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Linalool Based Herbal Mosquito Repellent

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Abstract

The mosquito is one of humanity's most lethal enemies. One of the most effective interventions for lowering illness rates is protecting people from mosquito bites.. To ensure the continuation of many plant species, linalool also plays a crucial part in the intricate biology of pollination. In addition to being a precursor in the creation of vitamins A and E, linalool is a lead ingredient in the commercial manufacturing of a wide range of aroma compounds. These include geraniol, nerol, citral, and their derivatives. Linalool's use in environmentally friendly pest control is highlighted by the extensive research showing the molecule's repelling effects on a wide variety of crop-destroying insects. Most plants employ phytochemicals, which are found in their leaves, to ward against insect pests. This study efforts to produce herbal insect repellents that are both safe and effective. Insecticides derived from oranges have a long history. Most linalool has found uses in pest management. The essential oil has repelling properties. Limonene, a monoterpene that gives orange oil its distinctive odor and flavor and has repelling qualities. It can replace synthetic repellents because to its health benefits and minimal danger of negative effects. The purpose of this research is to examine whether or not phytochemical extracts (essential oil) from plants have any repelling properties.

Keywords: Linalool, mosquito repellent, essential oil, Geraniol, DEET

Introduction

Disease which are transmitted by the bites of mosquitoes are mainly responsible for the death causing situation of a person in the worldwide ^[1]. Mosquitoes are known as vector of many pathogenesis diseases. Around 3.3 billion of people are suffer from many tropical diseases that include malaria, dengue, chicken Ghuniya, Filariasis, Hemorrhagic fever in the 106 countries near the tropical and subtropical area ^[2] Mosquitoes are the main reason for people death from dengue and malaria especially in case of infants and small children ^[3]. Control of mosquito growth and personal hygiene from the vectors of mosquitoes at present time is important measure to control mosquitoes that caused diseases. For the protection from mosquitoes bites the use of mosquito's repellent are highly recommended. Mosquitos' repellent are the only option in many situations specially for outdoors. Exposure of mosquito's repellent on the skin may be one suitable way to protect from the bites of mosquitoes ^[4].

Mosquitoes are the vector of the many diseases that caused such as Malaria, Dengue, Filariasis, Chicken Ghuniya, Japwnws encephalitis are a major public health problem in many countries because of tropical and subtropical climate ^[5]. Many types of synthetic product and formulations are design to fight against the malaria and many diseases transfer vector but they are not successful because many mosquitos are increases their resistance property. Mosquitos are the reasons for many dangerous diseases. Mosquitos are not only one type but there is a huge range of variety of mosquitos in other words there is a group of arthropods like *Aedes aegypti* lin it caused the dengue and yellow fever, *Anopheles* species transfer the vector of malaria and filaria is caused *Culex quinquefasciatus*. The vector of dengue are transmitted in the large area of tropics and subtropics ^[6]. There are required to find the new formulation which is effective, less toxic and safe mosquito repellent compound ^[7].

In world it is estimated that *Anopheles stephensi*. L and group of different species of mosquitos is the main vector that caused about 40% of malaria case annually. Globally the vector of *Anopheles stephensi*.

L kills 500 million of people each year. It is about 2 million child most of them are about less 5 years old and also pregnant women die by the bite of mosquitoes vectors and suffered from diseases like malaria, dengue, schistosomiasis, trypanosomiasis, liashmaniasis every year. 9/10 number of patients that caused by the vector of mosquitos near the Sub-Saharan Africa and also all over the world [5].

There are a many number of effective mosquitos repellents contain a synthetic compounds like allethrin, N-N-diethyl -m-toluamide (DEET), N-N-diethyl-m-acetamide (DEBA), N-N-diethylmendellic acid amide (DEM) and Picaridin [1]. DEET are present time available in variou formulations and readily used as a mosquito repellent. Those repellent contain DEET are have great activity to irritate mosquitos for biting but they also have some sides effects like headache, eye irritation, shortness of breath, skin irritation, atania, weakness, cancer, motor capacity, memory and learning ability and defect in child birth [8, 9]. By the addition of DEET chemical, vectors can be control but they also not recommended for infants and children they cause encephalopathy and other side effects because of its high concentrations [10, 11].

