, ecological imbalance and harm to mammals. Hence, there is a constant need for developing biologically active plant materials as larvicides, which are expected to reduce the hazards to human and other organisms by minimising the residue accumulation in the environment. In silico, docking analysis was also carried out to assess the mosquito larvicidal potential of three terpene compounds isolated from *Calotropis gigantea*[38].

5. Microbial insecticides

5.1. Early history

The science of invertebrate pathology provides the scientific foundations of microbial control. Invertebrate pathology has its origin in the study of diseases in beneficial organisms such as silkworm and honey bee. The first observations of diseased silkworms were made in China as early as 2 700 BC and by Aristotle on honey bees in 335 BC. It was not until the work of Bassi in 1834 that a microorganism, the fungus *Beauveria bassiana*, was associated with the production of disease in an animal, the silkworm.

Thirty years later, Louis Pasteur followed up with a more thorough study of the various diseases of the silkworm. Both of these 19th century pioneers suggested that microorganisms could be used to control insect pests[39]. Approximately 1 500 naturally occurring microorganisms by products have been identified as potentially useful insecticidal agents. Metabolites from 942 microbial isolates were screened for insecticidal and properties[40].

The isolates included 302 *Streptomycetes*, 502 novel actinobacteria including representatives of 18 genera, 28 unidentified aerobic actinobacteria, 70 fungi and 40 bacteria other than actinobacteria. The most important component of such approach is the biological suppression of insect pest by employing pathogens like bacteria, virus, and fungus (Table 3). These microbials tend to be highly selective and established as an alternative to eco-destabilizing chemical insecticides especially against lepidopteran insect[41,42].

Table 3

Insecticidal activity of secondary metabolites from microorganisms[43].

Genera	Number of isolates examined	Number of isolates with insecticidal activity
Streptomycetes	302	26
Micromonospora	134	2
Actinomadura	59	3
Nocardiopsis	22	1
Thermoactinomyces	19	0
Bacteria other than actinobacteria	40	3
Fungi	70	7

In many instances, alternative methods of insect management offer adequate levels of pest control and pose fewer hazards. This interest in microbial insecticides is largely a result of the many problems associated with the extensive use of chemical insecticide. Not only do chemical insecticides generally affect beneficial insects as well as pest species, but insects tend to acquire resistance to the chemicals so that new pest problems rapidly develop.

Furthermore, chemical residues pose environmental hazards and health concerns. Thus microbial insecticides are seen as an alternative means of pest control that can play an important role in integrated pest management systems and reduce our dependence on chemical insecticides.

6. Entomopathogenic actinobacteria

Actinobacteria are noteworthy as antibiotic and enzymatic producers, making three quarters of all known products; the *Streptomyces* are especially prolific and can produce a great many of antibiotic and other class of biologically active secondary metabolites.

Some antibiotics have been found to possess insecticidal properties. They include inhibitors of respiration (antimycin A, patulin, piericidins) and protein synthesis (cycloheximide and tenuazonic acid) and membrane active agents (dextruxin, beauvericin and some polyene macrolides antibiotics. Other microbial products have been studied specifically for their insecticidal activities, *e.g.* nikkomycins, prasinous, milbemycins. If we include secondary metabolites with biological activities other than antimicrobial, actinobacteria are still out in front, over 60%; *Streptomyces* sp. accounting for 80% of these[43]. Some antibiotics have been found to possess insecticidal properties. Actinobacteria play an important role in the biological control of insects through the production of insecticidal active compounds against the house fly *Musca domestica*[44].

Marine microorganisms have been the topic for the investigation of number of natural products. The marine actinobacteria have different characteristics from those of terrestrial counterparts. Almost 80% of the world's antibiotics are known to come from actinobacteria, mostly from the genera *Streptomyces* and *Micromonospora*. Terrestrial actinobacteria are noteworthy producers of a multitude of antibiotics; however, the marine representatives are much less studied in this regard. The marine environment is an untapped source for many useful drugs and an assessment of this potential is imperative. It is well known that the actinobacteria are the potential sources of antibiotics, which could profitably developed in the pharmaceutical industries and the best known example is the product of *Streptomyces*. There is an increasing demand for the new type of antibiotics to control mosquitos. Actinobacteria gave a good effect, shown as lowest pupal formation percentages of *Drosophila melanogaster*[45].

