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Entomotherapy medicinal significance of insects: A review

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Abstract
Insects and the substances extracted from them have medicinal importance and have been used in both traditional and modern medicines since long. Around thousand species of insects in the world are reported to have therapeutic uses. The tribes and the rural communities are very close to nature and its resources, thus have ample knowledge which is worthy of scientific and commercial exploitation for curing different kinds of diseases. Moreover, it will provide a good source of income to these local communities. This review focuses on the utilization of diverse insect biodiversity for their pharmacological properties and their significance in the development of modern drugs and treatment methods.

Keywords: Medicinal insects, traditional medicines, modern uses, conservation

Introduction
The term "entomotherapy" is derived from the Greek words entomon (insect) + therapy (treatment in medical terms). "Entomotherapy" is defined as preventative or therapeutic use of insects and insect-derived products (Costa-Neto 2005) [7]. Since ancient times, many species of insects and the substances extracted from them have been used as therapeutic resources in the medical systems of many cultures (Costa-Neto 2005) [7]. They are termed as "medicinal insects".

Global Scenario
Worldwide, at least 1000 species of insects are reported to be used therapeutically. Approximately 300 medicinal insect species are reported from China alone, distributed in 70 genera, 63 families and 14 orders. Hundreds more of insects have been reported from other parts of the world including India, Japan, Turkey, Korea, Africa, Tibet, Spain, South America, etc. (Meyer-Rochow 2017) [14].

Indian Scenario
India is a mega-diverse nation which is endowed with rich insect biodiversity due to its varied eco-climatic conditions. In Arunachal Pradesh, Nyishi and Galo tribes used about 102 species of insects for food and medicine purpose. Some major species considered medicinally important by the Galo and Nyishi are listed in **(**Table 1). The local people use the insects in home remedies not only for themselves but for their domesticated or semi-domesticated livestock as well (Chakravorty *et al*. 2011) [5]. In Satpura Plateau of Madhya Pradesh, 10 insect species (Table 2) belonging to different families are used as food and medicine by the tribal and rural people of the remote villages of Chhindwara & Betul district (Bhowate and Kumar 2020) [3]. In Nagaland, 50 species of medicinal insects belonging to 11 orders and 28 families were identified in treatment of at least 50 human ailments. Some major species considered medicinally important by the ethnic communities are listed in (Table 3). The dominant families reported in this study are the Libellulidae (16%), followed by Apidae (12%), Cerambycidae (8%) and Vespidae (6%) and the orders represented in the study are Odonata (8 spp.; 16%), Orthoptera (5 spp.; 10%), Mantodea (2 spp.; 4%), Phasmatodea (1 spp.; 2%), Blattodea (2spp.; 4%), Hemiptera (7 spp.; 14%), Neuroptera (1 spp.; 2%), Coleoptera (8 spp.; 16%), Hymenoptera (10 spp.; 20%), Lepidoptera (5 spp.; 10%) and Diptera (1 spp.; 2%) (Mozhui *et al*. 2021) [16].

Table 1: Major insect species used for medicine purpose by Nyishi and Galo tribes of Arunachal Pradesh

Scientific Name	Common Name	Disease
Apis spp.	Honey bee	Cough, fever, stomach pain
Bothroponera rufipes	Black ant	Scabies, toothache, wounds, high blood pressure, malaria
Oecophylla smaragdina	Weaver ant	Stomach ache & dysentery
Ephemera danica	May fly	Stomach disturbance
Cantharid spp.	Beetle	Skin allergy

Table 2: Insects used for medicine purpose by rural & tribes of Satpura plateau of Madhya Pradesh