Mosquito repellents are those compounds which are work locally at the distance for disturb the arthropod for flying, landing, biting on the human and animal skin [12, 13]. For the formulation of mosquito repellent plant essential oil are used as fragrances and flavouring agents and because of their volatile property. Essential oil are rubbed on skin in the same way that other conventional mosquitos repellent and they have little or no side effects. Large variety of plants have been tested for their insecticidal activity against mosquitos and plants essential oil are have tested for their promising effect. Essential oil and their complex mixture that are isolated from the volatile compounds of plants which contain the mosquito repellent property [14].

Role of Different essential oil in mosquito repellent activity

Plant based essential oil is type of herbal based essential oil or in the other words the formulations of plant base essential oil are made from the natural and organic sources for make it less harmless and with the great effect against the mosquitos. There are some active ingredients which play an important role in to distract the mosquitos or irritate the mosquitos there are name of those active ingredients are myrcene, limonene, Dihydrotagetone, Z-ocimene, E-caryophyllene, Piperitone, terpinene, lauric acid, Tagetone, alpha terthienyl. Limonene are contain from the layer of citrus fruits and vegetables [15, 16, 17]. The aroma and flavour of citurs fruits and vegetables are discourage and irritate the mosquitos. The aroma of the limonene which is collect from the all types of citrus fruits are unfavourable for the mosquitos [17].

Fatty acids are used as insecticidal from last few years for controlling the mosquitos vector diseases. lauric acid the main active constituent or chemical constituent in the citrus fruits and vegetables or plants which have high fragrance or aroma [18]. Lauric acid are mainly found in fatty acids of vegetables which help to discourage the mosquitos from biting on the skin of human and animals it is harmless for both peoples and animal [19]. High sources of lauric acid are present in coconut oil, Palm kernel oil, fish oil, eggs and vegetables [20].

Bay leaf oil

Bay leaf essential oil are reported to have repellent activity against the insects. The rich source of limonene acid as compare to Bay leaf, carrot contain less amount of limonene acid and lauric acid show the great insecticidal activity [21].

Beta caryophyllene are also a active constituent present in herbal plants which have the great mosquitos repellent property for the group of arthropods and all types of mosquitos which are the responsible for the dangerous diseases like malaria, dengue, chicken ghuniya, filaria, yellow fever. We can save our self from these dangerous diseases by using herbal mosquito repellent.

Monarda oil

Monarda oil and their species is effective against the adult mosquito vector they show the repellent activity for adult mosquitos [22, 23]. In the monarda oil the dominant chemicals are thymol and carvacrol which are responsible for the repellent activity against the vectors. At the low concentration the repellent activity of monarda oil were reported against the mosquito [24]. This study were investigates the repellent activity of monarda fistulosa with the different essential oil which contain the mosquitos repellent activity for the different group of mosquitos [25]. Different different variety of monarda oil have the different-different chemical constituents which have the mosquito repellent activity for the variety of vectors which cause the various diseases. Monarda fistulosa have the carvacrol, thymol, eugenol, carvacrol methyl ether. Monarda bradburiana have the carvacrol, thymol theses active constituent are active against the mosquitos [26].

Tagetes minuta

The essential oil of *Tagetes minuta* is active against the mosquito species. Chemical constituents of repellent activity of *Tagetes minuta* essential on female *Anopheles* mosquitos were observed by the human biting technique [27]. The main chemical constituents of *Tagetes minuta* are (z)-beta-ocimene, (E)-beta-ocimene, (Z)-tagetone, (E)-tagetone, dihydrotagetone, piperitenone. In other studies the repellency effect of *Tagetes minuta* are effective against the three mosquitos species which are *Aedes aegypti*, *Culex quinquefasciatus* and *Anopheles stephensi* are investigated [28]. *Tagetes minuta* are investigate for there repellent activity against the mosquitos. At the concentration of 0.5%(w/v) *Tagetes minuta* essential oil produce a mosquito repellent activity 94.7% [29]. *Tagetes minuta* is belong to the family of Asteraceae. It leaves are glossy, green and partially dissected in four to six pairs [30]. *Tagetes minuta* essential oil are used in the various medicine and grows at the high temp regions of south America [31].

Sweet basil oil

Sweet basil plant leaves (*Ocimum basilicum*), is also contain the larvicidal properties. On the basis of studies on genus ocimum that sweet basil contain many useful chemical constituents such as alkaloids [32], tannin, flavonoids, saponins, triterpenoids, linalool [33]. Many research were held to check the ability of sweet basil leaves as a larvasides against the *Aedes aegypti* mosquitos [34]. Many previous studies are conducted by the researcher around the various areas of the world which also include the India [35].

