Journal of Pharmacognosy and Phytotherapy Vol. 1(5) pp. 052-063, November, 2009
Available online at http://www.academicjournals.org/jpp

Review

A review on prospects of essential oils as biopesticide in insect-pest management

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Accepted 29 September, 2009

Plant essential oils in general have been recognized as an important natural source of pesticides. They represent a market estimated at US $700.00 millions and a total world production of 45,000 tons. The genera capable of elaborating the compounds that constitute essential oils are distributed in a limited number of families but the widespread range of activities of essential oils is being considered for both industrial and household uses. Essential oil compounds and their derivatives are considered to be an alternative means of controlling many harmful insects and their rapid degradation in the environment have increased specificity that favours beneficial insects. Essential oils based commercial products are being developed for a wide range of human and animal uses, including pest control. Unfortunately, most of the natural products used for pest control, are not always subject to rigorous testing. In view of the above points, the present paper focuses on the work done in the field of essential oils as biopesticides with special emphasis on essential oil chemistry, extraction, pesticidal properties, mode of action, synergism, phytotoxicity, commercialization prospects, safety aspects, socioeconomic impacts and sustainability.
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Key words: Essential oil, insecticide, repellent, phytotoxicity, safety, economics.

INTRODUCTION

Essential oils are volatile natural complex secondary metabolites characterized by a strong odor and have a generally lower density than that of water (Bruneton, 1999; Bakkali et al., 2008). There are 17,500 aromatic plant species (Bruneton, 1999) among higher plants and approximately 3,000 esential oils are known out of which 300 are commercially important for pharmaceuticals, cosmetics and perfume industries (Bakkali et al., 2008) apart from pesticidal potential (Franzios et al., 1997; Chang and Cheng, 2002).

They are lipophilic in nature and interfere with basic metabolic, biochemical and physiological and behavioural functions of insects (Brattsten, 1983). Genera capable of elaborating the compounds that constitute essential oils are distributed in a limited number of families, such as Myrtaceae, Lauraceae, Rutaceae, Lamiaceae, Asteraceae, Apiaceae, Cupressaceae, Poaceae, Zingiberaceae and Piperaceae.

Essential oil compounds and their derivatives are considered to be an alternative means of controlling many harmful insects and their rapid degradation in the environment have increased specificity that favours beneficial insects (Pillmoor et al., 1993). Recent research has demonstrated their larvicidal and antifeedant activity (Gbolade, 2001; Adebayo et al., 1999; Larocque et al., 1999), capacity to delay development, adult emergence and fertility (Marimuth et al., 1997), deterrent effects on oviposition (Naumann et al., 1995; Oyedele et al., 2000), and arrestant and repellent action (Landolt et al., 1999). Despite these most promising properties, problems related to their volatility, poor water solubility and aptitude for oxidation have to be resolved before they are used as an alternative pest control system (Moretti et al., 2002).

Although a number of review articles have appeared in the past on the various aspects of essential oils bio-activities (Saxena and Koul, 1978; Gora et al., 1988; Brud and Gora, 1989; Inagaski, 1989; Klocke and Barnby, 1989; Sharma, 1993; Singh and Upadhyay, 1993; Xu and Chiu, 1994; Regnault-Roger, 1997; Tripathi et al., 1999; Isman, 2000; Kumbhar et al., 2000; Bindra et al., 2001; Peterson and Coats, 2001; Singh et al., 2001; Kumbhar and Dewang, 2001; Tripathi, 2004; Isman et al., 2007;

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Bakkali et al., 2008) but the present paper emphasizes on sustainability, safety and economics of essential oils in insect-pest management.

ESSENTIAL OIL CHEMISTRY

The volatile components of essential oils can be classified into four main groups: terpenes, benzene derivatives, hydrocarbons and other miscellaneous compounds (Haagen-Smit, 1948; Ngoh et al., 1998). Monoterpenoids are the most representative molecules constituting 90% of the essential oils and allow a great variety of structures with diverse functions. They are ten carbon hydrocarbon or their related compounds such as acyclic alcohols (e.g. linalool, geraniol, citronellol), cyclic alcohols (e.g. menthol, isopulegol, terpeniol), bicyclic alcohols (e.g. borneol, verbenol), phenols (e.g. thymol, carvacrol), ketones (carvone, menthone, thujone), aldehydes (citronellal, citral), acids (e.g. chrysanthemic acid) and oxides (cineole). The main group is composed of terpenes and terpenoids and the other of aromatic and aliphatic constituents, all characterized by low molecular weight terpenes mainly the monoterpenes (C10) and sesquiterpenes (C15), but hemiterpenes (C5), diterpenes (C20), triterpenes (C30) and tetraterpenes (C40) also exist. Aromatic compounds occur less frequently than the terpenes and are derived from phenylpropane e.g. aldehyde: cinnamaldehyde; alcohol: cinnamic alcohol; phenols: chavicol, eugenol; methoxy derivatives: anethole, elemicine, estragole, methyl eugenols; methylene dioxy compounds: apiole, myristicine, safrole.