Dhanasekaran *et al.* found that the actinobacteria isolates producing strong larvicidal activity against *Anopheles* mosquito larvae[46]. However, actinobacteria were effectively used against *Cx. quinquefasciatus*[47]. Many actinobacteria strains caused larval mortality of the cotton leaf worm *Spodoptera littoralis*, ranging from 10% to 60%[48].

Actinobacteria are notable not only for their potent therapeutic activities but also for the fact that they frequently possess the desirable pharmacokinetic properties required for clinical development. Actinobacteria are the most widely distributed groups of microbes in nature. These are Gram positive bacteria frequently filamentous and sporulating organisms with DNA rich in GC from 57% to 75%. *Streptomyces* sp. is by far the most prolific genus, and has provided about 10 000 known antibiotics, 45%-55% produced[49-54]. Most of the antibiotics are extracellular metabolites which are normally secreted in culture media and have been used as herbicides, anticancer agents, drugs, immune regulators and antiparasitic drugs[55].

The secondary metabolites of new strain of *Streptomyces* displayed growth inhibition on the test pathogenetic insects (Table 4)[56-58], such as *Spodoptera exigua*, *Dendrolimus punctatus*, *Plutella xylostella*, *Aphis glycines* and *Culex pipiens*[59].

On the other hand, *Streptomyces* metabolites not only are effective against insect but may also protect the insect themselves from other microbial pathogen and other insect as in beewolf wasps which cultures a strain of antibiotic producing *Streptomyces philanthi* within specialized glands on horn antenna. *Streptomyces philanthi* then excrete antibiotics into the cocoons, protecting the beewolf larvae from harmful pathogen[60].

There is an increasing demand for the new type of antibiotics to control mosquitos. Exploration of microbial secondary metabolites has led to the discovery of hundreds of biologically active compounds which possess pharmacological activities which are currently being used for the treatment of various diseases in humans, animals, and plants. Abamectin and ivermectin derived from the actinobacteria *Streptomyces avermectinius* exhibited extraordinary anthelmintic activity[61]. The pure compound, (2S, 5R, 6R)-2-hydroxy-3,5,6-trimethyloctane-4- one produced by *Streptomyces* sp. VITDDK3 showed acaricidal and larvicidal activities against blood-sucking parasites[62].

7. Entomopathogenic bacteria

Most of the insect pathogenic bacteria occur in the families; such as, Pseudomonadaceae, Enterobacteriacea, Lactobacillaceae, Micrococcaceae, Bacillaceae except for the Bacillaceae, these families contain non sporulating microorganisms. Most spore-forming bacteria are pathogenic to insects belong to the family Bacillaceae. About 100 bacteria have been reported as entomopathogens, but only four

Table 4

Actinobacterial insecticidal agent against insects.

Name of the microorganisms	Insecticidal compound	Target insect	Reference
Streptomyces avermectinus	Abamectin and ivermectin	Mosquito	[52]
Streptomyces sp. VITDDK3	(2S,5R,6R)-2-hydroxy-3,5,6-trimethyloctan-4-one	Acaricidal and larvicidal activities against blood-sucking parasites	[53]
Streptomyces NRRL 30562	Munumbicins E-4 and E-5	Protozoan most biologically active for *Plasmodium falciparum*	[54]

[*Bacillus thuringiensis* (*B. thuringiensis*), *Bacillus popilliae, Bacillus lentimorbus, Bacillus sphaericus*] have been closely examined as insect control agents. Of these four organisms, *B. thuringiensis* is the only bacterium that has been developed successfully as a commercial insecticide on a very large scale and now is sold in several countries (Table 5).