Peppermint oil

Peppermint oil are also show mosquito repellent property. M.piperita show the great and effective mosquito repellent property against the *aegypti* adult mosquito [36]. Peppermint oil show the high percentage of mosquito repellent activity against the *A.aegypti*, *Anopheles.S*, *C.quinque*. The percentage of repellent activity are 100%, 92.3% and 84.5% [37]. The active components of peppermint oil are methone and the major chemical constituents of peppermint oil are p-

Menthane-3, 8-diol are registered for the activity of mosquito repellent from the year 2000[38]. Peppermint oil are used for the various pharmacological activity in various pharmaceutical formulations. The essential oil of peppermint oil has a many therapeutics value and also used as a active ingredients in the preparations of mouthwash, toothpaste, aromatherapy and for the topical preparations. It also used for the treatment of diabetes, fever, hypertension, jaundice, pain, respiratory and urinary tract infections [39].

Neem oil

Essential oil of Neem are the natural occurring repellent which is obtained from the seeds of neem tree. Essential oil of neem are used from many for the repellent and pesticidal activity. Neem oil mainly contain the triglycerides, terpenoids which gave the bitter taste. Essential oil of neem are the most active oil for the repellent property. The active chemical constituents of oil are Azadirachtin, Nimbin, Nimbidin, Nimbidol, Sodium nimbinate, Gedunin, Salannin, Quercetin [40]. Neem oil are the strongest weapon for fight against the malaria and mosquito borne diseases. In 1994 malaria research center Delhi India prove that kerosene lamp with 1% of essential oil of neem are effective for the protection from mosquitos [41]. 2% essential oil of neem on the addition with coconut oil or mustard oil are the 100% protection against the mosquitoes which are responsible for spreading the many disease. The repellent time period of this mixture are 7 hours [42].

Cinnamon oil

Essential oil of cinnamon show that they were kill the eggs of mosquito this process is reported in the conducted study in Taiwan. Adult mosquito are deterred by the cinnamon oil [43]. Essential oil of Cinnamon are recommended as a mosquito repellent and also as an insect repellent. Chemical constituents of cinnamon oil are work as an insecticidal chemical that is used for controlling the unit of insects and mosquitos name of those chemical which is work as an insect or mosquito repellents such as cinnamaldehyde. Cinnamon oil of leaf is reported to kill the larvae of mosquito. Cinnamaldehyde, eugenol, ethanol and cinnamyl acetate all chemical constituents are found in the cinnamon leaf with the activity to kill the mosquito larvae [44].

Lavender oil

Essential oil of lavender shows the mosquito repellent activity. Many chemical constituents are reported in the essential of lavender which show the repellent activity against the vector of mosquito borne diseases. The name of chemical

such as limonene, camphor, linalool, eucalyptol these chemical are reported with the activity of mosquitos repellent activity [45, 46].

Clove oil

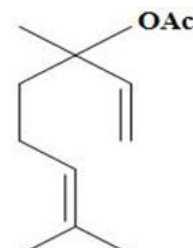
Essential oil of clove are reported with activity of antimicrobial, antibacterial and antifungal for many infectious symptoms of bacterial infection and it is reported to show the safe and effective for the peoples. On the other hands they also show high percentage of repellent property for the vector of mosquito borne diseases. Health care experts were recommended the essential oil of clove as an alternative of DEET [47].

Chemistry of Linalool

With the comparison of essential oil based chemical constituents are show the great water solubility. Linalool present in two forms of enantiomeric which are R(-) linalool and S(+)-linalool both are different in physiological and olfactory properties [48]. R(-)-linalool have the aroma of lavender and S(+)-linalool have the petitgrain aroma [49].