ESSENTIAL OIL EXTRACTION

Composition of oil varies to a large extent depending on the isolation method used. The chemical profile of the essential oil products differs not only in the number of molecules but also in the stereochemical types of molecules extracted. Steam distillation is the procedure most frequently used to isolate essential oils by Clevenger-type apparatus. However, distillation may influence the composition of the oil isolated, because isomerization, saponification and other reaction may occur under distillation conditions. The other methods of isolation of essential oils are solvent extraction, simultaneous distillation extraction, supercritical carbon dioxide and microwave ovens. The extraction product can vary in quality, quantity and in composition according to climate, soil composition, plant organ, age and vegetative cycle stage (Masotti et al., 2003; Angioni et al., 2006).

PESTICIDAL PROPERTIES

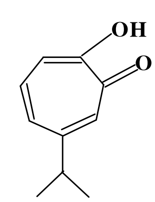
The toxic effect of essential oils, apart from the variability of phytochemical patterns, involves several other factors. The point of entry of the toxin is one of them. Commonly, essential oils can be inhaled, ingested or skin absorbed by insects (Ozols and Bicevskis, 1979). Survey of the literature on biopesticidal potential of essential oils from the year 2000 onwards indicates that the plants of families Myrtaceae, Lamiaceae, Asteraceae, Apiaceae and Rutaceae are highly targeted for anti-insect activities against specific insect ordrers like lepidoptera, coleoptera, diptera, isoptera and hemiptera. Essential oils have been explored for repellent, fumigant, larvicidal and adulticidal activities against the insects of the above orders.

Essential oils of *Artemisia* species have been reported for vapour toxicity and repellent activity against coleopteran beetles (*Sitophilus* sp., *Tribolium castaneum* and *Callosobruchus maculatus*) (Tripathi et al., 2000; Kordali et al., 2006; Negahban et al., 2007). Similarly, essential oils of *Cinnamomum camphora*, *C. cassia* and *C. zeylanicum* have been found to have repellent action against mosquitoes (Prajapati et al., 2005; Kim et al., 2003). Chaiyasit et al (2006) determined toxic effect of essential oil of *Curcuma zedoaria* with LC_{50} ranging from 5.44 - 8.52 µg/mg of mosquito adults.

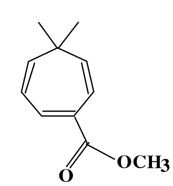
β-Ocimene is repellent to the leaf cutter ant, *Atta cephalotis* in both field and laboratory experiments (Harborne, 1987). Experiments with the aphid *Carvariella aegopodii*, which feeds on umbelliferae species in summer, indicate that the aphid can be captured in traps baited with carvone, but is repelled by linalool (Chapman et al., 1981; Harborne, 1987). Carvone occurs in the essential oils of several plants of the Apiaceae.

A number of monoterpenes and methyl esters of fatty acids were evaluated for their repellent and attractant properties towards *Denroctonus* species. Although activity was observed in the laboratory, none of the compounds tested were active in field tests (Seigler, 1983).

The wood of Western red cedar (*Thuja plicata*) is renowned for its ability to withstand insect attack in timberstands and as lumber. This may be attributed to the presence of a monoterpene β-thujaplicin which is toxic to larvae of the old house borer (*Hylotrupes bajulus*). Both α and β-thujaplicine showed low activity against the termite, *Reticulothermes flavipes*. Interestingly, methyl thujate was much more active. This compound is active against a number of other insects. (+)-3-thujone and (-)-3-isothujone, which make up most of the leaf essential of this plant (80 - 90%) are feeding deterrents to the white pine weevil (*Pissodes strobe*) (Alfaro et al., 1981).



β-thujaplicin



Methyl Thujate

Cineole, geraniol and piperidine found in Bay leaves (*Laurus nobilis*, Lauraceae) possess repellent properties towards cockroaches (Verma and Meloan, 1981). Female carribean fruit flies, *Anastrepha suspense*, lay their eggs readily in ripe grape fruit but do not oviposit in immature grape fruit because of the presence of linalool, which is toxic to the eggs and larvae of insects. Limonene found in sour oranges (*Citrus aurantium*) is toxic to adult bean weevils (*Callosobruchus phasecoli*), but highly attractive to male mediterranian fruit flies (Jacobson, 1982).

MODE OF ACTION OF ESSENTIAL OILS

Most monoterpenes are cytotoxic to plants and animal tissue, causing a drastic reduction in the number of intact mitochondria and golgi bodies, impairing respiration and photosynthesis and decreasing cell membrane permeability. At the same time they are volatile and many serve as chemical messengers for insects and other animals. Furthermore, most monoterpenes serve as a signal of relatively short duration, making them especially useful for synomones and alarm pheromones. The doses of essential oils needed to kill insect pests and their mechanism of action, are potentially important for the safety of humans and other vertebrates. The target sites and mode of action have not been well elucidated for the monoterpenoids and only a few studies have examined this question (Watanabe et al., 1990; Rice and Coats, 1994; Lee et al., 1997).