8. Entomopathogenic viruses

Insect-specific viruses can be highly effective natural controls of several caterpillar pests. Different strains of naturally occurring nuclear polyhedrosis virus and granulosis virus are present at low levels in many insect populations. Epizootics can occasionally devastate populations of some pests, especially when insect numbers are high. No threat to humans or wildlife is posed by insect viruses. Virus diseases of caterpillar pests may cause indirect mortality of some beneficial larval parasitoids if the host insects die before the parasitoids have completed development. Predators and adult parasitoids are not directly affected.

Viruses can over winter in the environment or in over wintering insects to infection in subsequent seasons. The success of insect pathogenic viruses has been limited. Thus far, nucleopolyhedrovirus (NPV) strains have only been mass produced in living insects, a costly procedure. Viral insecticide development is further hindered by the fact that the viruses are specific to one species or genus, ensuring a relatively small market. Most crops and habitats are affected by caterpillar pests. Naturally occurring viruses may affect many caterpillar pests. Preparations of granulosis virus have been isolated from several caterpillar species, including imported cabbage worm, cabbage looper, army worm, fall webworm, and mosquitoes, among many others.

9. Baculoviruses

Scientific advancements built on an understanding of what nature already provides are leading to environmentally friendly crop-pest control by either biological agents or specifically designed synthetic anti-insect compounds. Baculoviruses are rod-shaped DNA viruses, many of which begin their life cycle reproducing inside cells. In the nuclei of caterpillar cells infected with baculoviruses, viral progeny multiply and are incorporated into protective polyhedron-shaped protein structures called occlusion bodies. Infected caterpillars die and contaminate the leaf surfaces with the occlusion bodies. Then, healthy caterpillars ingest the occlusion bodies and release the virus when feeding on contaminated leaves, thus continuing the life cycle of infection and replication (Table 6)[63].

Table 6

Genetically engineered viral insecticides selected crop insect controlled with baculoviruses.

Insect	Baculovirus	Crop
Neodiprion sterifer Hymenoptera (European pine sawfly)	NPV	Pine
Lymanteria disper Lepidoptera (gypsy moth)	NPV	Broadleaved trees
Helithis sp. Lepidoptera (cotton bollworm)	NPV	Cotton, sorghum
Cydia pomonella Lepidoptera (colding moth)	GV	Wallnuts, apple
Oryctes rhinoceros (rhinoceros beetle)	NPV	Coconuts

NPV: Nucular polyhedrosis viruses. GV: Granulosis viruses.

10. Entomophagous fungi

Entomophagous fungi belong to divisions Ascomycota, Basidiomycota, Chytridiomycota, Oomycota and Zygomycota[64]. Entomopathogenic fungal genera are currently under research, especially members belonging to the classes Entomophthorales (Zygomycota) and Hyphomycetes. It is important to mention that fungal infections occur in pestilential and non-pestilential insects For example, *Gibellula* species infects spiders and several species of *Cordyceps* and *Erynia* infects ants. In India, of 2 000 fungal species, only 750 belonging to 56 genera attack terrestrial and aquatic arthropods. Agricultural crops are being affected by many fungi and bacteria. Agricultural pests so far identified include 10 000 species of insects and 8 000 fungi[65].

Mohanty and Prakash have described that the filtrate metabolites of *Trichophyton ajelloi* are effective on larvae of two mosquito species, *Cx. quinquefasciatus* and *Anopheles stephensi* (*An. stephensi*)[66]. The culture filtrate metabolites of *Chrysosporium tropicum* were also found to be toxic and toxicity for all larval instars of *An. stephensi* tested at different concentrations.

Table 5

Microbial secondary metabolites as insecticide agent: commercial insecticide product to control for various insects.

