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Melaleuca alternifolia : A review of the medicinal uses, pharmacology and phytochemistry

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Abstract : *Melaleuca alternifolia* also known as Tea tree oil belonging to family Myrtaceae. This plant has diverse and therapeutic uses in traditional herbal medicine for treating Skin care, First Aid, Household Cleaning, Hair care, Aromatherapy, Feminine care, Chronic illness, and Dental care in Australia. Phytochemical investigation shows that *Melaleuca alternifolia*c onsists of terpene hydrocarbons, such as monoterpenes, sesquiterpenes, and their associated alcohols. Studies indicate *Melaleuca alternifolia* possesses various pharmacological activities such as Anti-anxiety, Antibacterial, Antioxidant, Antimycotic and Antimicrobial, Antiviral, and Ant inflammation and Antiprotozoal. The finding of toxicity study topical use of the oil is relatively safe, and that adverse effect are minor and occasional TTO is toxic if ingested in higher doses and can cause skin irritation at higher concentrations. However, further research on chemical components and their mechanism of action show biological activities which are required to clarify the complete phytochemical profile and assess to confirm their suitability for future drugs. These reviews summarize the pharmacology and phytochemistry and medicinal uses of *Melaleuca alternifolia* to reveal its therapeutic effects.
Key Words : *Melaleuca alternifolia,* Phytochemical, Monoterpenes, Antiviral.

Introduction

Myrtaceae is the family of dicotyledonous plants placed within the order Myrtales. The plants such as clove, guava, all are members of this group. All species are woody, which contain essential oils, and flower parts in multiples of four or five. The Myrtaceae Family include over 5650 species[1].which occur in some 130-150 genera. The Myrtaceae family is the eighth largest flowering plant family, it comprises of several genera of outstanding ecological and economic relevance worldwide. The centers of diversity of myrtaceae family particularly in South America, with occurrences in Africa and Europe. The family is mainly found in world's Rain forest in Brazil where up to 90 species of Myrtaceae per hectare.

Melaleuca alternifolia is also called tea tree oil (TTO), the volatile essential oil derived mainly from the Australian native plant. Employed largely for its antimicrobial properties, TTO is used as the active ingredient in many formulations used to treat cutaneous infections. *Melaleuca alternifolia* available over the counter in Australia, Europe, and North America and is marketed as a remedy for various ailments[2].

This plant is very important for medicinal uses and herbal products. The leaves of "tea trees" were used for the treatment of cough or were spread on wounds,[3] and tea tree leaves were soaked to make an infusion for treatment of sore throats or skin ailments[4].

Botany

Common name: Australian Tea tree, Narrow leaved Paper bark
Scientific Name : *Melaleuca alternifolia* (Miaden & Betche) Cheel
Family : Myrtaceae

Scientific classification

Kingdom : Plantae
Subphylum : Euphyllophytina
Infraphylum : Radiatopses
Subclass : Magnoliidae
Superorder : Rosanae
Order : Myrtales
Suborder : Myrtineae
Family Myrtaceae
Genus : Melaleuca
Species : *M. alternifolia*

Description

Melaleuca alternifolia is a shrub, 7 m tall, with layered, and papery bark. Leaves are arranged, scattered to whorled often on one branchlet; and petiole 1 mm long; linear-acute, having size 10-35 mm x 1 mm, 3-veined (often only mid-vein visible), puberulous, dotted with oil glands visible with a lens. Inflorescence a many flowered, open to dense, upper-axillary flowers is solitary within each bract with tubular calyx up to 3 mm long and white corolla 2-3 mm long, stamens having 30-60, white, clawed, pistil having 3-4 mm long and capitate stigma. Fruit a many-seeded, globose, 2-3 mm in diameter[5]. (Figure 1).