As insecticide

Little is known about the physiological actions of essential oils on insects, but treatments with various essential oils or their constituents cause symptoms that suggest a neurotoxic mode of action (Coats et al., 1991; Kostyukovsky et al., 2002). A monoterpenoid, linalool has been demonstrated to act on the nervous system, affecting ion transport and the release of acetylcholine esterase in insects (Re et al., 2000).

Octopamine has a broad spectrum of biological roles in insects, acting as a neurotransmitter, neurohormone and circulating neurohormone - neuromodulator (Evans, 1980; Hollingworth et al., 1984). Octopamine exerts its effects through interaction with at least two classes of receptors which, on the basis of pharmacological criteria, have been designated octopamine-1 and octopamine-2 (Evans, 1981). Interrupting the functioning of octopamine results in total break down of nervous system in insects. Therefore, octopaminergic system of insects represents a biorational target for insect control (Figure 1).

The lack of octopamine receptors in vertebrates likely accounts for the profound mammalian selectivity of essential oils as insecticides. A number of essential oil compounds have been demonstrated to act on octopaminergic system of insects (Enan et al., 1998).

Enan (2005) showed that eugenol mimicked octopamine in increasing intracellular calcium levels in cloned cells from the brain of *Periplaneta americana* and *Drosophila melanogaster* and this was also found to be mediated via octopamine receptors. Furthermore, the toxicity of eugenol was increased in mutant *D. melanogaster* that were deficient in octopamine synthesis, suggesting that the toxicity is mediated through the octopaminergic system, though this was not the case for geraniol. It was suggested that these cellular changes induced by eugenol are responsible for its insecticidal properties (Price and Berry, 2006). Kostyukovsky et al. (2002) reached a similar conclusion, suggesting possible competitive activation of octopaminergic receptors by essential oil constituents; they found significant effects at low concentrations in abdominal epidermal tissue of *Helicoverpa armigera*.

As repellent

It is unclear if repellents work by common mechanisms in different arthropods, and conflicting evidence exists in the literature. For example, tick detects repellents on the tarsi of the first pair of legs (Haller's Organ) and insects detect the same substances on the antennae. Furthermore, the difference in sensitivity to the same repellent between different classes, orders and families are differences of degree only; no fundamental difference in type of response are observed (Rutledge et al., 1997). However, degree of differential sensitivity were stable over several generations in mosquitoes, indicating a genetic, heritable basis of tolerance (Rutledge et al., 1985). Hairs on the mosquito antennae are temperature and moisture sensitive. The repellent molecules interact with the female mosquito olfactory receptors, thereby blocking the sense of smell. Very little is known about the receptors responsible for the repellent responses in cockroaches. Oleic acid and linoleic acid have been indicated in death recognition and death aversion (repellency) in cockroaches and the term 'necromone' has been proposed to describe a compound responsible for this type of behaviour (Rollo et al., 1995).

As fumigant

Well known essential oils with bioactivity, either as an insecticide or repellent, are clove, thyme, mint, lemon grass, cinnamon, rosemary and oregano oils. Bioactivity can vary greatly because of variability in chemical composition but despite of these variabilities, certain plant species, namely thyme, oregano, basil, rosemary and mint, are consistently bioactive (Isman and Machial, 2006).