Scientific Name	Common Name	Disease
Trombidium grandisimum	Red velvet mite	Pneumonia & fever
Oecophylla smaragdina	Weaver ant	Gastritis
Polistes carolina	Red wasp	Piles & general wound
Apis dorsata & Apis indica	Honey bee	Cracks & scars
Mylabris pustulata	Blister beetle	Dog bite & Hydrophobia
Microtermes obesi	White ant	Liver disorder
Hieroglyphus banian	Grasshopper	Dog bite
Pachliopta aristolochiae	Common Rose	Snake bite
Bombyx mori	Silk moth	Pneumonia
Sceliphron spp.	Mud wasp	Vomiting & migraine

Table 3: Insects used for medicine purpose by ethnic communities of Nagaland

Scientific Name	Common Name	Disease
Apis spp.	Honey bee	Cold, cough, diarrhea, mouth ulcers, stomach pain, wounds
Batocera parryi	Beetle	Malaria, joint pain, typhoid
Mylabris spp.	Beetle	Blisters & warts
Samia cynthia ricini	Silk moth	Analgesic, blood pressure, diabetes
Vespa mandarinia	Asian giant hornet	Nutrient supplement, diabetes

History

The belief that insects exist for the benefit of human beings can be found in the book Insectotheology, published in 1699 (Berenbaum and May 1995) [2]. The *Ebers papyrus*, an Egyptian medical treatise dated to the sixteenth century B.C., contains several accounts of medicines obtained from insects and spiders (Weiss 1947) [24]. Silkworms (*Bombyx mori* L., 1758) have been used in Chinese traditional medicine for at least three thousand years (Zimian *et al.* 1997) [28]. The larvae of certain flies have been recognized for centuries as beneficial agents for the healing of infected wounds (Sherman *et al.* 2000) [20]. In *Naturalis historiae*, Pliny the Elder recorded some entomotherapeuticals (insect-derived medicines) for the treatment of several illnesses in the Roman Empire in the first century A.D. (Carrera 1993) [4]. In *Materia medica*, Dioscorides mentioned some insect remedies like bedbugs (quartan fever), cockroaches (ground with oil or cooked - earache), cicadas (fried - bladder complaints), locusts or grasshoppers (dried - scorpion stings). In another book, On Poisonous Animals, Dioscorides dealt with the treatment of people stung by wasps and bees (Morge 1973) [15].

Why to study insects as medicine?

Insects and their products have been used directly and indirectly in the medical systems of different human cultures throughout the world since early times. Insects have immunological, analgesic, antibacterial, diuretic, anesthetic and anti-rheumatic properties, thus, they have proven as sources of drugs for modern medicine (Yamakawa 1998) [26]. Moreover, insect by-products are very important both as folk medicines and potential modern drugs. As of now, no resistance problem has been found for any disease. The medicinal use of insects can be a potential source for the discovery of new drugs in future.

Entomotherapy

Entomotherapy can be studied into two parts:

1. Traditional & historical use of insects in medicine
2. Modern & scientific use of insects in medicine

Traditional & historical use of insects in medicine

Traditional medicines in China

The traditional Chinese medicine includes the use of herbal medicine, acupuncture, massage, exercise and dietary therapy. Insects are incorporated as part of the herbal medicine component of traditional Chinese medicine. For example; Chinese Black Mountain Ant, *Polyrhachis vicina* prolongs life, anti-aging properties and increases fertility. Ant extract is typically consumed mixed with wine. It contains a lot of zinc, thus, acts as immune stimulant and antioxidant (Wilkinson 2002) [25]. *Polyrachis lamellidens*, a medicinal ant used in Chinese medicine, was confirmed to exert potent analgesic and anti-inflammatory actions (Kou *et al.* 2005) [12].