Figure 1: *Melaleuca alternifolia* Plant

Traditional Uses

Tea Tree oil is an active ingradient of many topical preprations for the treatment of cutaneous infections including wound infections,[6] fungal dermatoses,[7] otitis media,[8] and acne[9].Although several clinical studies suggest that tea tree oil possesses antimicrobial activity. Tea tree oil is present in variety of household products

including moisturizing cream,l aundry detergents, fabric softners, mouth washes, massage oils,often as a substitute of nutmeg oil. The single component isolated from Tea tee oil which have antibacterial and antifungal benefits. Another study from 2012[10] used tea tree oil as a control scent against orange aroma when testing anxiety, found the test aroma (sweet orange) created less anxiety and tension.. Particularly, two substances in tea tree oil, terpinen-4-ol and alpha-terpineol, have shown significant successes against fungi and bacteria[11].

Phytochemistry

Melaleuca alternifolia is consist of terpene hydrocarbons, which contain monoterpenes, sesquiterpenes, and their associated alcohols. Brophy and colleagues [12] examined over 800 Tea Tree oil samples by gas chromatography and GC-MS and report approximate 100 components and their Percentage composition (Table 1).

The relative Density of Tea Tree Oil is 0.885 to 0.906 which is soluble in water and insoluble in non polar solvents.

The composition Tea tree oil is regulated by an international standard for "melaleuca oil which containterpinen-4-ol type," which sets maximum and minimum for 14 components ofthe oil[13].Six varieties of *M. Alternifolia* have been found or chemotypes, each producing oil with a distinct chemical composition. These containa terpinen-4-ol chemotype, a terpinolene chemotype, and four 1,8-cineole chemotypes[14]. The terpinen-4-ol chemotype contains terpinen- 4-ol of between which is about 30 to 40% and chemotype used in commercial TTO production. The antimicrobial activity of TTO is due to terpinen-4-ol, a major component of the oil.

The bark and stem of *Melaleuca alternifolia*(Myrtaceae) led to the isolation and identification of 3,3' dimethylellagic acid and five pentacyclictriterpenes: 2 το3β, 23 trihydroxyolean12en28oic acid (arjunolic acid) 3 βhydroxylup20 (29) en27,28dioic acid (melaleucic acid),Betulinic acid, betuline, 3 β-*the*-acetylurs12en28oicacid and the mixture of fatty acids and esters, and several hydrocarbons [15].

The Tea Tree Oil stored for 9 months under sunlight there is the formation of the endoperoxideascaridole was proven using a GC-MS analytical procedure.[16]As a further oxidation product such as 1,2,4-trihydroxymenthane was identified[17].

The Structure of Bioactive components of *Melaleuca alternifolia* as shown in (Figure 2) and (Figure 3).