Elucidation of mode of action of essential oils is important

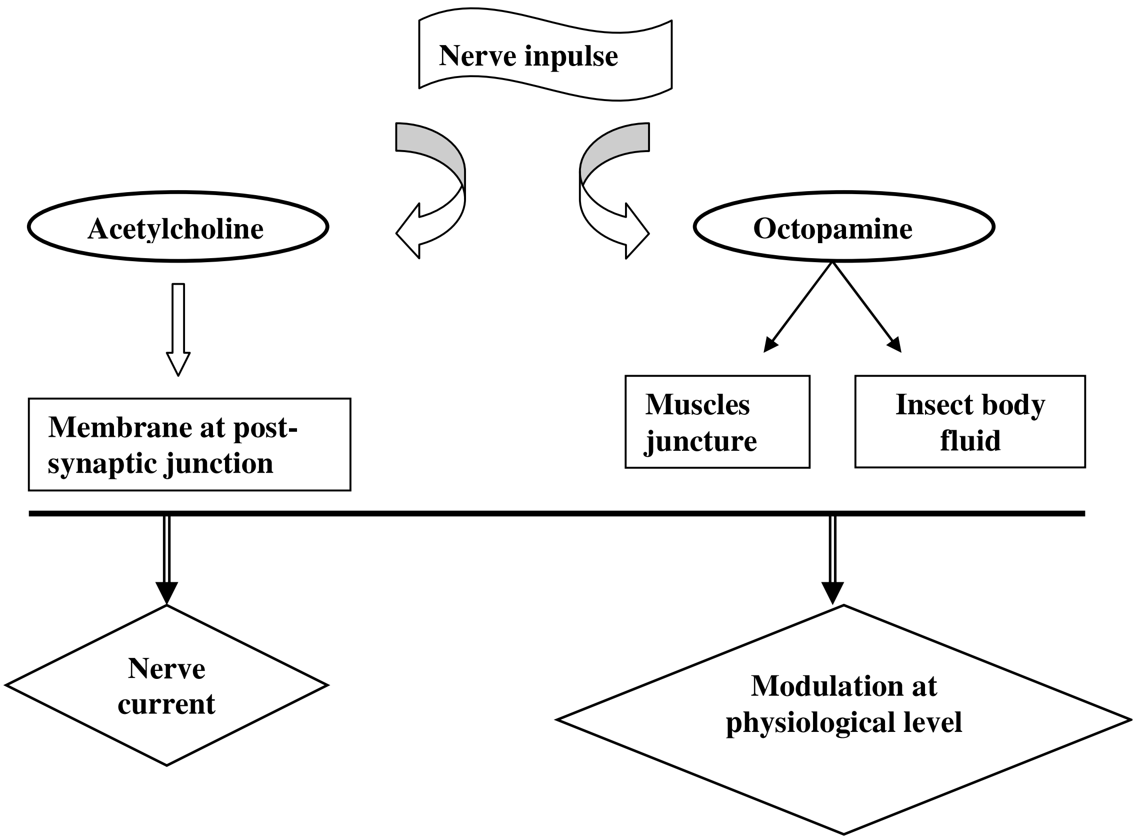


Figure 1. Target sites in insects as possible neurotransmitter mediated toxic action of essential oils.

for insect control because it may give useful information on the most appropriate formulation, delivery means and resistance management (Sim et al., 2006). Many plant essential oils and their isolates have fumigant action (Kim et al., 2003). Esential oil of *Artemisia annua* (Tripathi et al., 2000), *Anethum sowa* (Tripathi et al., 2001), *Curcuma longa* (Tripathi et al., 2002), *Lippia alba* (Verma et al., 2001) and isolates like d-limonene (Tripathi et al., 2003a), carvones (Tripathi et al., 2003b) and 1,8-cineole (Aggarwal et al., 2001a) have been well documented as fumigants. These findings indicate that the route of action for the oils was largely in the vapour phase via respiratory system, although the exact mode of action of these oils remains unknown.

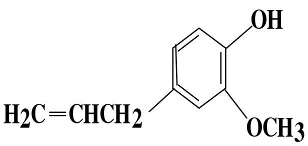
There are no established natural fumigants in use against pests attacking grains, dry stored food and other agricultural products. Fumigants in use today are phosphine, methyl bromide and DDVP (2,2-dichlorovinyl dimethyl phosphate). Phosphine is the major cause of suicidal deaths in India, whereas methyl bromide as compound with ozone-depleting potential (UNEP, 2000) and DDVP used for space treatment has a possible human carcinogen potential (Lu, 1995). Thus, there is urgent need to develop safe alternative that have the potential to replace the toxic fumigants, yet they should be simple and convenient to use. Many aromatic plants have capacity to synthesize chemicals which, when isolated, are deadly or repellent to many insect species but harmless to mammals.

Physical properties of essential oils such as high boiling point, high molecular weight and low vapour pressure are barriers for application in large scale fumigation (Daglish, 2006). Although essential oils have the potential for small scale treatments and space fumigation, but there is lack of data for single or multiple components of essential oils on sorption, tainting and residues in food commodities (Rajendran and Sriranjini, 2008).

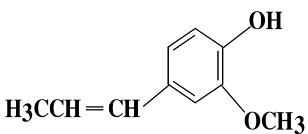
STRUCTURE-ACTIVITY RELATIONSHIPS

The structural modifications of natural monoterpenoids may lead to improved biological activity (Kumbhar and Dewang, 1999). The biological activities of natural products as well as monoterpenoids are related to functional groups. The activities are dependent upon nature and position of the functional groups and molecular configuration rather than volatility and molecular size (Kumbhar and Dewang, 2001). Through the establishment of structure-activity relationships with the knowledge of required functional group, optimal structure can be elucidated through biorational design of the derivatives on the basis of bioassays.

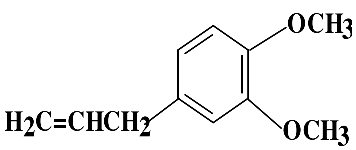
Ngoh et al. (1998) evaluated nine essential oil constituents comprising benzene derivatives and terpenes for toxic properties against *P. americana*. They found that benzene derivatives (eugenol, isoeugenol, methyl eugenol, safrole and isosafrole) are generally more toxic and repellent to *P. americana* than the terpenes (cineole, limonene, p-cymine and α-pinene). As evident from the following figure, the distance of the side chain double bond from the aromatic ring and the substitution of the methoxy group of theses compounds appeared to be important determinants of their toxicity and repellency as evident from the structure of eugenol and its analogues isoeugenol and methyl eugenol.