Traditional medicines in India

Termite is used to cure a variety of diseases, both specific and vague. Typically the mound or a portion of the mound is dug up and the termites along with the architectural components of the mound are ground into a paste which is then applied topically to the affected areas or, more rarely, mixed with water and consumed (Srivastava *et al.* 2009) [21]. This treatment was said to cure ulcers, rheumatic diseases, and anemia and was also suggested to be a general pain reliever and health improver (Chakravorty *et al.* 2011) [5]. The Jatropha Leaf Miner, a lepidopteran which feeds preferentially on Jatropha, is an example of a major agricultural pest which is also a medicinal remedy. The larvae are harvested, boiled, and mashed into a paste which is administered topically and is said to induce lactation, reduce fever, and soothe gastrointestinal tracts (Srivastava *et al.*

2009) [21]. Pierisin, a protein purified from pupa of cabbage butterfly, *Pieris rapae* exhibits cytotoxic effects against human gastric cancer. Butterflies produce several antibacterial proteins including cecropins, defensins and lysozymes. Cercopin has also been reported to be cytotoxic against mammalian lymphoma and leukemia cells. Butterflies may become a good source of novel bioactive materials such as anti-bacterial, anticancer drug. In India, 1,501 species of butterflies are found having a tremendous potential in butterfly bioprospecting (Srivastava *et al.* 2009) [21].

Traditional medicines in Africa

Unlike China and India, the traditional insect medicines of Africa are extremely variable. Grasshoppers are typically collected, dried in the sun, and then ground into a powder which can then be turned into a paste when mixed with water and ash and applied to the forehead to alleviate the pain of violent headaches (Srivastava *et al.* 2009) [21]. Termites mound parts are dug up, boiled, and turned into a paste, which can then be applied to external wounds to prevent infection or consumed to treat internal hemorrhages. Termites are not only used as a form of medicine, but also as a medical device. If the "healer" wants to insert a medicine subcutaneously, they will often spread the medicine on the patient's skin, and then agitate a termite and place it on the skin of the patient and when the termite bites, its mandibles effectively serve as an injection device (Srivastava *et al.* 2009) [21].

Traditional medicines in America

Grasshoppers are said to serve as diuretic to treat kidney diseases, to reduce swelling, and to relieve the pain of intestinal disorders when they are consumed (Ramos *et al.* 1988) [17]. Much like the termites of Africa, ants were sometimes used as medicinal devices by the indigenous people of Central America. The soldier cast of the Army ant would be collected and used as the living sutures by agitating an ant and holding its mandibles up to the wound edges and when it bites down, the thorax and abdomen were removed, leaving the head holding the wound together. The ant's salivary gland secretions were reputed to have antibiotic properties (Ramos *et al.* 1988) [17]. The Red harvester ant's venom was used to treat rheumatism, arthritis, and poliomyelitis via the immunological reaction produced by its sting. This technique, in which ants are allowed to sting afflicted areas in a controlled manner, is still used in some arid rural areas of Mexico (Ramos *et al.* 1988) [17]. The silkworm, *Bombyx mori*, was also commonly consumed for medicinal purposes in Central America. Only the immatures are consumed. Pupae were boiled and eaten to treat apoplexy, bronchitis, pneumonia, convulsions, hemorrhages, and frequent urination. The excrement produced by the larvae is also eaten to improve circulation and alleviate the symptoms of cholera (intense vomiting and diarrhea) (Ramos *et al.* 1988) [17].

Modern & scientific use of insects in medicine

Though insects were used widely throughout the history for medical treatment on nearly every continent, relatively very little medical entomological research has been conducted since the revolutionary advent of the antibiotics. Thus, arthropods represent a rich and largely unexplored source of new medicinal compounds (Dossey 2010) [8]. It consists of Maggot Therapy, Apitherapy, Blister Beetle or Spanish Fly Therapy, Blood-feeding insects.

Maggot therapy

Maggot therapy is the intentional introduction of live, disinfected blow fly larvae (maggots) into soft tissue wounds to clean out the necrotic tissues selectively. This helps to prevent infection; it also speeds healing of chronically infected wounds and ulcers (Sun *et al.* 2014) [22]. The maggots perform three actions *viz*., clean wounds by dissolving the dead (necrotic) infected tissue, disinfect the wound by killing bacteria, and stimulate wound healing (Sherman *et al.* 2000) [20]. Maggots secrete several chemicals that kill microbes, including allantoin, urea, phenylacetic acid, phenylacetaldehyde, calcium carbonate, proteolytic enzymes, and many others (Heuer and Heuer 2011) [10]. The flies responsible belong to order Diptera and family Calliphoridae (the Blow Flies) and Sarcophagidae (the Flesh Flies). The commonly found/used species are *Phormia regina, Lucillia sericata*.