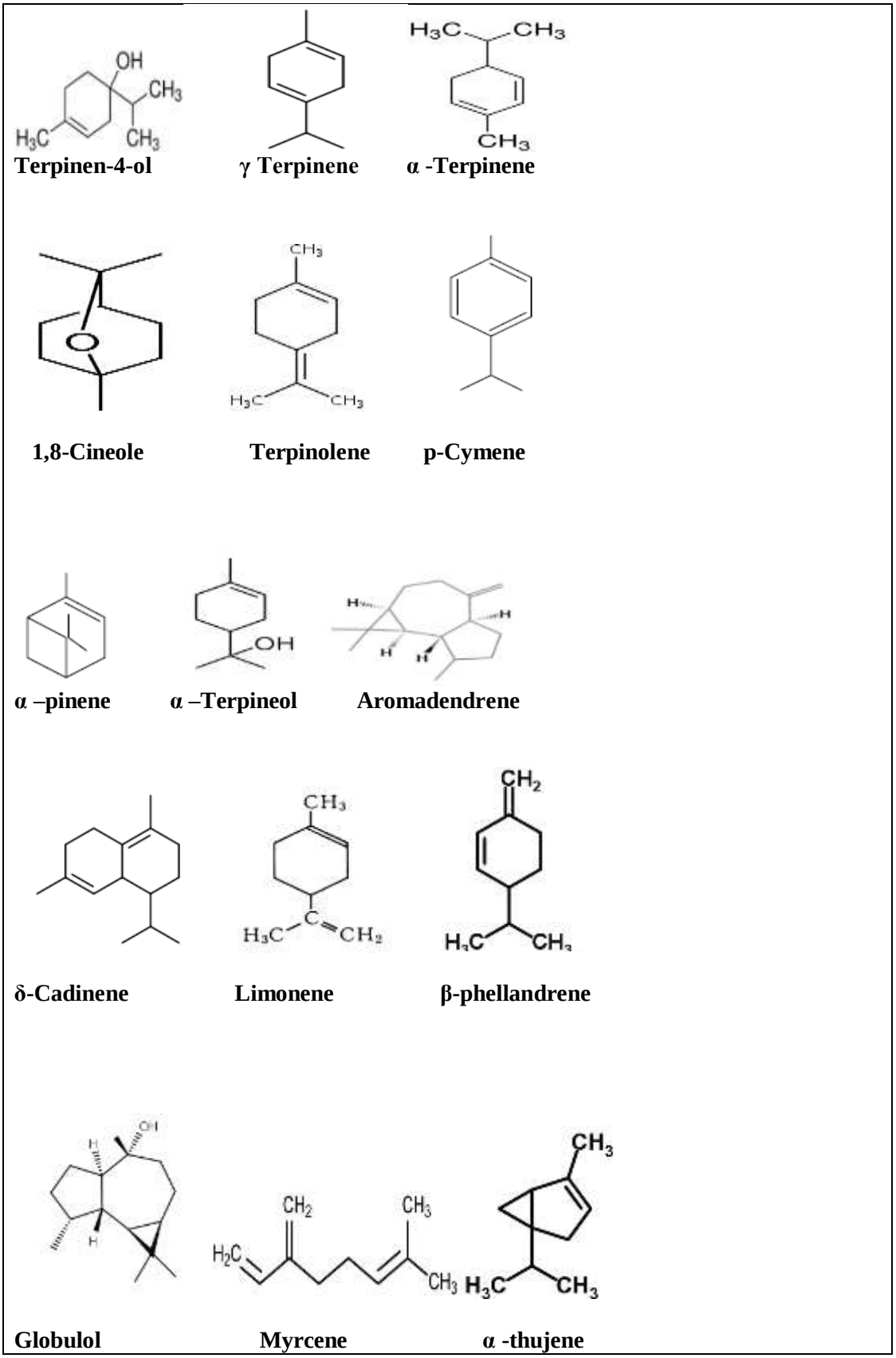

Figure 2: Structure of Bioactive components of *Melaleuca alternifolia*

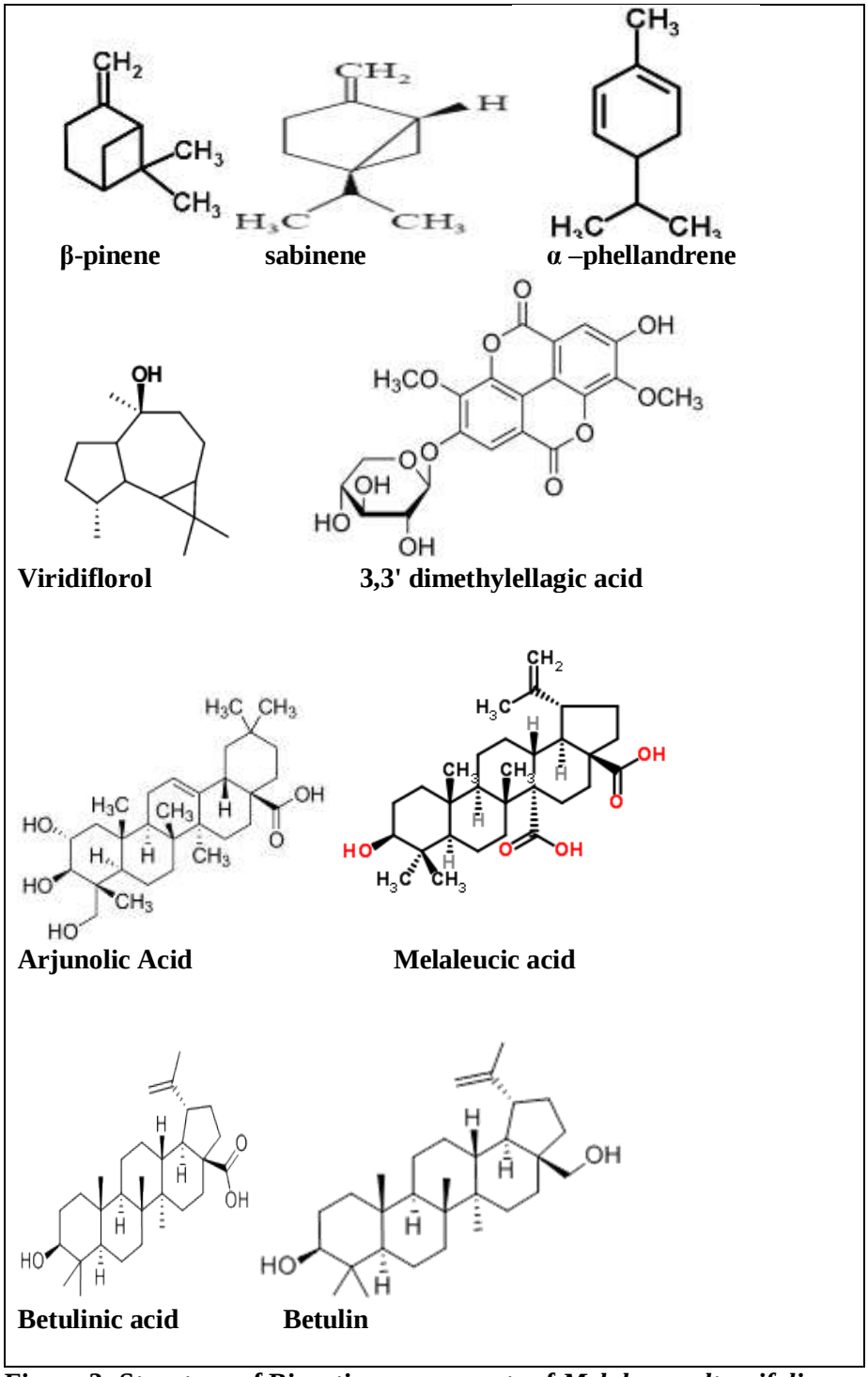

Figure 3: Structure of Bioactive components of *Melaleuca alternifolia*

Pharmacological Effects

Antibacterial activity

Antibacterial activity has been determined by using agar or broth dilution methods. However, activity has determined by time-kill assays,[18] [19],[20],[21] suspension tests, [22] and "ex vivo"-excised human skin [23] . In addition, vaporized TTO can inhibit bacteria, including *Mycobacterium avium* ATCC 4676,[24]*Escherichia coli*, *Haemophilus influenzae*, *Streptococcus pyogenes*, and *Streptococcus pneumonia*[25].

Antifungal activity

Data shows that a yeasts, dermatophytes, and other filamentous fungi are susceptible to TTO.[26],[27],[28],[29],[30],[31],[32]Various test methods differ, MICs range between 0.03 and 0.5%, and fungicidal concentrations generally range from 0.12 to 2%. The exception is Aspergillus niger, contain minimal fungicidal concentrations (MFCs) of as high as 8% reported for this organism.[33]However, assays are performed with *fungal conidia*, which are known to be relatively impervious to chemical agents. Subsequent assays that have been shown that germinated conidia are significantly more susceptible to TTO than nongerminated conidia suggesting conidial wall conferim considerable protection. Vapours of TTO have also been demonstrate to inhibit fungal growth[34], [35]and affect sporulation. [36]

Antiviral Activity

The antiviral activity of TTO was first shown by using tobacco mosaic virus and tobacco plants.[37]The trials with *Nicotinia naglutinosa*, plants sprayed with 100, 250, or 500 ppm TTO or control solutions and were experimentally diseased with tobacco mosaic virus. Later 10 days, there were significantly smaller amount lesions per square centimeter of leaf in plants treated with TTO than in controls. The effects of TTO were examined by incubating viruses by several concentrations of TTO and formerly using these treated viruses to infect cell monolayers. After 4 days, the plaques amount made by TTO-treated virus and untreated control virus were determined and compared. The TTO concentrationpreventing50% of plaque formation stood 0.0009% for HSV type 1 (HSV-1) and 0.0008% for HSV-2, relative to controls. These studies also presented that at the higher concentration of 0.003%, TTO reduced HSV-1 titers by 98.2% and HSV-2 titers by 93.0%.