Eugenol

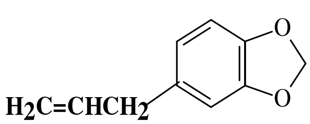


Isoeugenol

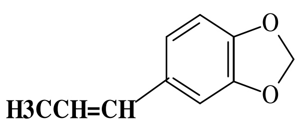


Methyleugenol

Furthermore, in this group of compounds, the additional methoxy functional group in methyl-eugenol increases the knockdown capability without significantly affecting its lethality. Similarly, fumigant activity decreases when the side chain double bond is



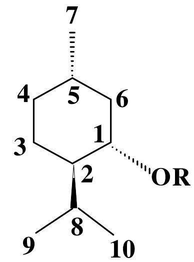
Safrole



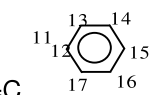
Isosafrole

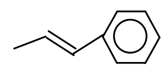
closer to the aromatic ring (isosafrole), therefore ring closure (safrole and isosafrole) appears to be also important for fumigant toxicity. It appears that benzene derivatives are more toxic and repellent than monoterpenes.

Further, Aggarwal et al. (2001b) evaluated L-menthol isolated from *Mentha arvensis* and seven of its acyl derivatives for bioactivities against four stored product insects. They observed that the number of methyl group in the side chain was a significant factor in the observed activity among the derivatives as compared to L-menthol. As the number of methyl groups on the side chain increases, there is a decrease of positive charge on the



1. L-menthol, R = H; **2.** L-menthyl formate, R = OCH; **3.** L-menthyl acetate, R = $COCH_3$; **4.** L-menthyl propionate, R = $COCH_2CH_3$; **5**. L-menthyl butyrate, R = CO $(CH_2)_2CH_3$
6. L-menthyl isovalerate, R = $COCH_2CH\ (CH_3)_2$

7. L-menthyl benzoate, R = O=C 

8. L-menthyl cinnamate, R=OC 

(L-Menthol and its derivatives)

carbon atom attached to the oxygen atom due to electron donating (nucleophilic) character of methyl group. The activity of the functional carbon atom in the chain decreases with reduction of its electrophilic character. Due to absence of a methyl group in methyl formate, the positive charge of the carbon atom attached to oxygen remains high. In case of menthyl acetate, one methyl group is attached to the side chain, which causes slight decrease in positive charge. Menthyl propionate has two methyl groups, which decreases the positive charge on the carbon atom even further. A possible reason for lack of activity displayed by menthyl benzoate may be the absecnce of methyl group and presence of a benzene ring attached directly to the menthyl carbon atom. Menthyl cinnamate was found to be moderately active and this may be due to presence of double bond and benzene ring not being directly attached to the carbon atom.

Synergistic action of essential oils

Concerning pesticide activity, the aim of creating synergistic combinations is to reduce the dose of potentially polluting substances and reduce the risk of developing resistance. A broad array of pest-repellent products, including homemade herbal teas, plant extracts and fermentation products and industrial clay and rock powder products (e.g. kaolin) are authorized for use in organic agriculture. Nevertheless, the use of homemade products has declined in recent years because of the commercialization of standardized industrial products (Isman, 2006). Sinzogan et al. (2006) found that damage to cotton by the bollworm, *Helicopverpa armigera* (Hubner), can be minimised by mixtures of coventional insecticides at one half the recommended rate by combining extracts of three local plants (*Azadirachta indica, Khya senegalensis*, and *Hyptis suaveolens*) which provided greater efficacy than the conventional products alone at their recommended rate. However, none of the plant extracts alone provided adequate crop protection. Such a direct demonstration of the utility and value of botanical preparations increased the farmers confidence in indigenous technology (Isman, 2008).

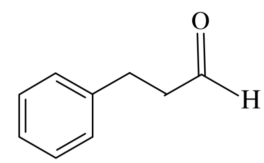
The synergistic rationale for using combination products looks to producing a dynamic product that has multiple modes of action, respecting the principle that the action of the combined product is greater than the sum total of known and unknown chemical components. Both positive and negative synergism can occur between the essential oil or their components and the other ingredients present in the total formulation. This is an important factor to take into account as one can create a synergy between essential oils that can subsequently be negated by the base product. The pH and the salinity of base may also significantly impact the activity of the essential oil.

Several studies (Lachowicz et al., 1998; Tassou et al., 1995) have confirmed that a low pH and saline (5% NaCl) environment can potentiate the activity of the whole product. Essential oils combinations such as thyme, anise and saffron have been demonstrated for synergistic activity (Youssef, 1997). Hummelbrunner and Isman (2001), reported that mixtures of different monoterpenes produced a synergistic effect on mortality, and they developed a proprietary monoterpene mixture containing 0.9% active ingredient for use against foliar feeding pests.