R(-)-LINALOOL



S(+)-LINALOOL

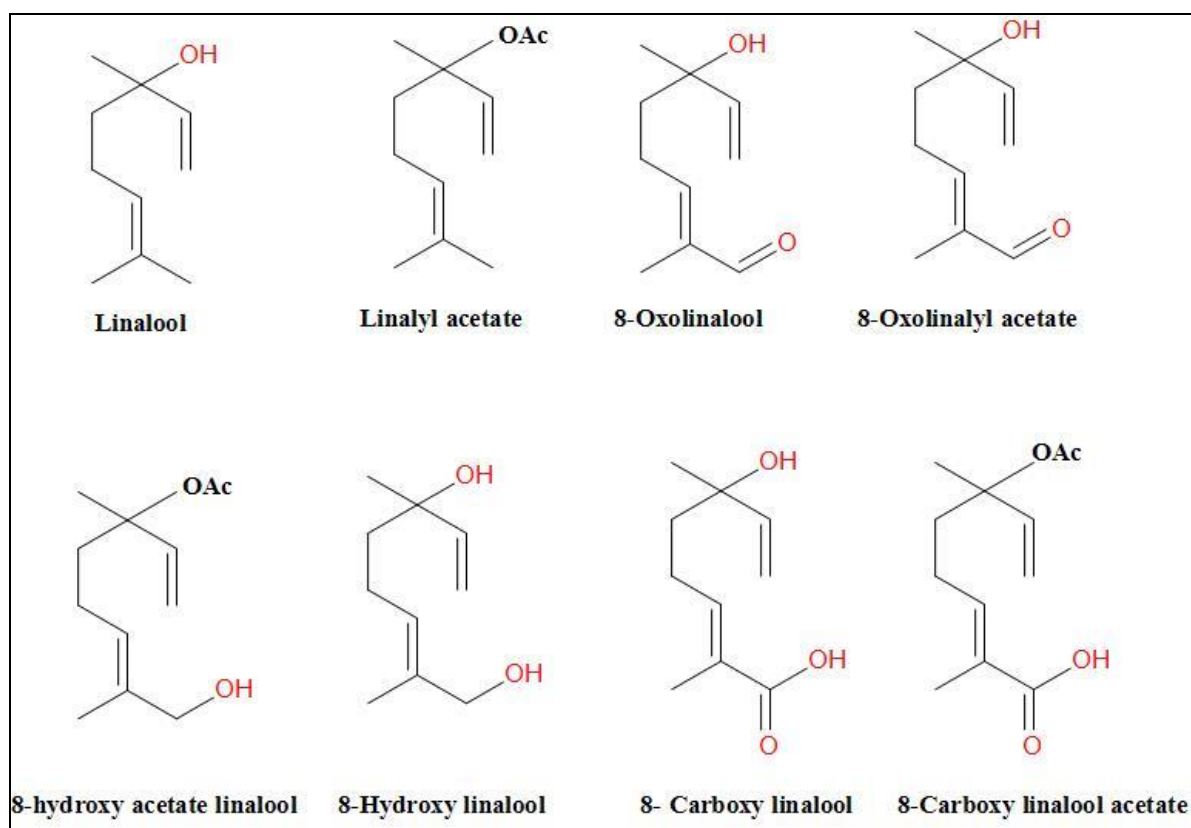
The chemical constituent of linalool are isolated by the plant which contain the high percentage of linalool. The chemical constituent of linalool are can be produced by the industrially by the hemi synthesis method from the natural pinene or by the fractional distillation. Isolation of single chemical constituents of linalool from the mixture of essential oil are achieve by the various technique of chromatography such as column chromatography or by the fractional distillation. The biosynthesis of linalool is based on the alpha and beta pinene [50]. Alpha pinene are hydrogenated by the cis pinane and oxidised by the cis and trans mixture of pinane hydroperoxide which is reduce the pinanols and at the last they were prylsed as a d- or l-linalool [51, 52].

Chemical properties

Table 1: Chemical Properties of Linalool

Chemical Properties		
1	Chemical formula	C ₁₀ H ₁₈ O
2	Appearance	Colorless to pale-yellow
3	Odor	spiciness; like a bergamot oil or French lavender Pleasant floral or woody scent,
4	Taste	woody, spicy, floral, sweet
5	Molecular weight	154.25 g/mol
6	Density	At 25 °C (0.87 gm/ml)
7	Solubility of water	At 25 °C (0.00159 gm/ml)
8	Flash point	78 °C (< 0–74) freezing point
9	Melting point	Greater than 20 °C
10	Partition Coefficient	At the 25 °C (2.84)
11	Surface tension	8.3 mN/m at the 20 °C
12	Viscosity	0.004465 Pa/s at 25 °C

