Review Article

A review of plants and essential oils effective as natural remedies against bedbugs

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ABSTRACT

Called *Cimex lectularius* and *Cimex hemipterus*, the bedbug has made its return to daily life in many developed countries since the 1990s, although it had practically disappeared since the 1950s. The resurgence of bedbug infestations can be explained partly by the evolution of the lifestyle and by the mode of consumption favoring second-hand purchasing. One of the main factors behind their resurgence is the excessive use of synthetic insecticides with similar modes of action, which has led to the development of insecticide resistance. The application of synthetic insecticides indoors or in the environment is a public health concern due to the toxic effects that can result from prolonged exposure to these chemicals. It is for this reason that there is an increased demand from the public for the use of effective "green" products for urban pest control. Natural insecticides, including EOs are considered safe due to their low toxicity to humans and animals. Thanks to a search in ethnobotanical studies, we identified a list of 10 plants used in the fight against bedbugs: *Lavandula latifolia spica, Corymbia citriodora, Syzygium aromaticum (L), Cymbopogon winterianus jowitt, Thymus vulgaris, Chrysanthemum cinerariaefolium, Phaseolus vulgaris, Oreganum vulgare L., Tagetes paluta L. and Cinnamonum camphora.* The study of the literature that we subsequently carried out showed that these plants/essential oils/components act according to 4 mechanisms, namely: topical, neurological, mechanical or fumigant effects. We therefore conclude that the use of preparations of natural origin has the advantage of avoiding the toxic and polluting harm of substances of chemical and synthetic origin and that it is desirable to continue research and investigation of the composition details of its plants and essential oils.

Keywords: Cimex Lectularius, Cimex Hemipterus, Bed Bugs, Plants, Essential Oils, Green Product, Natural Insecticides.

he bed bug has made a comeback in daily life in many developed countries since the 1990s, although it had practically disappeared since the 1950s. The increase in bedbug infestations is partly explained by changes in lifestyle and consumption patterns favoring second-hand purchases [1]. One of the main factors behind their resurgence is the excessive use of synthetic insecticides with similar modes of action, which has led to the development of insecticide resistance [2-5]. Called Cimex lectularius L. and Cimex hemipterus, the bedbug belongs to the Cimicidae family, exclusively hematophagous throughout its life, it has always cohabited with humans. It is an insect that has been known for thousands of years, specimens found in Egyptian tombs bear witness to this. Without functional wings, brown to reddish in color. It can measure 5 to 8 mm as an adult, its body is flattened dorso-ventrally, with a rounded shape [6,7].

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After a blood meal, fertilized female bed bugs lay, throughout their adult life, around five eggs per day in a place protected from light. At room temperature, the eggs hatch into first instar larvae in approximately 7 to 15 days. Insects pass through four larval stages and one nymphal stage, each requiring a blood meal before they can progress to the next stage, the fifth instar molting into an adult. The lifespan of bed bugs is approximately 12 months in total. They are nocturnal, photophobic and gather during the day in aggregates located near the resting sites of human beings, sheltered from light [1]. The bedbug must feed every three to fifteen days on average; this duration varies depending on the digestion time, egg laying and temperature and humidity conditions and the availability of the host. Certain populations of bed bugs have been shown to be highly resistant to various chemicals including neonicotinoids and to possess reduced sensitivity to pyrrole compounds [4,5].

Correspondence to: Mohamed Yafout, Pharm D, 19, Rue Tarik Ibnou Ziad B.P. 9154, Casablanca, MAROC, Laboratory of Drug Sciences, Biomedical Research, and Biotechnology, Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, Morocco. **Email:** <u>yafoutm@yahoo.fr</u> An amino acid substitution mutation, F348Y (or F331Y in standard numbering), occurring at an acyl binding site of the AChE paralog gene (*p-Ace*), was identified among AChEi - resistant colonies of common bedbugs [8]. The difficulty of eliminating resistant bed bug populations requires pest management that uses both chemical and non-chemical or alternative treatments [9-11]. Substances of natural origin such as plant essential oils, which are secondary metabolites derived from the outer glandular cells of the leaves and stems of aromatic plants [12], are one of the treatment alternatives used to combat bedbugs. And many other urban and agricultural insect pests [13–20].

