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REVIEW ARTICLE

Exploring Tea Tree Oil's Potential in Combatting Fungal Infections

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Abstract: *Melaleuca alternifolia*, or tea tree, is a shrub native to Australia, particularly New South Wales' north-east coast. Due to its broad-spectrum antibacterial activity, Aborigines employ it in traditional medicine. Terpinen-4-ol in Melaleuca alternifolia has many antibacterial and antifungal properties. Non-toxic, biodegradable, and easily accessible, it is a useful therapeutic product. In traditional medicine, it treats skin infections, acne, vaginal fungus, throat infections, and cold sores. However, high tea tree oil popularity has raised worries about adulteration, driving the development of analytical tools to distinguish authentic from adulterated products. Skin mycoses are a growing danger, according to the WHO's Fungal Priority Pathogens List. Infections afflict 20-25% of the world's population. Antifungal drug resistance and immunocompromised patients are contributing to skin mycoses. Skin mycoses are a developing problem that requires increasing awareness, surveillance, and study. Several WHO and UN guidelines on health and the environment focus on environmental factors and illness burden. Fungal infections, which can harm humans and the environment, are rising due to climate change. Climate change increases endemic mycosis' global footprint, susceptibility to fungal infection, and selection for pathogenic characteristics. The risk of a fungus epidemic is rising. Also Compared to allopathic drugs, herbal treatments are safer, more effective, and cheaper. They're more accessible, culturally compatible, and synergistic. Additionally, herbal medications offer superior therapeutic outcomes and fewer side effects than allopathic treatments. Herbal skin treatments have several benefits. Their antibacterial, anti-inflammatory, antioxidant, and healing capabilities help treat complex skin and soft tissue infections. Modern pharmaceuticals are more expensive and have more negative effects than these natural cures for skin diseases. Due to its synergistic properties and long history of use, herbal remedies are a sensible and efficient treatment for different skin problems.

Keywords: Tea tree; Fungal infections; WHO; Climate change; Traditional medicine.

1. Introduction

1.1. An overview of tea tree oil

Melaleuca alternifolia, commonly known as tea tree, is a shrub native to Australia, particularly the north-east coastal area of New South Wales [1]. It has been used in traditional medicine by the Aborigine people due to its broad-spectrum antimicrobial activity [2]. The plant's essential oil, which is rich in monoterpenes and other compounds, has been found to possess effective antibacterial and antifungal properties [2]. This species has been the subject of intense scientific analysis in Brazil, where it is considered an important medicinal plant with various applications, including in agriculture, aquaculture, and public health [3].

Melaleuca alternifolia, is a natural product with a wide range of antimicrobial and antifungal activities due to its major constituent, terpinen-4-ol [1,4]. It is non-toxic, easily accessible, and biodegradable, making it a beneficial therapeutic product [4]. However, there is a risk of adulteration, which can be detected using various analytical technologies [5]. The oil has been used for almost a century in Australia and is known for its antiseptic and anti-inflammatory properties [1]

Research on *Melaleuca alternifolia*, the source of tea tree oil, has identified key factors influencing its annual production. Small (1981) found that plant spacing significantly affects growth and oil yield, with higher population densities leading to increased yields [6]. Stuepp (2017) further explored this by analyzing the use of renewable substrates for clonal plant production, with a substrate composed of 70% coconut fiber and 30% carbonized rice husk showing the best results [7]. Butcher (1994) highlighted the

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importance of genetic diversity in improving oil production, suggesting that utilizing seed sources of 'Type' trees can enhance productivity [8]. Baskorowati (2010) provided insights into the reproductive biology of *M. alternifolia*, including the correlation between flowering intensity and spring rainfall [9]. These studies collectively underscore the significance of plant spacing, substrate composition, genetic diversity, and environmental factors in the annual production of *Melaleuca alternifolia* [6, 7].

1.2. Historical uses and significance

Tea tree oil, derived from the leaves of the *Melaleuca alternifolia* plant, has a long history of use for its antibacterial, antiviral, antifungal, and anti-inflammatory properties [10]. It has been used in traditional medicine for skin infections, acne, vaginal fungus infections, throat infections, and cold sores [10]. The oil's antimicrobial and anti-inflammatory activities have been well-documented, and it has been used in a variety of products [1]. Its use in museum conservation for controlling mold has also been explored [11] . However, the increasing popularity of tea tree oil has led to concerns about adulteration, prompting the development of analytical technologies to differentiate between authentic tea tree oil and adulterated products [5].