Monoterpenoids are targeted to the insect selective octopaminergic receptor. On the basis of their insect selectivity, a mixture of essential oil trademarked hexahydroxyl (EcoPCO EcoSMART Technologies, Franklin, Tennessee) and based on distinct combinations of different plant essential oils that significantly enhance the activity of these oils against insect was formulated. This patented technology demonstrates rapid insecticidal activity by combining oils with common molecular structure (a six membered carbon ring with an oxygenated functional group attached) and since they are directed at octpaminergic sites, they are also classified as Generally Recognized as Safe (GRAS) and have been approved for food and breverage consumption by US Food and Drug Administration (FDA) (Isman and Akhtar, 2007).

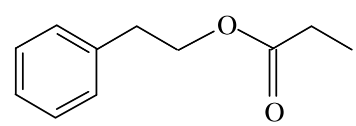
COMMERCIALIZATION OF ESSENTIAL OIL-BASED PESTICIDES

The most attractive aspect of using essential oils and/or their constituents as crop protectants is their favorable mammalian toxicity because many essential oils and their constituents are commonly used as culinary herbs and spices, pesticide products containing certain of these are actually exempt from toxicity data requirements by the Environmental Protection Agency, USA (EPA). Some American companies have recently taken advantage of this situation and have been able to bring essential oil based pesticides to market in a far shorter time period than would normally be required for a conventional pesticide. Mycotech Corporation produces CinnamiteTM, an aphidicide/miticide/fungicide for glasshouse and horticultural crops and ValeroTM, a miticide/fungicide for use in grapes, berry crops, citrus and nuts. Both products are based on cinnamon oil, with cinnamaldehyde (30% in EC formulations) as the active ingredient.



Cinnamaldehyde

EcoSMART Technologies as mentioned above is aiming to become a world leader in essential oil-based pesticides. They currently produce aerosol and dust formulations containing proprietary mixtures of essential oil compounds, including eugenol and 2-phenethyl propionate aimed at controlling domestic pests (cockroaches, ants, feas, fies, wasps, etc.). Commercial success with these products based on well-known chemistry will likely provide an impetus for the development and commercialization of future pesticides based on more exotic essential oils with even greater potency (Shaaya and Kostjukovsky, 1998).



2-Phenethyl propionate

Several essential oil constituents are already in use as an alternative to conventional insecticides. For example, d-limonene is an active ingredient of commercially available flea shampoos, pulegone and citronellal are used as mosquito repellents, 1- 8, cineole is the structural base of the herbicide cinmethylin. These constituents are favourable for development as environmentally friendly safe insect control agents because of their insect toxicity and repellency, low mammalian toxicity and biodegradability.

The essential oil based repellents are designed as topical preparations or combustible products that are able to protect the user or environment from harmful insects (Oyedele et al., 2000). Many commercial products like Buzz Away® (containing oils of citronella, cedarwood, eucalyptus and lemongrass), Green Ban® (containing oils of citronella, cajuput, lavender, safrole free sassafrass, peppermint and bergaptene free bergamot oil) and Sin-

So-Soft® (containing various oils and stearates), although effective but failed in scientific validation in an olfactometer assay against *Aedes aegypti* (Chou et al., 1997).

Therefore, natural ingredients must be scientifically validated for their activity, efficacy and safety before making any formulations. Three barriers to the commercialization of new products of this type were identifed: (i) the scarcity of the natural resource; (ii) the need for chemical standardization and quality control; and (iii) difficulties in registration.

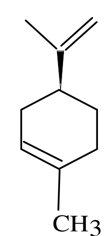
Formulation of essential oil based product is an important area of concern. The choice of formulation is influenced by several factors, such as the physical, chemical and biological properties of the pesticides and the mode of applications. Controlled released formulations allow smaller quantities of pesticides to be used and are highly effective over a given period of time (Kydonieus, 1980). Encapsulation process is suitable method for entrapping essential oil of a very different chemical compositon.This method reduces loss of the active principles, leading to high loaded microparticles that offer protection against environmental agents and also offers the possibility of controlled drug release (Moretti et al., 2002). Essential oils can also be incorporated with polymers into sheets. Attractant adhesive films with essential oils were prepared to control insects in agriculture and horticulture (Klerk, 1990).

PHYTOTOXICITY AND SAFETY OF ESSENTIAL OILS

Natural products are not always safer than synthetic pesticides. Just because a plant has been used for centuries does not mean it is safe or even desirable (Hinkle, 1995). Phytotoxicity of essential oils requires serious attention when formulating products for agricultural and landscape use (Lindberg et al., 2000). Interest in natural products is growing rapidly. Given the size of the market, an increasing interest in all natural, it is not surprising that commercial products are being developed for a wide range of human and animal uses, including pest control. Unfortunately, most of the natural products used for pest control, are not always subject to rigorous testing. Repellents may have an increasingly important role in eliminating insects from certain environments such as schools, hospitals and food preparation areas. Many of the commercial products including essential oils are included on the GRAS list fully approved by FDA and EPA in USA for food and brevarage consumption (EPA, 1993). However, this does not ensure that the preparation or product will function effectively as formulated or advertised by a specific producer.