Review of plants and essential oils (EO) used against bedbugs

The application of synthetic insecticides indoors or in the most environment is a public health concern due to the toxic effects **Table 1: List of identified plants and essential oils used against bedbugs:**

that may result from prolonged exposure to these chemicals [21–23]. It is for this reason that there is an increased demand from the public for the use of effective "green" products for urban pest control. Natural insecticides including EOs are considered safe due to their low toxicity to humans and animals [12-13]. Theses EOs is marketed under a lot of brand names as: Sereni-d[®] (Bouclier[®] punaise de lit), EcoWidow[®] (BED BUG REPELLENT[®]), ANBE[®] (BED BUG spray[®]), Ready Steady Defend® (BED BUG KILLER® spray) and other. In this context, EOs of plant origin in particular have emerged as an interesting option in the fight against harmful insects [24-25]. To identify plants and EOs used to treat bedbugs, we searched scientific article or book databases as well as Google Scholar for publications containing ethnobotanical data on plants and EOs. used to treat these parasites. This research allowed us to establish a list of the ten most cited plants or EOs and their constituents (Table 1).

Plant / source of HE	Botanical family	English common name	Active molecule
Lavandula latifolia spica	Lamiaceae	Aspic lavender	Linalool
Corymbia citriodora	Myrtaceae	Lemon eucalyptus	Eucalyptol Geraniol
Syzygium aromaticum (L)	Myrtaceae	Clove	Eugenol
Cymbopogon winterianus jowitt	Poaceae	Java lemongrass	Citronellol
Thymus vulgaris	Lamiaceae	Thyme	Thymol
Chrysanthemum cinerariaefolium	Asteraceae	Pyrethrum flowers	Pyrethrin
Phaseolus vulgaris	Fabaceae	Common bean	-
Oreganum vulgare L.	Lamiaceae	Wild oregano	Carvacrol
Tagetes paluta L.	Asteraceae	French marigold	Terthyenyl
Cinnamonum camphora	Lauraceae	Camphor tree	Camphor, monoterpene

Lavandula latifolia spica: Spike Lavender is a shrub with a woody, square stem from the Lamiaceae family that can reach 80cm high. Its stems branch into forks and its narrow, linear leaves can reach 10cm. Its spike-shaped inflorescences have small purple flowers with a shape characteristic of lamiaceae [26]. The extraction of lavender essential oil is done by steam distillation, the resulting oil is very light yellow, almost colorless [27], its composition is not constant, this variation is probably due to various conditions including environment, genotype, geographic origin, drying location, temperature and extraction method. EO is rich in linalool (25-50%), 1,8-cineole (20-35%) and camphor (8-20%) [28,29]. Lavender owes its repellent activity and mortality rate to its predominant component Linalool which provides neuro-excitatory effects on the nervous system of bedbugs [30].

Corymbia citriodora: Also called *Eucalyptus citriodora*, is a species of the genus *Corymbia*. It is a large tree 50 meters high whose foliage gives off a lemony smell. Its bark is fibrous, gray or gray brown coming off in long ribbons. The small branches are green in color. The leaves are green, concolorous, narrow, lanceolate, pointed and measure 7 to 15 centimeters long and 0.7 to 1.5 centimeters wide. They give off a peppermint smell when kneaded. The EO is extracted from the leaves and branches, which has medicinal properties thanks to the known active ingredients: Aldehydes

(citronellal), eucalyptol (3%), Alcohols: citronellol, geraniol [31]. Eucalyptus essential oil is composed of an average of 70% Citronellol, effective against insects and against bedbugs [32].

Syzygium aromaticum (L): The clove or clove tree is a large tree with a light gray trunk 12 to 15 meters high which can reach up to 20 meters high. It has an erect and pyramidal port. Its foliage is aromatic, leathery, evergreen, dark green and glazed with a lighter underside. Its leaves are opposite, entire, elliptical. It is a tree native to the Moluccas Islands in the Indonesian archipelago. The nails are actually flower buds. Green in color then red once ripe, the nails take on their pretty brown color during the drying phase, which takes place in the open air for a month [33]. The biochemical composition is likely to change depending on the production conditions and the quality of the oil. However, we can rely on this composition to evaluate the quality of an oil: Main chemical compound: Phenols 70 to 85% (Eugenol) [34]. Clove essential oil appears to exhibit insecticidal activity against bedbugs. However, its application requires direct spraying on the insect, which can prove difficult in practice [16].