Tea tree oil, was introduced in India with the establishment of tea tree plantations in the late 20th century (Combest, 2005). The oil's composition, including its key components terpinen-4-ol and 1,8-cineole, has been analyzed and compared with Australian tea tree oil [12] . However, the potential for adulteration of tea tree oil has also been noted, with the need for analytical technologies to differentiate between authentic oil and adulterated products [5]. Despite the challenges, the demand for tea tree oil has continued to grow, leading to its commercial cultivation in various parts of India [13].

The WHO's Fungal Priority Pathogens List, released in response to the COVID-19 pandemic, highlights the growing threat of fungal infections, including skin mycoses [14]. These infections are a significant global health concern, affecting 20-25% of the world's population [15]. The rise of skin mycoses is attributed to factors such as increased antifungal drug resistance and immunocompromised patient populations [14]. In particular, infections with *Candida glabrata, Aspergillus terreus*, and non-Aspergillus moulds are on the rise, posing a challenge due to their resistance to common antifungal agents [16]. This underscores the need for increased awareness, surveillance, and research to address the growing threat of skin mycoses

1.3. Tea Tree Oil as an alternative

A range of WHO and UN guidance on health and the environment is available, with a focus on the impact of environmental factors on disease burden [17]. This guidance emphasizes the need for preventive measures to address modifiable environmental risk factors, which contribute significantly to global deaths and diseases. The WHO's role in providing objective and reliable information on environmental health services is also highlighted.

The World Health Organization's Fungal Priority Pathogens List, released in 2022, identifies 19 fungal pathogens with the greatest threat to public health [14]. This list has significant implications for global health, where it has prompted a call for strengthened public health interventions, improved laboratory testing and clinical supervision, and increased investment in research and development [18]. The need for a collaborative, multisectoral, and trans-disciplinary approach, including the One Health approach, to address fungal diseases is underscored, given their significant impact on human and animal health [19]. In the context of antimicrobial resistance, the development of new strategies to combat multidrug-resistant bacteria is also highlighted as a priority [20].

Climate change is contributing to the rise of fungal infections, with the potential to cause significant harm to both human and environmental health [21]. The expansion of the geographic footprint of endemic mycosis, increased susceptibility to fungal infection, and the selection for pathogenic traits are all linked to climate change [22]. Furthermore, environmental disruptions due to climate change, such as floods and storms, can disperse and aerosolize fungi, leading to infections by previously rare or unknown species [23]. The potential for a pandemic of fungal origin is a growing concern [24].

A comprehensive One Health approach is crucial in addressing the urgent threat of antimicrobial resistance (AMR) [25]. This approach should involve improved communication, cooperation, and collaboration among various professional disciplines and organizations [26]. Key priorities include strengthened surveillance and monitoring for resistant organisms, antimicrobial stewardship programs, infection-control programs, and the development of new antimicrobial agents [26]. The irresponsible and excessive use of antimicrobials in various sectors, including agriculture, livestock, and human medicine, is a major contributor to AMR [25]. To combat AMR, there is a need for a One Health – One Europe – One World framework that targets innovation in antibiotic drug discovery and development [27]. [28]

Also Herbal medicines offer several advantages over allopathic medicines, including safety, efficiency, and cost-effectiveness [29]. They are also more readily available, align with cultural preferences, and have synergistic effects [30]. Furthermore, herbal medicines have been shown to have better therapeutic effects and fewer adverse effects than allopathic medicines [31].

Herbal medicines offer a range of benefits in the treatment of skin diseases. They possess antimicrobial, anti-inflammatory, antioxidant, and healing properties, making them effective in addressing the complex pathophysiology of skin and soft tissue infections [32]. These natural remedies are particularly valuable in managing skin disorders due to their lower cost and reduced side effects compared to modern medicines [33]. The use of herbal extracts and phytomedicines, such as Aloe, Neem, and Ginger, has been shown to be potent and safe in treating dermatological infections (Ahuja, 2020). Furthermore, the synergistic components of herbal preparations, as well as their long history of use, make them a rational and effective treatment option for various skin diseases [34]