Apitherapy

Apitherapy is the medical use of honeybee & bee products such as honey, pollen, propolis, royal jelly, bee wax & bee venom against disease & disorders.

Bees wax

Bee wax is rich in Vitamin A and helps in cell development & skin epithelium antiseptic property; used in body lotions and coating for pills which facilitates ingestion (Ramos *et al.* 1988) [17].

Bee venom

Apipuncture is the therapy by means of bee sting. The major peptide in bee venom is Mellitin which blocks expression of inflammatory genes and is used to treat inflammation in rheumatoid arthritis & multiple sclerosis (Ratcliffe *et al.* 2011) [18]. Apitoxin, or honey bee venom, can be applied via direct stings to relieve polyneuritis, asthma, etc. (Ramos *et al.* 1988) [17].

Honey

Honey is consumed for digestive problems and as a general health restorative, and can be heated and consumed to treat head colds, cough, throat infections, laryngitis, tuberculosis, and lung diseases (Ramos *et al.* 1988) [17]. It can be applied to skin to treat excessive scar tissue, rashes, and burns (Feng *et al.* 2009) [9]. It can be used to prevent cancer as it contains phenols with anti-cancer properties (quercetin, hesperidin, caffeic acid, apigenin, etc.) (Abubakar *et al.* 2012) [1].

Pollen

Bee bread, or bee pollen, is eaten as a generally health restorative, and is said to help treat internal and external infections, skin diseases, ulcers. It is a rich source of vitamins (A, B1, B2, B6, C and E), amino acids, Ca, Fe, K, P and Na (Ramos *et al.* 1988) [17].

Propolis

Propolis is a resinous, waxy mixture collected by honeybees and used as a hive insulator and sealant, is often consumed by menopausal women because of its high hormone content, and it is said to have antibiotic, anesthetic, and anti-inflammatory properties (Ramos *et al.* 1988) [17].

Royal jelly

Royal jelly is used to treat anemia, gastrointestinal ulcers,

arteriosclerosis, hypo- and hypertension, and inhibition of sexual libido and helps in cell regeneration & bone marrow production, and balance the endocrine system (Ramos *et al.* 1988) [17].

Blister Beetle or Spanish Fly Therapy

Spanish fly is an emerald-green beetle belonging to order Coleoptera and family Meloidae. *Mylabris pustulata* (India) and *Lytta vesicatoria* (Europe) are the commonly used species. Cantharidin is a defensive chemical produced by blister beetles to ward off predator attacks by reflex bleeding. Beetles contain up to 1% cantharidin by weight. This was accepted by the FDA in 2004 as treatment for warts, skin problems; inhibit ovarian cancer cell, uro-genital tract and kidney infections (Ratcliffe *et al.* 2011) [18].

Blood-feeding insects

Several blood-feeding insects like ticks, horseflies, and mosquitoes inject multiple bioactive compounds into their prey. They have been used to prevent blood clot formation or thrombosis (Yang *et al.* 2000) [27]. The saliva of blood feeding insects has strong drug development potential. Currently, over 1280 different protein families have been associated with them *viz*., anticoagulants (blood clot), antihistamines (allergy & inflammation), anaesthetics (surgery), etc. (Ratcliffe *et al.* 2011) [18].