Cymbopogon Winterianus Jowitt: Java Lemongrass is a genus of herbaceous plants of Asian species, many crops of which have been introduced throughout the world. Java

lemongrass is robust, aromatic, and persistent. A tuft of erect leaves arises from a short rhizome and can reach a height of 2 meters. It is widely cultivated in Java and South-East Asia. The fresh aerial parts, from which Java Lemongrass essential oil is extracted, are rich in terpene aldehydes (35 to 65%): citronellal Alcohols (30 to 40%): geraniol, citronellol and Esters (10%): citronellal acetate [35]. A recent study demonstrated the toxic effects of lemongrass against various insects including bedbugs. The authors reported that some compounds contained in this plant have strong activity as membrane channel activating cations. They observed that this effect is similar to the mode of action of pyrethrin [36].

Thymus vulgaris: Native to the Mediterranean basin, Thymus vulgaris L. is an aromatic shrub with branched stems, which can reach 40 cm in height. It has small leaves curved on the edges, dark green in color, and which are covered with hairs and glands (called trichomes). The trichomes contain the essential oil mainly composed of monoterpenes. The color of its small flowers varies from white to purple to pink. Thymus vulgaris is characterized by floral and therefore chemical polymorphism as well [37]. The essential oil of T. vulgaris has a high content of oxygenated monoterpenes (56.53%) and low contents of monoterpene hydrocarbons (28.69%), sesquiterpene hydrocarbons (5.04%) and oxvgenated sesquiterpenes (1.84%) [4]. The predominant compound among the components of essential oils is thymol (51.34%) [38]. Maximum mortality and repellency of up to 100% have been reported for Thymus vulgaris in previous studies [30].

Chrysanthenum Cinerariafolium: Perennial flower native to mountainous regions of Europe, with the appearance of a large daisy. The term "pyrethrum" is the powder produced from the flowers harvested and air-dried to avoid fermentation and loss of pyrethrin. The dried flowers are crushed and extracted with hexane or other suitable solvent, the plant undissolved and the material is filtered and the solvent is flashed to leave a crude oleoresin which generally contains about 30% pyrethrins: pyrethrins I and II, cinerins I and II, jasmoline I and II [39]. Pyrethrins act by contact or ingestion on the nervous system of bedbugs. It is the most economically important natural insecticide, comprising a group of six closely related monoterpene esters. Industrial production is based on the extraction of Chrysanthemum flower heads cinerariaefolium (Pyrethrum) [40]. These alkaloids are toxic to the central nervous system of insects, but also to that of cold-blooded animals. Their toxicity for humans is much lower. These biodegradable natural products are quickly inactivated by light, their effectiveness is therefore quite limited and also cause resistance [41]. Pyrethrum is still found today in organic insecticides in the form of dry powder or combined with other components such as lavender essential oil [41].

Phaseolus vulgaris: The bean is an herbaceous, annual plant, which can take several types of growth depending on the

variety. There are two large groups, climbing beans (called pole beans), with a twining habit. The bean has a nondominant main root which is very quickly supplemented by lateral roots. The roots can reach a depth of one meter if the soil is suitable [42]. In the past, common bean leaves were used by dropping them in infested areas to capture bed bugs after using them the leaves were destroyed or burned. This capturing power was analyzed, by microscopy, it revealed the presence of tiny sharp needles on the surface capable of piercing the integument of the legs of bedbugs, and these are the trichomes). The imprisonment and death of bedbugs is therefore purely physical [43].

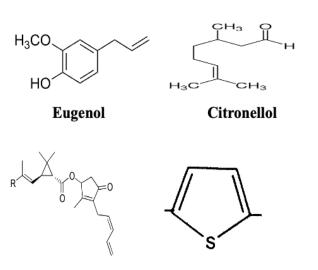
Origanum vulgaris: A perennial herbaceous plant that measures 30 to 80 cm high, with fragrant foliage and flowers when crushed. It is thus recognizable by its odor and its phenolic, spicy and hot flavor [44]. It grows from sea level to 4000 m altitude, mainly on limestone substrates and flowers from May to October. The aerial parts die during the bad season, and the plant can therefore start again from renewal buds [45]. It is a plant that is often slightly reddish-purple and is covered with hairs. Oregano is a plant with erect stems, generally hairy, sometimes glabrous. They have leaves with entire or toothed edges. Oregano essential oil contains carvacrol (61.9%), which is the majority component followed by p- cymene (25.2%) and g- terpinene (2.24%) [46]. This 39% oil gives 99% bed bug repellency in the petri dish test, it has been used against 4th and 5th instar nymphs and bed bug adults using a rabbit and human host [47].