No	Name of the microorganisms	Commercial insecticide product	Insect host range
1.	*B. thuringiensis* var. kurstaki	Bactur, bioworm caterpillar killer	Caterpillars (larvae of moths and butterflies)
2.	*B. thuringiensis* var. israelensis	LarvX, mosquito attack	Larvae of *Aedes* and *Psorophora* mosquitoes
3.	*Bacillus sphaericus*	Vectolex WDG	Larvae of *Culex*
4.	*Beauveria bassiana*	Mycotro	Aphids
5.	*Lagenidium giganteum*	Laginex	Larvae of most pest mosquito species
6.	*Nosema locustae*	NOLO Bait	Grasshoppers
7.	Gypsy moth nuclear polyhedrosis (NPV)	Gypchek	Gypsy moth caterpillars
8.	Pine sawfly NPV	Neochek-S	Pine sawfly larvae
9.	*Steinernema feltiae*	Scanmask	Larvae of a wide variety of soil-dwelling and boring insects
10.	*Steinernema scapterisci*	Nematac	Adult stages of mole crickets

Similarly, the same metabolites were used to control *Cx. quinquefasciatus* larvae and have shown LC_{50}, LC_{90} values[67]. Further, Vijayan and Balaraman have already reported the metabolites of 17 fungi and actinobacteria to be highly larvicidal against the third instar of *A. stephensi* and *Cx. quinquefasciatus*[68]. Natural contamination of food commodities with microflora and their toxins continue to be one of the major problems particularly in tropics[69]. Fungi cause most of the microbiological problem inherent in stored grains and agricultural crops.

In contrast, the extracellular secondary metabolites produced by entomopathogenic fungi have become a focus of interest for insect pathologists[70]. Some entomopathogenic fungi, *Beauveria bassiana*, *Paecilocyces fumosoroseus*, and *Fusarium moniliforme* produce mosquito larvicidal compounds like cyclodepsipeptide, including beauvericin and the enniatin complex[71]. Dhanasekaran and Thangaraj found that biogenic nanoparticles from bacteria and fungus can be an alternative source for present chemical larvicides[72].

11. Advantages of microbial insect pest control

An important benefit of microbial control agents is that they can be used to replace, at least in part, some more hazardous chemical pest control agents. At the present time, chemical controls are far more commonly used in the world than microbial controls. It is unclear whether or not all chemical pesticides are environmentally harmful, so replacing all of them with microbial agents would not necessarily guarantee fewer environmental risks. Nonetheless, for the numerous chemical pesticides known to have toxic effects beyond their target pests including toxic effects to animals and human, the opportunity to substitute safer, more selective, and biodegradable biocontrol agents can provide important ecological benefits. One of the ecological advantages of microbial control agents is that they tend to be highly selective, infecting or killing a very narrow range of target pests. Microbial insecticides are especially valuable because their toxicity to non target animals and humans is extremely low. Compared to other commonly used insecticides, they are safe for both the pesticide user and consumers for treated crops. Microbial insecticides are also known as biological pathogens and biocontrol agents (Table 7).

12. Future considerations

Currently, microbial insecticide has the greatest potential in intelligently designed and carefully applied insect management programs. Expanded use of microbial insecticide will depend heavily on the balance between production costs and ecological considerations. Broad range chemical insecticides disrupt ecosystems and affect natural balances in insect populations. The abundance and variety of extra chromosomal elements in *B. thuringiensis*, for example, should allow their isolation and purification in sufficient quantities for detailed investigation of the structure and biological properties of these molecules. Genetic manipulation of promising plasmids by simple transformation or recombinant DNA techniques, may ultimately improve the efficacy, pathogenicity and commercial production of *B. thuringiensis* as well as other entomopathogenic bacteria. Likewise, the genetic manipulation of viruses by both classical selection techniques and recombinant DNA technology may achieve increased efficacy and broadened host range. Thus far, classical genetic selections have been used to increase resistance to ultraviolet light and to increase occluded virus production. Genetic engineering of *Autographa californica* nuclear polyhedrosis virus by recombinant DNA techniques is currently under way. Future possibilities include the introduction of an insect-specific toxin (for example, a paralytic neurotoxin) gene into the genome of *Autographa californica* nuclear polyhedrosis virus by recombinant DNA technology.