2. Chemical composition and properties

2.1. Chemical constituents

Tea tree oil, derived from Melaleuca alternifolia, is a complex mixture of monoterpenes, sesquiterpenes, and their alcohols, with β-terpinene, α-pinene, and p-cymene being the major components [35]. It exhibits a range of biological activities, including antiradical, antibacterial, and antifungal properties [35] [13]. However, its hydrophobic nature and sensitivity to environmental factors present challenges in its formulation and delivery [13]. α-Pinene, 2,4(10)-Thujadien, β-Terpinene, β-Pinene, α-Thujene, 3-Carene, α-Terpinene, p-Cymene, Limonene, cis-Ocimene, Thujol, γ-Terpinene, α-Terpinolene, 2-β-pinene, Thujone, 4-Thujen-3-ol, trans-Sabinene hydrate, trans-Anethole, Germacrene-D, β-Bourbonene, Humulen-(v1), a-Amorphene, Aromadendrene, (+)-Sativen are the constituents of the tea tree oil. [15]. The main chemical constituents are shown in Figure 1 while the percentage of each chemical constituent is shown in Figure 2. Tea tree oil, derived from the leaves of Melaleuca alternifolia, is a complex mixture of monoterpenes, sesquiterpenes, and their alcohols, with β-terpinene, α-pinene, p-cymene, 3-carene, trans-anethole, and limonene being the major components [13,35]. It exhibits a range of biological activities, including antimicrobial, antiradical, and antifungal properties [13,35]. The oil's chemical composition and concentration can vary depending on factors such as the plant's vegetative cycle and the specific species of tea tree [37]

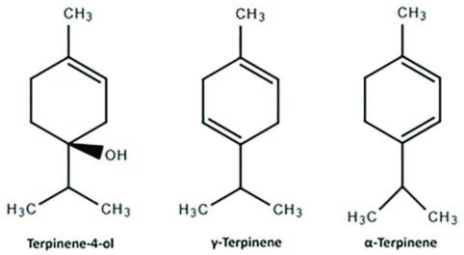

Figure 1. Major chemical constituents of tea tree oil

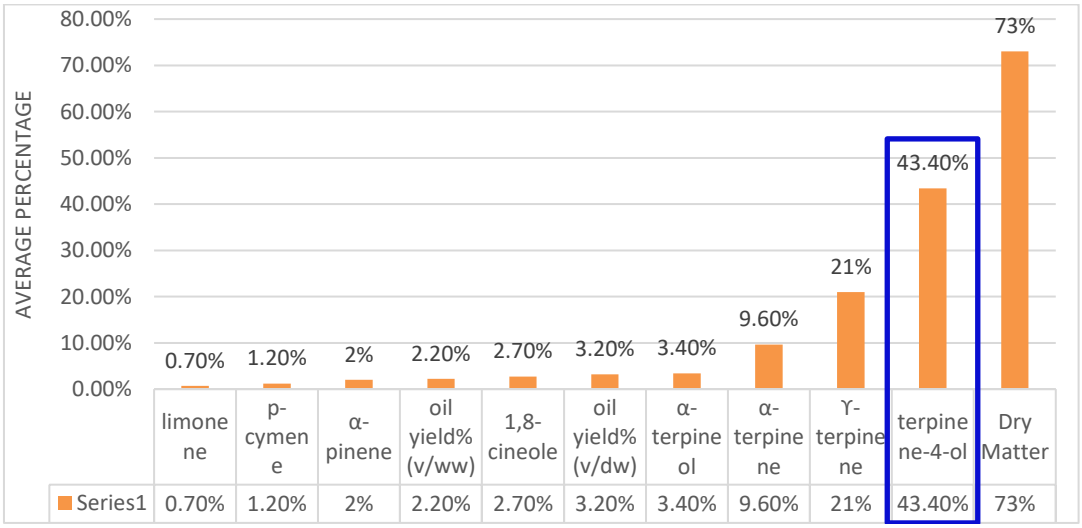

Figure 2. Chemical composition of the major constituents of tea tree oil and oil concentration [37]
(nd =not determined; (v/ww) =volume/wet weight; (v/dw) =volume/dry weight; DM =dry matter)

2.2. Key components responsible for therapeutic properties

The therapeutic properties of Melaleuca alternifolia, commonly known as tea tree oil, are attributed to its key components, including terpenoids, phenolic compounds, flavonoids, and steroids [38]. These components contribute to its antioxidant, antimycotic, antiseptic, anti-inflammatory, and insecticidal properties (Oliva 2003; Kasujja 2021; Liao 2017). Notably, the presence of terpinen-4-ol, γ-terpinene, α-terpinene, α-terpineol, α-pinene, terpinolene, and 1,8-cineole in the essential oil of Melaleuca alternifolia is responsible for its therapeutic effects [39].

2.3. Physicochemical properties

Tea tree oil (TTO) is a volatile essential oil extracted from the leaves of the Melaleuca alternifolia plant native to Australia. It possesses a unique combination of physical and chemical properties that contribute to its therapeutic and industrial applications. Table 1 list outs the key physical and chemical properties of tea tree oil: [40]

Table 1. Physical and chemical properties of tea tree oil.