Antiprotozoal Activity

TTO has antiprotozoal activity. TTO produced a 50% reduction in growth (compared to controls) of the protozoa *Leishmania major* and *Trypanosoma brucei* at concentrations of 403 mg/ml and 0.5 mg/ml, respectively.[38]

Antioxidant activity

Antioxidant activity of *Melaleuca alternifolia* (TTO) examined by usingtwo different assays. In the 2,2diphenyl1picrylhydrazyl assay, 10 μL/mL crude TTO in methanol had 80% free radical scavenging activity, and in the hexanoic acid assay, 200 μL/mL crude TTO showed 60% inhibitory activity against the oxidation of hexanal to hexanoic acid over 30 days. These results were equal to the antioxidant activities of 30 mMbutylatedhydroxytoluene in both tests at the same experimental conditions. These results suggest that the TTO could be a good alternative antioxidant. [39]

In Vitro Larvicidal Activity

Tea tree oil indicated a significant dose-dependent lethal effect on Anisakis simplex L3. Concentrations of 5 μL/mL and above weaken the larvae survival after 24 h exposure . Otherwise, 4 μL/mL of TTO required 48 h to reduce larval vitality. The most effective concentrations were 10 μL/mL, which showed a total lethal effect at 24 h and 7 μL/mL that produced 93% and 100% mortality after 24 h and 48 h incubation.[40]

Anti-inflammatory activity

Tea tree oil possesses anti-inflammatory activity. The water-soluble components of TTO can inhibit the lipopolysaccharide-induced productions of the inflammatory mediators tumor necrosis factor alpha (TNF-α), interleukin-1β(IL-1β), and IL-10 by human peripheral blood monocytes by around 50% and that of prostaglandin E2 by about 30% after 40 h.[41]Further examination of the TTO water soluble fraction identified terpinen-4-ol, α-terpineol, and 1,8-cineole as the main components, but of these, only terpinen-4-ol remained capable to diminish the production of TNF-α, IL-1β, IL-8, IL-10, and prostaglandin E_2 by lipopolysaccharide-activated.

Anticancer activity

Tea tree oil and terpinen-4-ol inhibited the growth of two murine tumor cell lines in a dose and time-dependent which means that more mesothelioma and melanoma tumor cells died induced more tree oil and terpinen-4-ol. rk. Tea tree oil and terpinen-4-ol stimulated G1 cell cycle arrest – the compounds stopped the cancer cells from multiplying. The compounds induced necrotic cell death and low level apoptotic cell death in both cell lines. [42]

Dental affects

Tea tree exposure kill Periodontopathic bacterial strains tested, including *Porphyromonas gingivalis, Actinobacillus actinomycetem comitans,Fusobacterium nucleatum, Streptococcus mutans, and Streptococcus sobrinus*. Tea tree oil showed significant inhibiting activity against *P. gingivalis.*[43]

Toxicity

TTO can remain toxic if ingested, as verified by studies with animals and from cases of human poisoning. The 50% lethal dose for TTO in rat model is equal to 1.9 to 2.6 ml/kg.[44] and rats dosed with 1.5 g/kg TTO appeared lethargic and ataxic Incidences of oral poisoning in children [44],[45],[46] and adults [47],[48]have been reported.

Clinical Trials

Treatment of acne

Tea tree oil usein the treatment of acne by comparing with 5% benzoyl peroxide (BP).[49]The study found that mutually treatments reduced the numbers of inflamed lesions, though BP performed significantly better than TTO. The BP group indicated significantly less oiliness than the TTO group, whereas the TTO group displayed significantly less scaling, ,and dryness. Significantly fewer overall side effects were reported by the TTO group (27 of 61 patients) than by the BP group (50 of 63 patients).