Pharmacological Significance of Insects

Insects have large number of biologically active compounds, such as molecules that kill cancer cells, proteins that prevent blood from clotting, enzymes that degrade pesticides, proteins that glow in the dark and antimicrobial peptides and toxins (Trowell 2003) [23]. Antibacterial proteins extracted from insects include cecropin A and B (from *Hyalophora cecropia*), sarcotoxin IA, IB, IC and sapecin (*Sarcophaga peregrine*), defensin and diptericin (*Drosophila melanogaster*), attacin, moricin and drosocin (*Bombyx mori*) (Yamakawa 1998) [26]. The novel peptide neurotoxins, pompilidotoxins (PMTXs), have been identified from the venom of the spider wasps *Anoplius samariensis* and *Pseudagenia* (*Batozonellus*) *maculifrons* in Japan (Konno *et al.* 1998) [11]. Promising anticancer drugs, such as isoxanthopterin and dichostatin, have been isolated from the wings of Asian sulphur butterflies (*Catopsilia crocale*) and the legs of Taiwanese stag beetles (*Allomyrina dichotomus*) respectively (Kunin and Lawton 1996) [13].

Constraints

With the degradation of natural resources & rapid population growth, the traditional wisdom of entomotherapy is at risk of being lost (Chakravorty *et al*. 2011) [5]. Despite having strong potential, insect-derived products have yet to establish the recognition & market success (Ratcliffe *et al.* 2011) [18]. There is lack of motivation and facilities provided to the scientists to study and work for entomotherapy. Heavy reliance on antibiotics, coupled with discomfort with insects limited the field of insect pharmacology until the rise of antibiotic resistant infections sparked pharmaceutical research to explore new resources (Dossey 2010) [8].

Conservation and Sustainability

Conservation of insect species could be promoted through their value in the treatment of human ailments and diseases (Cheesman and Brown 1999) [6]. Species involved in traditional remedies should be among the highest priorities for conservation (Kunin and Lawton 1996) [13]. According to Zimian *et al.*, the two main ways to protect natural insect resources are to develop mass-rearing methods to enhance commercial production of valued insects in order to meet growing market needs] and to find the natural substitutes and to develop synthetics through basic research e.g. researchers have synthesized sodium of cantharidin, which is used to treat lung and liver cancers (Zimian *et al.* 1997) [28].

Future Perspectives

The discovery of pharmaceuticals coming from insects should follow the same general principles that are known in phytochemical research *viz*., theoretical and basic research in the fields of toxicology, pharmacology, and chemical components of medicinal insects; identification and taxonomic classification of insects; protection from over-collecting to guarantee their sustainable use and to avoid destruction of natural food chains including their natural enemies; reduction in the pesticide application by developing more efficient methods for collecting medicinal insects; development of a quality control standard for commercial species to guarantee the safety and effectiveness of the medicine for people (Costa-Neto 2005) [7].

Conclusion

Insects constitute an almost inexhaustible resource for pharmacological research having developed defensive chemicals over co-evolution with plants and predators. However, medicinal insect species have received very little attention probably due to the disdain that majority of people show towards these animals (Costa-Neto 2005) [7]. The exploitation of animal resources for medicinal purposes has ecological and cultural dimensions. Insect diversity must be maintained to provide future biological diversity and substances for new sources of pharmacological exploration in the coming years (Costa-Neto 2005) [7]. We must pay attention to the sustainable use of insects to avoid their extinction (Costa-Neto 2005) [7]. Insects have long been a significant remedy for illnesses in many regions of the world and we should further encourage their collection and commercialization, given the benefits to the environment and human health (Srivastava *et al*. 2009) [21]. The traditional and indigenous knowledge on medicinal significance of entomological products is important for value addition and benefit sharing for economic upliftment and poverty alleviation of local communities and indigenous people (Senthilkumar *et al.* 2008) [19]. The twenty-first century has witnessed severe infectious disease outbreaks. Thus, looking at the increased risk of emerging infectious diseases, there is a need to set certain standards or formulate national policies on the utilization of insects for therapeutic uses on the basis of no hazard to health so as to avoid the adverse effects, if any.

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