Sr. No.	Parameter	Specification
1	Appearance	Tea tree oil is typically a clear to pale yellow liquid with a characteristic medicinal aroma. The color can vary depending on factors such as the age of the oil, extraction method, and storage conditions.
2	Odor	Tea tree oil has a distinctively fresh, camphoraceous odor with herbal and medicinal notes. Its aroma is often described as pungent, earthy, and slightly spicy.
3	Density	The density of tea tree oil is approximately 0.885 to 0.906 g/cm³ at 20°C. It is less dense than water, which has a density of 1 g/cm³ at the same temperature.
4	Solubility	Tea tree oil is insoluble in water but soluble in organic solvents such as ethanol, acetone, and oils. This property allows it to be easily incorporated into various formulations, including creams, lotions, shampoos, and mouthwashes.
5	Refractive Index	The refractive index of tea tree oil ranges from approximately 1.475 to 1.482 at 20°C. This property can be used to identify and authenticate tea tree oil and assess its purity.
6	Boiling Point	The boiling point of tea tree oil is approximately 176 to 210°C (347 to 410°F). This relatively high boiling point allows for the steam distillation of tea tree oil from the leaves of the Melaleuca alternifolia plant.
7	pH	Tea tree oil is slightly acidic, with a pH typically ranging from 5 to 6. This acidity contributes to its antimicrobial activity and may help maintain the skin's natural pH balance when used topically.
8	Chemical Composition	Tea tree oil is composed primarily of terpenes and their derivatives, with terpinen-4-ol being the major component (typically comprising 30-48% of the oil). Other key constituents include gamma-terpinene, alpha-terpinene, alpha-terpineol, and cineole. The chemical composition of tea tree oil contributes to its antimicrobial, anti-inflammatory, and other therapeutic properties.

Tea tree oil's physical and chemical properties make it a versatile and valuable ingredient in various applications, including skincare, haircare, aromatherapy, and natural medicine. Understanding these properties is essential for its proper utilization and formulation in different products

3. Ethnomedical uses

3.1. Exploring the traditional uses of tea tree oil across various cultures

Tea tree oil, derived from the leaves of the Melaleuca alternifolia plant native to Australia, has a rich history of traditional uses in various cultures dating back centuries. Known for its potent antimicrobial, antiseptic, and anti-inflammatory properties, tea tree oil has been incorporated into diverse cultural practices for its medicinal benefits [1].

In Australian Aboriginal culture, tea tree oil has long been recognized for its healing properties. Indigenous Australians used crushed tea tree leaves to treat wounds, cuts, and skin infections. They would apply the crushed leaves directly to the affected area or soak them in water to make a healing poultice. This traditional use reflects the plant's efficacy in treating bacterial and fungal infections, promoting wound healing, and reducing inflammation.

In traditional Chinese medicine, tea tree oil is valued for its ability to clear heat and toxins from the body. It is commonly used topically to treat skin conditions such as acne, eczema, and fungal infections. Additionally, tea tree oil may be inhaled or used in steam inhalation to alleviate respiratory ailments like coughs, colds, and sinus infections. Traditional Chinese medicine practitioners believe that tea tree oil helps to balance the body's energy and restore harmony, making it a versatile remedy in Chinese herbal medicine.[18] Indigenous Australian and Traditional Chinese medicine practices have influenced the adoption of tea tree oil in Western herbal medicine. European settlers in Australia learned about the medicinal properties of tea tree oil from Indigenous Australians and began incorporating it into their own folk remedies. In the early 20th century, tea tree oil gained recognition in Western medicine for its antiseptic properties, particularly during World War II when it was used to disinfect wounds and prevent infection among soldiers.

Today, tea tree oil is widely used in aromatherapy for its uplifting and purifying effects on the mind and body. Its fresh, medicinal scent is believed to promote mental clarity and emotional well-being while also purifying the air. In aromatherapy, tea tree oil is often diffused or added to massage oils and bath blends to relieve stress, anxiety, and fatigue. Tea tree oil has a diverse range of traditional uses in various cultures. From its origins in Australian Aboriginal medicine to its integration into Chinese and Western herbal practices, tea tree oil has been valued for its healing properties for centuries. Whether applied topically, inhaled, or used in aromatherapy, tea tree oil continues to be esteemed for its antimicrobial, antiseptic, and anti-inflammatory benefits across cultures worldwide [18]