13	Refractive index	at 20 °C 462
14	UV spectra	It not absorbs in region between 290-700 nm [53,54,55,56]



Pharmacological Properties of Linalool and their reported activity

Infectious diseases

Infectious diseases are caused by the microorganism which is affected millions of people in the developed countries. Some studies are reported the activity of essential oil which helps to make the person anti-infected. *Bursera aloexylon* essential oil which contain the high percentage of linalool (96%) chemical constituent have the anti-infected properties. Linalool is effective against the *Staphylococcus epidermidis* (0.15 mg/mL), *Rhodococcus equi* (0.60 mg/mL) [57]. *Croton cajucara* are the linalool enriched essential oil which reduce the growth of *Candida albicans*, *S. aureus*, *Lactobacillus casei*, *Porphyromonas gingivalis* and also *Streptococcus mutans* cell suspensions. All of these agents are associated with the oral cavity infection. Scientific evidence provides results that use of linalool as a active pharmaceutical ingredients in mouthwash formulation and gargle formulations that claim to give the relief from sore throats, ulcers of mouth and gums. [58]. Linalool chemical constituent are showing the antimicrobial activity against the pathogens using the minimum inhibitory concentration (micro plate assay) method [59].

Anti-oxidant activity

Essential oil contains the anti-oxidant properties are the point of attraction now days. Synthetic anti-oxidants products are replaced by the natural compound contain essential oil [60]. *Cinnamomum osmophloeum* (Lauraceae) oil report the property that they can scavenge DPPH compound radical IC50 value: 29.7 micro gram per ml [61]. Linalool as the single

chemical constituent have the little anti-oxidant property that contain the IC50 value less than six hundred forty-eight micros.

Anti-inflammatory activity

Swelling is caused when the body exposed around the infective agents or when physical or a chemical change is occurring [62]. Essential oil is also beneficial in the aromatherapy, anticancer or anti-plasmodial activity. From the traditional time linalool/linalyl compound producing plants are used as an active ingredient to relieve from the treat the both chronic and acute ailments [48]. Linalool constituent contain plants are has been observed to give the good anti-inflammatory property and also possess the peripheral analgesic activity [63, 48]. Linalool as a dose (25 mg/kg) body weight, does not show any activity after the 1hrs administration of carrageenin, but after the 3 to 5 hours significant reduction of oedema 28%, P = 0.008 and 25%, P = 0.0004, was seen [64].

Anticancer activity

In the worldwide cancer is a public health problem around the 11 million people are affected by the cancer diseases every year. In 2020 16 million new case are reported annually [65]. Plants and plants based essential oil are used to prevent and treat the symptoms of cancer. Some studies are done on the cancer cell which is derived from the 8 organs of human and use pure compounds which contain the linalool and flavonoids such as luteolin [66]. It is observed that Linalool reported strongest activity against broad range of cancerous cells which is carcinoma of cervix IC50: 0.37 µg/mL, in

stomach IC50: 14.1 µg/mL, in skin IC50: 14.9 µg/mL, in lung IC50: 21.5 µg/mL, in bone IC50: 21.7 µg/mL. ^[67].

The effects of linalool on CNS:

In some studies linalool psycho pharmacological activity is reported on mice, while the study linalool show the fix dose dependent, sedative effects on CNS. They protect from the picrotoxin, pentylentetrazol, hypnotic, hypothermic, trans corneal electroshock-induced convulsions ^[68, 69]. A practical is conduct in which 40 different extracts are used and also include the 9 essential oil in it to report the ability for decrease the motility of the test animals ^[70]. The reported result show that linalool is able to decrease the motor activity on the 6–8-week-old mice after the one-hour inhalation of linalool contain compound and the percentage of linalool activity on the mice are more than 60%. Those plant species are containing the high percentage of linalool are able to use as an anticonvulsant by the expert of traditional medicine in the brazilin amazon ^[71]. From the traditional time many essential oil and plant derived products are used in the treatment of mental related problems ^[72]. At the 400 mg/kg linalool show the significant anticonflict effects on both Geller and Vogel test but linalool alone not able to show anticonflict effects the lavender oil also shows the major contribution for show the anticonflict effect. Some studies are report that people with the Alzheimer's diseases are have decrease level of acetylcholine in brain. Inhibition of acetylcholinesterase enzyme helps to accumulate the acetylcholine. Increase the level of acetylcholine decrease the mental decline on the people with Alzheimer's diseases and also some related conditions diseases. The terpenes compound which contains the linalool are examined for the anticholinesterase activity by the *in-vitro* method and the reported result show that linalool blocks the acetylcholinesterase enzyme ^[73].