Tagetes patula L: Marigold is an annual or perennial plant. Its stems are erect, glabrous, or hispid, with opposite branches erect in the upper part. Leaves all stem opposite, External flowers feminine or absent with short yellow, white or orange ligule, tubular internal flowers. In the essential oil of T. patula, 21 compounds were identified, and α - terthienyl (43.1%), pentatriacontane (23.9%) and 2-ethyl-l-dodecanol (7.9%) %) are the main constituents [48]. The phytochemical constitution of the essential oil attests to a rich composition of monoterpenes, sesquiterpenes, and secondary metabolites closely linked to the insecticidal potential [49]. Most reports indicate that these compounds exhibit inhibitory effects, growth retardation, maturation damage, reduction of reproductive capacity, appetite suppression or direct toxicity [49]. Thus, we find that its essential oil is reported in studies giving maximum mortality and repellency of up to 100% [30].

Cinnamonum camphora: Also called camphor, it is a tree that can reach 15 to 40 meters high, although it rarely exceeds 20 meters in Europe. Its longevity is of the order of a thousand years [50]. The trunk is branched at the base, and has rough, chapped bark. The fragrant camphor tree (*Cinnamonum camphora*) and its products, such as camphor essential oil, have been coveted since ancient times. Having a rich history of traditional use, it was particularly used as a fumigant [51].

OH

Camphor essential oil is extracted from the bark of the camphor tree. The distillation of this bark gives an essence. This is sublimated a certain number of times, to obtain a very aromatic white crystallized product: crystallized camphor. The latter must be mixed with other vegetable oils to be able to use it. The benefits of camphor essential oil are mainly explained by its high content of camphor, monoterpenes, and terpene oxides [52]. Indeed, camphor essential oil owes its action to monoterpenes which give it toxic effects (fumigants and contact toxicity), repellent, anti-feedant, ovicidal and sterilizing effects against bedbugs [53].



alpha- terthyenyl

Figure 1: Chemical structures of certain molecules

Pyrethrin

DISCUSSION

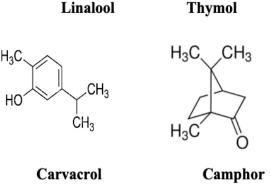
The analysis of the data that we collected concerning the plants and EOs most cited for their effectiveness studied against bedbugs allowed us to classify their effects into four main mechanisms of action summarized in (Table 2). We subsequently discuss each of these mechanisms.

Topical toxicity: According to the studies that we have cited for oregano and thyme, it clearly appears that their common mechanism of action is exerted by topical activity due to the most predominant components, namely carvacrol and thymol, which have two properties major [13.54]:

- Saturated compounds (carbon-carbon single bonds outside the benzene cycle)

- Presence of functional hydroxyl groups, on the benzene ring

These structural properties allowed thymol and carvacrol, after undergoing slight detoxification, to quickly penetrate through the cuticle and interact effectively with their target sites [13,54,55]. Lipophilicity of essential oil compounds is another important property that plays a role in penetration through the insect cuticle [50]. Therefore, the plant essential oils of thyme (Thymus vulgaris L.) and oregano (Origanum vulgare L.), which contain large amounts of thymol and carvacrol, respectively, can be included in the formulation of natural insecticide products. Eucalyptol and eugenol also in one study showed topical toxicity towards bedbugs, but with resistance for adult males [56].



HO

Physical toxicity: Artichoke leaves have tiny hairs that attach to the exoskeleton of bed bugs. A bean leaf barrier therefore traps bedbugs, which eventually die. Researchers are trying to reproduce by synthesis this type of trap naturally present in bean leaves but have not succeeded in reproducing its effectiveness [43]. If researchers could synthesize a comparable leaf, it could be an effective alternative biological tool to use in combination with other techniques.