Figure 3. Tea Trees harvested by ancient aborigine people of Australia

3.2. Historical applications

Tea tree oil, though not native to India, has found its place in traditional Indian medicine, primarily through the principles of Ayurveda. While not as deeply ingrained in Indian traditional medicine as in some other cultures, tea tree oil has gained recognition in recent decades for its therapeutic properties. In Ayurveda, which dates back thousands of years, there is a concept of "Gandha Taila," which refers to aromatic oils used for therapeutic purposes. While tea tree oil is not explicitly mentioned in classical Ayurvedic texts, its use aligns with Ayurvedic principles of promoting balance and wellness. [41]

Tea tree oil's antibacterial, antifungal, and anti-inflammatory properties make it suitable for various Ayurvedic treatments. It is often used topically to treat skin conditions such as acne, eczema, and fungal infections, aligning with Ayurvedic practices of caring for the skin using natural remedies. Furthermore, in Ayurvedic aromatherapy, certain aromatic oils are used to promote mental clarity, relaxation, and emotional balance. Tea tree oil's invigorating scent and purifying properties make it a suitable choice for this purpose.

While tea tree oil may not have as deep a historical association with Indian medicine as some indigenous herbs and oils, its adoption into Ayurvedic practice reflects its efficacy and versatility in promoting health and well-being. As interest in natural remedies and alternative medicine continues to grow, tea tree oil is likely to find further applications within the framework of Ayurveda in India and beyond [20]

4. Pharmacological properties and biological activities

4.1. Pharmacological properties of tea tree oil.

Tea tree oil, derived from Melaleuca alternifolia, has a range of pharmacological properties. It has been shown to have antiseptic, antimicrobial, and antioxidative effects, making it a valuable topical application in modern medicine and cosmetics [42]. Furthermore, it has been found to have bactericidal and fungicidal effects, as well as potent antioxidant properties, making it a potential natural antimicrobial and preservative agent in the food, agriculture, and pharmaceutical industries [43]. Additionally, its anti-inflammatory and immunomodulatory effects suggest a potential role in neuroprotection [44].

4.2. Antimicrobial, antifungal, and anti-inflammatory activities related to tea tree oil.

Tea tree oil, derived from Melaleuca alternifolia, has been extensively studied for its antifungal properties. Its components, including terpinen-4-ol, α-terpineol, linalool, α-pinene, β-pinene, and β-myrcene, have been found to exhibit high inhibitory antifungal activity [45]. This oil and its components have been shown to be effective against a range of fungal pathogens, including Botrytis cinerea and various plant pathogens [46,47]. In a study by Concha (1998), tea tree oil demonstrated inhibitory activity against a variety of clinical isolates, suggesting its potential use in the treatment of yeast and fungal infections. These findings collectively support the antifungal properties of tea tree oil [48].

4.3. Recent studies regarding biological activities of tea tree oil.

Recent studies have highlighted the diverse biological activities of tea tree oil, including its antioxidant and antimicrobial properties. Lakatos (2022) found that tea tree oil exhibited significant antimicrobial activity against Salmonella enteritidis [49], while Yasin (2021) reported its bactericidal effect against various bacterial species and its potential use as an organic fungicide, herbicide, and insecticide in agriculture[43]. Rutoa (2022) emphasized the antioxidant and antimicrobial activities of tea seed oil, a related product, further underscoring the potential of these natural oils in various applications.[50]

5. Clinical Applications and Efficacy

5.1. Clinical studies assessing the efficacy of tea tree oil.

A systematic review by Ernst (2000) found limited evidence for the efficacy of tea tree oil (TTO) in dermatological conditions, despite promising results in trials for acne and fungal infections [51]. However, Hadaś (2017) reported 100% effectiveness of TTO in treating Acanthamoeba infection, a type of eye disease [52]. May (2000) demonstrated the antimicrobial activity of TTO, particularly against multidrug-resistant organisms, including MRSA [53]. In contrast, Arweiler (2000) found no significant effect of TTO on supragingival plaque formation and vitality[54]. These studies collectively suggest that while TTO may have potential in treating certain conditions, further research is needed to establish its efficacy. [55]

5.1.1. Acne:

Several clinical trials have demonstrated the effectiveness of tea tree oil in treating acne. Research has shown that tea tree oil formulations significantly reduce acne lesions and improve overall skin condition. Its antimicrobial and anti-inflammatory properties help to clear acne lesions and prevent new ones from forming.

5.1.2. Fungal Infections:

Tea tree oil has been studied for its antifungal properties in treating conditions such as athlete's foot, nail fungus, and fungal skin infections. Clinical trials have shown that tea tree oil can effectively eradicate fungal pathogens and alleviate symptoms associated with these infections.