Insect repellent activity

Various biological pesticides are showing the adverse effect on the environment and search of safe pest management are become difficult. For the protection of crops and their products from the pesticide's pollution the use of less toxic and safe botanical pesticides are important to use. For controlling the insect's pests chemical and biological treatment methods are used ^[74, 75]. In essential oil many compounds are present which are able to fight against the plant enemies ^[76]. Plants and their chemical constituents are used as a source of alternative fumigant which is suggested by the many practitioner ^[77, 78]. Insecticidal activity of many essential oil and monoterpenes are have been studied on the variety of insects ^[79, 80]. Insects like mosquitos are the

important alignment of the aquatic and terrestrial chain of food. Mosquitos posses a many health risk that may cause a many diseases like skin allergy and the vector of many dangerous diseases like malaria, dengue, yellow fever and the west Nile fever ^[81, 82]. Protection from the mosquito borne diseases is still difficult to control in Africa and in the world its seems like a human crisis. Some aromatic plant species are used as repellent in African countries ^[83]. In many studies the aromatic plants which contain the linalool, eugenol and geraniol, terpineol are reported to show the positive repellent activity. Larvicidal assay are conduct to evaluate the LC50 and LC90 after the 24 and 48 hrs of essential oil and their chemical constituents against the seaside mosquitos *ochlerotatus caspius*. All the examined essential oil are reported to have high larvicidal activity LC50:15-156ppm. Coriander fruit oil which contain the high amount of linalool as used as a most potent oils [84]. Oxygenated monoterpenes like linalool are also toxic for the rice weevil ^[85]. Some monoterpenes like camphor are test for the practitioner observed linalool log IC50 value: 0.5 mg/L are most toxic for all the compounds which is investigated ^[86]. Linalool are more effective and produce the 100% mortality for *rhyzopertha daminica* and 85% mortality for the rice weevil after the 24hrs administration at the concentration of 0.1 µl/720 mL ^[87].

Mosquito repellent activity

essential oils used as a natural insecticide The phrase "Green Pesticides" is used to refer to any environmentally safe and effective method of pest control. pest-repellent and effective. Their low toxicity, little environmental effect, and compatibility with non-target organisms make them superior to synthetic pesticides ^[96].

Linalool are aromatic and pleasant odour natural occurring terpene compound which is commonly collect from the flowers and plant species. It is isolated from various plants that are used from the traditional time for the mosquito repellent activity by the local African peoples like *Ocimum forskolei*, and *Thymus vulgaris* ^[88, 89]. Some studies are examined that electrophysiological effect of mosquito repellent on the mosquito olfactory receptors observed the same odor receptor that is respond for the DEET also respond for the linalool on the *Culex quinquefasciatus* ^[90]. volunteer hand bioassay test are perform by using the *Culex pipiens pallens* report that linalool can produce 92.00% protection from bites of mosquitos around the 1 hr ^[89]. In the addition of olfactometric study the repellency response of *stegomyia aegypti* show that the combination of linalool and the dehydrolinalool produce the 33.60% repellency in comparison to the control ^[91]. The repellency testing of linalool are done in the fileld or in the formulation of oil candles ^[92].

Table 2: Repellancy of Essential oil

S. No.	Essential oil	Biological source	Family	Linalool %	Repellancy % of pure oil	Reference
1	Lavender	<i>L.angustifolia</i>	Asteraceae	20-50	80.90	93,95
2	Sweet Basil	<i>Ocimum Basilicum</i>	Asteraceae	30-50	-	94,95
3	Bay leaf	Laureal leaf	Lauraceal	2.0	-	95
4	Coriander	<i>Coriandrum sativum L</i>	Apiaceae	60-80	-	95
5	Lime	<i>Aurantifolia</i>	Rutaceae	0.5	43.1	93,95
6	Mentha	<i>Mentha piperita L.</i>	lamiaceae	20-50	57.1	93,95
7	Rosemary	<i>Rosemarinus officinalis</i>	Labiatae	2.0	100	93,95

Conclusion

Linalool contains many pharmacological properties but

mainly they work as mosquito repellent to discourage the mosquito for biting the people by the help of linalool-based

mosquito repellent people can protect themselves from the vector of many dangerous diseases like malaria, chicken ghuniya, yellow fever, dengue. Linalool is a chemical constituent which is present in various species of plants and trees and percentage of linalool chemical constituents vary with the plant species. The repellent property of linalool is depending on the percentage of linalool present in any formulation and plant species which contain the linalool. Linalool present in most of the plants in small percentage to high percentage the high percentage of linalool present in the bay leaf, lavender, peppermint, sweet basil.

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