Neurological toxicity: We can differentiate between two types:

- 1. A neuro-inhibition is exerted by the essential oils of plants (oregano, thyme, clove) due to the action at the level of possible target sites for the components: thymol, eugenol and carvacrol, respectively on gamma -amino butyric acid (GABA), octopamine / tyramine and nicotinic acetylcholine (nACh) receptors [57-58].
- Neuroexcitation has been reported in studies for EOs from lavender, pyrethrum flower and camphor plants containing linalool, pyrethrum derivatives and camphor respectively [18].

Linalool produced neuroexcitatory effects on the nervous system of bedbugs. Studies report that linalool acts as a reversible competitive inhibitor of the acetylcholinesterase enzyme [59]. Synthetic pyrethroid derivatives modify the gating characteristics of potential-sensitive sodium channels which result in a delay in their closure and thus cause a neuroexcitatory effect on the insect nervous system [60]. The same effect was noticed in lemongrass [36]. Camphor has been shown to inhibit catecholamine secretion by blocking acetylcholinesterase nACHR in bovine adrenal chromaffin cells [61]. Finally, molecular modeling studies suggest that the main compounds in the essential oils of *Tagetes patula L*. such as terthyenyl competitively inhibit acetylcholinesterase of C. lectularius [19].

Toxicity by fumigation: A study on the constituents of essential oils of plants: thyme, oregano, lavender, camphor shows that thymol was the most powerful, followed by carvacrol, linalool and camphor [17]. Indeed, thymol was more potent as a fumigant than any other essential oil constituent tested in this study. Therefore, thymol or thymol-containing essential oils have the potential to be used as fumigants to control bedbugs in the field. The behavior of

adult females, which lay eggs in isolated places, justifies the adoption of a more practical approach such as fumigating or fogging bedbug-infested objects by enclosing them in plastic bags with paper or a cloth impregnated with essential oils containing thymol [17,18].

Camphor has great potential for development as an alternative green commercial insect repellent to replace harmful synthetic agents currently in use [62]. Monoterpenes exert toxic (fumigant and contact toxicity), repellent, antifeedant, ovicidal and sterilizing effects against bedbugs [53]. A synergistic interaction between these monoterpenoids has been demonstrated by previous studies [63], which may provide information on the oily constituents that can be formulated together in botanical insecticide products, such as increased cuticular penetration and also great alteration of the nerve triggering activity [64].

Mechanism of action of bedbug toxicity	Plant or HE	Active molecule	References
Topical	Oreganum vulgare L.	Carvacrol	47,13,54,55
-	Thymus vulgaris	Thymol	13,30,54,55
	Corymbia citriodora	Eucalyptol, Geraniol	31
Mechanics (physics)	Phaseolus vulgaris	-	43
Neurological			
Neuro-inhibitory	Oreganum vulgare L.	Carvacrol	57.58
-	Thymus vulgaris	Thymol	30,57,58
	Syzygium aromaticum (L)	Eugenol	16,57,58
Neuro-excitatory	Lavandula latifolia spica	Linalool	18,30,59
	Chrysanthenum Cinerariafolium	Pyrethrin	40,18,60
	Cinnamomum camphora	Camphor	18,53,61
	Tagetes patula L.	Alpha- terthyenyl	30,49,19
	Cymbopogon winterianus jowitt	Citronellol	31.36
Fumigant	Thymus vulgaris	Thymol	18,17,30
-	Oreganum vulgare L.	Carvacrol	17
	Lavandula latifolia spica	Linalool	17.30
	Cinnamomum camphora	Camphor, monoterpene	17,51,53,62
	Cymbopogon winterianus jowitt	Citronellol	31.17

CONCLUSION

This present review summarizes the current knowledge available on the toxic potential: neurological, physical, fumigant and topical of the plants and EOs most studied for their effects against bed bugs. The studies indexed on the Scopus database, and which we have included in this review provide relevant scientific data which make it possible to elucidate the precise mechanism of action of the action observed against the bed bugs of these plants or HE. The major interest of our development is therefore to guide the research and development of effective insecticides of natural origin against these harmful insects. The use of preparations of natural origin has the advantage of avoiding the toxic and polluting harm of substances of chemical and synthetic origin. It is also desirable to continue research and investigation of the precise composition of its plants and EOs in order to extract and possibly purify the active molecules at the origin of their mechanisms of action.

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