Dental applications

The efficacy of TTO in dental applications has been evaluated. A 0.2% TTO mouthwash and two other active agents on the oral cavity of 40 volunteers suggested that TTO used once regular for 7 days can reduce the number of mutans streptococci and the total number of oral bacteria, which are compared to placebo treatment. The data also showingthat these reductions were sustained for 2 weeks after the use of mouthwash ceased.[50]A study comparing a 2.5% TTO gel, a 0.2% chlorhexidine gel, and a placebo gel showing thatTTO group had significantly reduced gingival index and papillary bleeding index scores, their plaque scores remained actually increased. These studies indicate that although TTO cancause decreases the levels of oral bacteria, this does not essentially equal to reduced plaque levels.

Production

The business TTO industry was conceived after the restorative properties of the oil were initially detailed by Penfold in the 1920s as a feature of a bigger study into Australian basic oils with monetary potential. Amid that incipient stage, TTO was created from common shrub stands of plants, apparently M. alternifolia, that delivered oil with the proper chemotype. The local living space of M. alternifolia is low-lying, swampy, subtropical, beach front ground around the Clarence and Richmond Rivers in northeastern New South Wales and southern Queensland and, dissimilar to a few other Melaleuca animal groups, it doesn't happen actually outside Australia. The plant material was hand cut and frequently refined on the spot in stopgap, versatile, wood-let go bramble stills. The business proceeded in this mold for a very long while. Legend has it that the oil was considered so imperative for its restorative uses that Australian fighters were provided oil as a major aspect of their military packs amid World War II and that bramble cutters were absolved from national administration. In any case, no proof to support these records could be found (A.- M. Conde and M. Pollard [Australian War Memorial, Canberra, Australia], individual correspondence). Generation ebbed after World War II as interest for the oil declined, probably because of the improvement of viable anti-infection agents and the disappearing picture of characteristic items. Enthusiasm for the oil was revived in the 1970s as a major

aspect of the general renaissance of enthusiasm for common items. Business manors were built up in the 1980s, permitting the business to automate and deliver expansive amounts of a steady item . Today there are manors in Western Australia, Queensland, and New South Wales, in spite of the fact that the dominant part are in New South Wales around the Lismore district. Ordinarily, manors are built up from seedlings sowed and brought up in nurseries preceding being planted out in the field at high thickness. The opportunity to first reap fluctuates from 1 to 3 years, contingent upon the atmosphere and rate of plant development. Gathering is by a coppicing procedure in which the entire plant is sliced off near ground level and chipped into littler pieces before oil extraction.

Conclusion

*Melaleuca alternifolia*is local to Australia, where it is found from Queensland to north-east New South Wales, at up to 300 m above ocean level.Tea Tree oil is a dynamic ingredient of numerous topical preprations for the treatment of cutaneous contaminations including wound diseases, contagious dermatoses otitis media, and skin inflammation. The Tea tree oil the plant have promising antibacterial, antifungal and antiviral, antioxidant, anticancer and anti-inflammatory activities. *Melaleuca alternifolia* contains different phytoconstituents, for example, terpenoids and basic oils, which might be in charge of the distinctive natural exercises. Thus, we can seclude some unadulterated phytopharmaceuticals, which thusly can be utilized as lead atoms for integrating the novel operators having great restorative movement. As to the advancement of value home grown solution institutionalization of the concentrates, phytopharmacology of various concentrates, confinement and portrayal of dynamic phytopharmaceuticals, clarification of the system of activity of the disengaged mixes and clinical trials of the mixes are truly necessary. In the changing worldwide situation, the enthusiasm toward plants with restorative esteem is expanding considerably in the essential medicinal services framework both in the created and in the creating nations. Accordingly, the data will help researchers and scientists to screen the mixes in charge of various bioactivities and to explain the atomic component of activity.

Conflict of Interest

We declare that we have no conflict of interest.

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