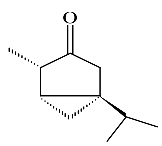
Many of the herbal products for pest control suffer from several non-trivial problems. The least important of these ranges from relatively minor misinterpretations to providing misinformation to the consumers. For example, a natural repellent such as oil of eucalyptus advertised for use against mosquitoes can serve as attractant for another blood feeding pest e.g. biting midges (Braverman et al., 1999). Plants produce a wide variety of insect toxins, many of which are dangerous to mammals as well as insects (D'Mello, 1997). Thus, simply assuming that natural is safe can be dangerous.

For example, the oil of tea tree, *Melaleuca alternifolia* has been used for centuries in Australia as traditional remedy for discomfort caused by insect bites (Budhiraja et al., 1999). The most active compounds in this oil are terpinen-4-ol, terpinene, 1,8-cineole and terpinolene. The International Standards Organization, ISO 4730 (ISO, 1996), mandates a minimum concentration of 30% for terpinen-4-ol and a maximum concentration of 1,8-cineole of 15% in the oil. This latter material is also one of the arthropod active ingredients in peppermint and rosemary essential oils (Veal, 1996). There have been several problems reported with the use of tea tree oil. The most common problematic response is contact dermatitis, with more than 30 human cases reported in the scientific literature in the 1990s (Hausen et al., 1999). This can be caused by fresh oil, but is enhanced by the formation of degradation products that develop with photodegradation in either open or closed containers (Hausen et al., 1999). These degradation product includes peroxides, epoxides and endoperoxides such as ascaridol. *Melaleuca* oil toxicosis in dogs and cats has been associated with depression, weakness, muscle tremours, and lack of co-ordination (Villar et al., 1994). Another bioactive compound d-limonene is a constituent of a number of essential oils like orange, lemon, mandarian and grapefruit (EPA, 1993). This compound is listed in US EPA's and GRAS list. As a pesticide, this compound can be found in flea dips for dogs and cats and pesticides used for indoor pest control. But d-limonene has been reported to cause dermatitis (Nilsson et al., 1999).

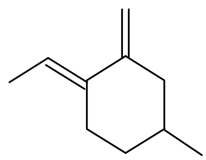


d-Limonene

It is hoped that repellent compounds may be applied at levels lower than those compounds that are acutely toxic thereby lowering the pesticide load on urban environment, but this hope is purely conjectural at this point. Further, essential oil of *Artemisia absinthium* contains active ingredient thujone which is potent neurotoxin impacting the gamma-amino butyric acid system (Hold et al., 2000). Similarly, essential oil of *Mentha pulegium* is widely used as insect control agent and contains an active ingredient pulegone. Pulegone, upon ingestion is oxidized by cytochrome P-450 system into toxic metabolited including toxic metabolites including methofuran (Nelson et al., 1992). These metabolites bind to proteins (Thomassen et al., 1992) causing loss of organ function, seizures, acute poisoning and death (Burkhard et al., 1999). Therefore, such uses are not advisable.



Thujone



Pulegone

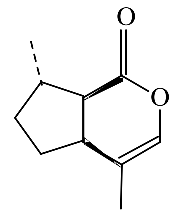
EFFECT OF ESSENTIAL OILS ON INDOOR AIR QUALITY

Monoterpenes with one or more unsaturated carbon-carbon bonds may also easily interact with oxidants such as ozone, hydroxyl and nitrate radicals in the general environment and generate consequently a variety of secondary organic pollutants in gas and particle phase (Weschler, 2000). The oxidation products of terpenes such as d-limonene, α-pinene and linalool have been characterized by atmospheric chemists to include a number of higher molecular weight oxidation products include aldehydes, ketones, organic acids and diacids (Shu et al., 1997; Reissell et al., 1999).

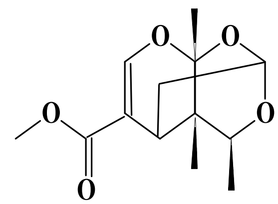
One major product derived from reaction between oxidants and terpenes is formaldehyde and serial studies have shown ozone/terpene reaction are important sources of secondary air pollutants including secondary hydroscopic organic aerosols which are mainly of sub-micron particles (Sarwar et al., 2004; Iinuma et al., 2004). These oxidation products have attracted rising concerns as many of them seem to be more irritating than their precursors (Wolkoff et al., 2000) and fine to ultrafine particles are known to penetrate into lower respiratory system more easily. Thus, evaporating essential oils could be another hidden source of indoor terpenes and deserve more attention for its potential impact on indoor air quality.