5.1.3. Dermatitis and Eczema:

Studies have explored the use of tea tree oil in managing dermatitis and eczema due to its anti-inflammatory and soothing properties. Research suggests that tea tree oil formulations can help reduce inflammation, itching, and redness associated with these conditions, providing relief to affected individuals.

5.1.4. Dandruff and Seborrheic Dermatitis:

Tea tree oil has been investigated as a natural remedy for dandruff and seborrheic dermatitis. Clinical studies have found that tea tree oil-based shampoos can effectively reduce dandruff severity and scalp itching, attributed to its antifungal and anti-inflammatory actions.

5.1.5. Oral Health:

Some research has explored the use of tea tree oil in oral care products for its antimicrobial properties. Clinical trials have shown that tea tree oil mouthwashes or dental products can help reduce oral bacteria, plaque formation, and gingivitis, contributing to improved oral hygiene.

5.1.6. Wound Healing:

Tea tree oil has been examined for its potential role in wound healing. Clinical studies have indicated that topical application of tea tree oil formulations can promote faster wound closure, reduce infection risk, and improve overall wound healing outcomes.

These clinical studies collectively support the efficacy of tea tree oil in various dermatological and oral health conditions. However, it's important to note that more research is needed to fully understand its mechanisms of action, optimal dosages, and potential side effects in different populations. Additionally, individuals should use tea tree oil cautiously and follow proper dilution guidelines to minimize the risk of skin irritation or allergic reactions.

5.1.7. Insect Bites and Stings:

Tea tree oil's anti-inflammatory and antipruritic properties make it useful for relieving itching, swelling, and discomfort caused by insect bites and stings. Applying diluted tea tree oil to the affected area can help soothe the skin and reduce irritation.

5.1.8. Minor Burns and Sunburns:

Tea tree oil can provide relief for minor burns and sunburns due to its cooling and soothing properties. It helps to reduce inflammation, alleviate pain, and promote healing when applied topically to the affected area.

5.1.9. Oral Health:

Tea tree oil has been incorporated into oral care products such as toothpaste and mouthwash for its antimicrobial properties. It can help reduce oral bacteria, plaque formation, and gingivitis when used as part of a regular oral hygiene routine.

5.1.10. Dandruff and Scalp Conditions:

Tea tree oil is commonly used in shampoos and hair care products to treat dandruff, dry scalp, and seborrheic dermatitis. Its antifungal properties help to eliminate dandruff-causing fungi and soothe the scalp.

Tea tree oil offers a natural and effective solution for addressing a variety of skin conditions, wounds, infections, and other health concerns. However, it's important to use tea tree oil safely and appropriately, as undiluted or improperly diluted tea tree oil can cause skin irritation or allergic reactions in some individuals.

Conventional treatments: Conventional wound care treatments may include antiseptic solutions, antibiotic ointments, and bandages. These treatments can be effective but may also increase the risk of antibiotic resistance and allergic reactions.

Tea tree oil can be a viable alternative or complementary treatment option for various skin conditions, wounds, and infections. However, it's essential to use tea tree oil safely and appropriately, and in some cases, conventional treatments may be more suitable or necessary, particularly for severe or persistent conditions. Consulting with a healthcare professional can help determine the most appropriate treatment approach based on individual needs and circumstances.

6. Safety and Toxicity

6.1. Safety profile of tea tree oil

Tea tree oil is generally considered safe when used appropriately, but it can cause adverse reactions in some individuals, especially when used in high concentrations or undiluted. Here's an overview of the safety profile of tea tree oil: [56]

6.1.1. Skin Irritation:

Undiluted or improperly diluted tea tree oil can cause skin irritation, redness, itching, and burning sensations, particularly in individuals with sensitive skin. It's important to always dilute tea tree oil with a carrier oil (such as coconut oil, olive oil, or almond oil) before applying it to the skin to minimize the risk of irritation. [56]

6.1.2. Allergic Reactions:

Some people may be allergic to tea tree oil, experiencing allergic contact dermatitis upon exposure. Symptoms of allergic reactions can include rash, hives, swelling, and difficulty breathing. If you experience any allergic symptoms after using tea tree oil, discontinue use and seek medical attention. [56]

6.1.3. Oral Toxicity:

Ingestion of tea tree oil can be toxic and should be avoided. Swallowing even small amounts of tea tree oil can cause nausea, vomiting, diarrhea, confusion, drowsiness, and potentially serious symptoms such as coma or seizures. Tea tree oil should never be ingested and should be kept out of reach of children. [56]

6.1.4. Eye Irritation:

Direct contact with tea tree oil can cause irritation to the eyes, leading to redness, burning, and tearing. If tea tree oil comes into contact with the eyes, flush the eyes with water immediately and seek medical attention if irritation persists. [56]

6.1.5. Hormonal Effects:

There is some evidence to suggest that tea tree oil may have hormonal effects, particularly in prepubescent boys. Topical application of tea tree oil has been associated with gynecomastia (enlarged breast tissue) in rare cases. However, more research is needed to fully understand the extent of this risk. [56]

6.1.6. Pets:

Tea tree oil can be toxic to pets, especially cats, if ingested or applied directly to the skin in high concentrations. Keep tea tree oil products away from pets, and consult a veterinarian if accidental exposure occurs.