13. Conclusion

Insect transmitted disease remains a major health source of illness and health worldwide. To prevent mosquito borne disease and improve public health, it is necessary to control them. In recent years, however, mosquito control programmes have failed because the ever increasing insecticide resistance. Microbial insecticides offer effective alternatives for the control of many insect pests. Biological control is the use of natural enemies to manage mosquito populations. There are several types of biological control including the direct introduction of parasites, pathogen and predators to target mosquitoes or by using the dead spores

Table 7

Components of integrated vector control[7].

Type	Intervention	Targets	Products
Community education	Behavioral change, application of other interventions	All vectors	-
Environmental management and sanitation	Natural environment changes improved housing quality physical barriers to breeding sites	Mosquitoes, blackflies, snails, *etc.* vectors of chagas disease, malaria (*Anopheles*), dengue (*Aedes*), (*Culex*) vectors of filariasis	Polystyrene beads in standing water bodies
Biological control (microbial secondary metabolites and plant products)	Larvivorous fishes predators and competitors larviciding	Mosquitoes snails urban mosquitoes, blackflies	Microbial larvicides, organophosphates, neem extracts and other herbal insecticides
Chemical control	Space spraying indoor residual spraying	Urban mosquitoes vectors of malaria lymphatic filariasis, leishmaniasis	Pyrethroids, organophosphates

of varieties of the natural soil bacteria and actinobacteria which used to interfering in the digestion systems of larvae. The use of microbial insecticides could decrease our dependence on chemical insecticide. Microbial metabolites could be an alternative source for mosquito larvicides because they constitute a potential source of bioactive compounds and generally free from harmful effects. Use of these microbial derivatives in mosquito control instead of synthetic insecticides could reduce the cost and environmental pollution. Further studies on identification of active compounds, toxicity and field trials are needed to recommend the active fraction of microbial metabolites for development of eco-friendly strategies for the control of insect vectors.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

Insect's transmitted disease remains a major source of illness and death worldwide. Metabolites from 942 microbial isolates were screened for insecticidal properties. The microbial insecticides are generally pest-specific, readily biodegradable and usually lack toxicity to higher animals. This review paper communicates the insect problem in the transmission of diseases in human, animals, plants and problem of chemical insecticides control of insects using microbial metabolites from actinobacteria, bacteria, fungi and viruses.

Research frontiers

For the numerous chemical pesticides known to have toxic effects beyond their target pests including toxic effects to animals and human, the opportunity to substitute safer. More selective and biodegradable biocontrol agents can provide important ecological benefits. Microbial insecticides are especially valuable because their toxicity to non target animals and humans is extremely low. Compared to other commonly used insecticides, they are considered to be safe for both the pesticide user and consumers of treated crops.

Related reports

Carbamates, the chemical control were developed in the 1950s and are still used today (Roberts *et al.*, 2007). The biological control to manage mosquito populations includes the direct introduction of parasites, pathogen and predators to target mosquitoes or by using the dead spores of varieties of the natural soil bacteria and actinobacteria which used to interfere in the digestion systems of larvae. The use of microbial insecticides could decrease our dependence on chemical insecticide.

Innovations & breakthroughs

Data regarding microbial secondary metabolites against zoonotic diseases are of significant importance. This study has categorized insect borne diseases, plant insecticidal agent to control the insects, insecticidal activity of secondary metabolites from microorganisms, actinobacterial insecticidal agent against insects, genetically engineered viral insecticides, selected crop insect controlled with baculoviruses, commercial insecticide product to control for various insects and components of integrated vector control.

Applications

Microbial insecticide has the greatest potential in intelligently designed and carefully applied insect management programs. Genetic manipulation of promising plasmids by simple transformation or recombinant DNA techniques, may ultimately improve their efficacy, pathogenicity and commercial production.

Peer review

This is a good study in which the authors categorized the broad spectrum of microbial secondary metabolites as alternatives to insect vector to prevent zoonotic diseases. Broad range chemical insecticides disrupt ecosystems and affect natural balances in insect populations. Hence these data could be informative for future possibilities of recombinant DNA technology.

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