ESSENTIAL OILS TRENDS AND DEVELOPMENT

Examination of some recent patents involving essential oils showed that a majority of the inventions have focused on household uses. Some patents are also devoted to the protection of domestic animals. A large number of the patents have been assigned to the preservation of clothes from moths and beetles. Beside these domestic uses, essential oils present applications in agriculture and the food industry. Essential oils also showed some usefulness for building materials. A wood preservative solution mixed eucalyptus essential oils with pyrethroids and borax (Urabe, 1992). The resistance of

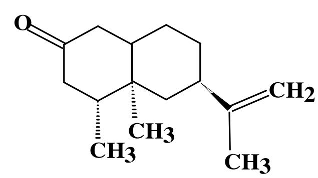


Nepetalactone

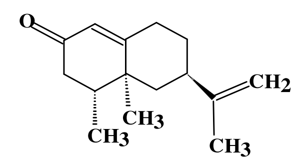


Dihydronepetalactone

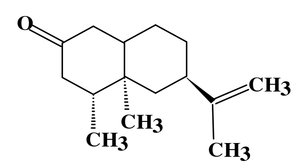
veneer-faced panels to insects is improved by a deep impregnation of the polymer layer with *Thujopsis dolobrata* essential oil (Akita, 1991; Tsubochi and Sugimoto, 1992). All these examples demonstrate the wide range of uses of essential oils. The most patented biorational repellent is based on nepetalactone and dihydronepetalactone from *Nepeta cataria* against cockroaches, mosquitoes, mites, ticks and other household insects (Hallahan, 2007; Scialdone and Liauw, 2006; Scialdone, 2006). Nootkatone from Vetiver oil and its derivatives, tetrahydronootkatone and 1,10-dihydronootkatone have



Nootkatone



1,10-dihydronootkatone



Tetrahydronootkatone

been patented as repellent against mosquitoes, cockroaches, termites and ants (Zhu et al., 2005; Henderson et al., 2005 a,b). Thyme oil and monoterpenoid like thymol, anethole, eugenol and citronellal combinations have been patented for pesticidal activity against cockroaches and green peach aphid (Bessette and Beigler, 2005, 2008; Ninkov, 2007). Similarly citronellal, cotronellol, citronellyl or a mixture of these have been patented as pest treat-ment composition against human louse (Ping, 2007).

ECONOMICS

Today essential oil represent a market estimated at US $700.00 millions and a total world production of 45,000 tons. Nearly 90% of this production is focused on mint and citrus plants (Verlet, 1993). Thus, the widespread range of activities of essential oils is being considered for both industrial and household uses. Essential oils are presently regarded as a new class of ecological products for controlling insect vectors. Therefore, development of safe and scientifically proven herbal products should be given priority.

Over the last 40 years, the market for pest management products for crop protection has shown a regular growth of 7 – 10% per year, a turnover of around 25 billion US dollars. This growth has been accompanied by a deep reorganization of the industrial sector, not only because of many takeovers and amalgamations of companies, but also because of modifications in the number and the nature of commercialized insecticidal molecules. Two factors contributed to this change: the expensive cost of commercialization licences and the numerous cases of ecotoxicity or toxicity of pesticides to mammals that occurred in the past.

Another economic aspect concerns producers of aromatic plants are continuous and bulk requirement of raw materials. To supply such large quantity of the herbs, large scale cultivation would be required, which in turn will generate good business opportunities and human resource development.

REGISTRATION OPPORTUNITIES FOR NATURAL PRODUCTS

Policies to reduce the use of plant protection products are being developed globally. To meet such objectives, viable low risk alternative products need to be developed and authorised. Until now the regulatory procedures based on synthetic chemical active substances have been regarded as a barrier to the commercialization of alternative products. Steps are being taken to encourage the development of natural plant extracts by proposing reduced data requirements. The Organisation for Economic Co-operation and Development (OECD), under the Pesticide Programme, has been working on the harmonisation of their plant protection product review procedures, sharing the evaluation of plant protection products and proposing policies for the reduction of risks associated with plant protection product use. The OECD has maintained its active role in this area, developing a guidance document for the preparation of a dossier to support pheromones and other semiochemicals (OECD, 2002). They recognise that semiochemicals act by modifying the behaviour of pest species rather than killing them and can be target specific. They are used at very low rates, are non-toxic and dissipate rapidly. Therefore, they can be regarded as low risk and the data requirements are not as enormous as for synthetic chemical substances.

Most promising potential for exploitation of these molecules as pest management agents lies in the synthesis of derivatives and analogues through simple synthetic procedures and environment friendly as well as remunerative approaches (Kumbhar et al., 2000). Such systematic derivatization of natural monoterpenoids based on structure-activity relationships warrants eva-luation both as sources and a model for new com-mercial pest management agents having natural base. Advantages of using monoterpenoids as lead compounds for new pest management agents is their bulk availability in plants (Kumbhar and Dewang, 2001).

ACKNOWLEDGEMENTS

The authors are thankful to Dr. P. S. Ahuja, Chairman, CSIR-Networking project on Development of Herbal Pesticides (Council of Scientific and Industrial Research, Ministry of Science and Technology, Government of India, New Delhi, India), for providing necessary funds, encouragement, defined directions and necessary facilities for the present work.

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