6.2. Recommendations for safe usage and dosage.

To ensure safe use, it's essential to follow these guidelines when using tea tree oil:[57]

- Always dilute tea tree oil with a carrier oil before applying it to the skin.
- Perform a patch test before using tea tree oil on a larger area of the skin to check for any adverse reactions.
- Avoid ingesting tea tree oil or using it near the mouth or eyes.
- Store tea tree oil securely and out of reach of children and pets.
- Discontinue use if any adverse reactions occur and consult a healthcare professional if needed.

Hence, when used properly and with caution, tea tree oil can be a safe and effective natural remedy for various skin conditions and ailments.

7. Formulations and Delivery Systems

7.1. Different formulations of tea tree oil being reported.

Different formulations of tea tree oil have been explored for various applications. Umar (2021) developed anti-dandruff shampoos containing tea tree oil [58], which demonstrated good quality attributes and antifungal activity. Köhler (1999) found that encapsulating tea tree oil in cyclodextrins can protect its sensitive terpenes against oxidation. Shao (2015) compared the chemical composition, thermal stability, and antioxidant properties of tea seed oils obtained by different extraction methods, with supercritical fluid extraction yielding the best oil quality. Williams (1998) highlighted the strong antimicrobial activity of tea tree oil, particularly when combined with lavender or manuka oil, making it suitable for therapeutic use in various formulations.

7.2. Novel delivery systems aimed at enhancing its efficacy and stability of tea tree oil.

Recent studies have explored various novel delivery systems for tea tree oil, aiming to enhance its efficacy and stability. Kwon (2023) developed core-shell nanofibers as carrier systems for sustained delivery of tea tree oil, demonstrating strong antibacterial effects. Assis (2020) reviewed the therapeutic potential of encapsulated tea tree oil in micro and nanoencapsulated systems, emulsified and hybrid systems, and liposomal formulations, all of which showed improved antimicrobial and anti-inflammatory activities. Morais (2020) focused on a cellulose-based delivery system for dermic applications, successfully incorporating tea tree oil and microalgae components. Chen (2021) explored the use of stable high internal phase emulsions solely stabilized by natural oil-based nonionic surfactants as a delivery system for tea tree oil, effectively protecting the oil and increasing its bioavailability. These studies collectively highlight the potential of these novel delivery systems in enhancing the efficacy and stability of tea tree oil.

8. Regulatory Status and Quality Control

8.1. The regulatory status of tea tree oil in different countries.

Tea tree oil is a widely used product in aromatherapy and cosmetics, but its regulatory status is under threat in the European Union (Wabner, 2006). Adulteration of tea tree oil has become a concern, and various analytical technologies have been developed to differentiate between authentic tea tree oil and adulterated products (Gafner, 2018). Safety concerns have also been raised, with a review of adverse reaction cases suggesting that oral administration should be avoided and that skin disorders may occur with topical use (Bekhof, 2022).

8.2. Quality Control measures and standards for tea tree oil production and distribution.

A range of quality control measures and standards have been proposed for tea tree oil production and distribution. Brophy (1989) and Piovan (2021) both emphasize the importance of chemical composition analysis, with Brophy focusing on gas chromatography and Piovan introducing a TLC protocol for easy evaluation. Wang (2015) and Gallart-Mateu (2016) further enhance these measures by using chiral GC/MS and headspace gas chromatography mass spectrometry, respectively, to detect deviations from ISO standards and ensure the accuracy and greenness of the analysis. These studies collectively provide a comprehensive framework for quality control in tea tree oil production and distribution. Quality control measures and standards play a crucial role in ensuring the safety, efficacy, and consistency of tea tree oil production and distribution. Here are some key quality control measures and standards commonly implemented in the tea tree oil industry:

8.2.1. Botanical Identification:

Quality control begins with ensuring the correct botanical identity of the tea tree (Melaleuca alternifolia) used for oil extraction. Botanical identification techniques such as macroscopic and microscopic examination, DNA analysis, and chemical fingerprinting are employed to authenticate the raw materials.

8.2.2. Good Agricultural Practices (GAP):

Tea tree oil producers often adhere to Good Agricultural Practices to ensure the cultivation of high-quality raw materials. This includes practices such as proper land preparation, irrigation, pest and disease management, and harvesting techniques to optimize plant health and oil yield.

8.2.3. Good Manufacturing Practices (GMP):

GMP guidelines are followed during the extraction, processing, and manufacturing of tea tree oil to ensure consistent quality and safety. This includes maintaining hygienic conditions, proper equipment calibration, documentation of procedures, and personnel training.

8.2.4. Quality Assurance (QA):

Quality assurance protocols are implemented to monitor and control the quality of tea tree oil throughout the production process. This may include regular testing of raw materials, in-process monitoring, and final product testing to ensure compliance with quality standards and specifications.

8.2.5. Chemical Analysis:

Tea tree oil undergoes chemical analysis to determine its composition and purity. Gas chromatography (GC) and mass spectrometry (MS) are commonly used techniques to identify and quantify the chemical constituents of tea tree oil, such as terpinen-4-ol, cineole, and alpha-terpineol.

8.2.6. Physical Properties:

Physical properties such as colour, odour, viscosity, and specific gravity are evaluated to assess the overall quality of tea tree oil. These properties can indicate factors such as freshness, purity, and potential contamination.

8.2.7. Microbiological Testing:

Microbiological testing is conducted to ensure that tea tree oil is free from harmful microorganisms such as bacteria, fungi, and yeast. This helps prevent contamination and ensures product safety for consumers.

8.2.8. Packaging and Labelling:

Tea tree oil packaging should be designed to protect the product from degradation, oxidation, and contamination. Proper labelling is essential to provide consumers with accurate information about the product, including its botanical name, extraction method, purity, and usage instructions.

8.2.9. Certifications:

Some tea tree oil producers may obtain certifications such as Organic, ISO (International Organization for Standardization), or GMP certification to demonstrate compliance with industry standards and regulatory requirements.

By implementing these quality control measures and standards, tea tree oil producers can maintain the integrity and quality of their products, ensuring consumer satisfaction and safety. Additionally, adherence to quality standards helps build trust and credibility within the industry and among consumers.

9. Current Trends and Future Directions

9.1. Emerging trends in tea tree oil research.

Tea tree oil (TTO) has a wide range of applications, from medicinal to household and cosmetic products. However, its potential for inducing contact sensitization and allergic reactions should be considered [59]. The quality of TTO is a growing concern, with increasing instances of adulteration [60]. Research has been conducted to assess the potential of TTO in museum conservation, particularly in controlling recurrent mold. The quality of Australian TTO has been evaluated using advanced analytical technologies, including chiral and multi heart-cuts multidimensional gas chromatography [61].

9.2. Potential future applications and areas of exploration for tea tree oil.

Tea tree oil, derived from Melaleuca alternifolia, has a wide range of potential applications. Its antimicrobial properties make it a promising treatment for dermatological disorders [13]. It also shows potential as a natural antioxidant, with stable properties and a high yield [62]. Tea seed oil, extracted from Camellia sinensis, has also been studied for its potential health benefits, including its high unsaturated fatty acid content and antioxidant activity [63]. These studies collectively suggest that tea tree oil and tea seed oil have a wide range of potential applications, from skincare to food and museum conservation.

9.3. Gaps in current knowledge and suggested areas for further research.

Current research on tea tree (Melaleuca alternifolia) has primarily focused on its oil properties, with little attention given to its leaves as a potential source of natural fibres for bio composites [64]. Similarly, there is a need for further investigation into the chemical variation within the species and the potential biomarker compounds for quality control. The indigenous knowledge of trees and shrubs used as tea in Benguet also presents an area for further exploration, particularly in understanding their habitat, flowering/fruiting periods, and health benefits. Also, the role of shade tree species in tea gardens, requires further investigation to determine their impact on the growth and yield of tea plants [65].

10. Conclusion

Tea tree oil, derived from the leaves of Melaleuca alternifolia, is a natural product with antibacterial, antiviral, antifungal, and anti-inflammatory properties. It has been used in traditional medicine for skin infections, acne, vaginal fungus infections, throat infections, and cold sores. The WHO's Fungal Priority Pathogens List highlights the growing threat of fungal infections, including skin mycoses, affecting 20-25% of the world's population. Climate change is also contributing to the rise of fungal infections, with the potential to cause significant harm to both human and environmental health. Therefore, further research should be necessary in the field of natural / herbal antifungals to overcome any future fungal infections threats

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