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Essential oils for the treatment of skin anomalies: Scope and potential

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ABSTRACT

Skin diseases contribute significantly to worldwide morbidity and mortality. It is the most common of all human diseases which can affect people of any age group. Most importantly, it is seen that the COVID-19 pandemic have further detrimentally contributed to dermatological manifestations. Due to the enormous socioeconomic burden created by skin disorders, the dermatological treatments have been added in the WHO List of Essential Medicines. Some of the major predominant diseases are acne, psoriasis, eczema, fungal infections and skin carcinoma. As a matter of fact, focus on treatment of skin diseases should be arguably considered as a matter of global urgency. Although treatments are available, they face numerous challenges which limit patient acceptability. Essential oils have a long history of pharmacological use; however their role in the treatment of dermatological disorders is vague. Therefore, in this review, the potential and mechanism of different essential oils obtained from various sources in the treatment of major dermal disorders has been summarized. This will help the formulation scientists and the clinicians to develop suitable formulation strategies for the prevention and cure of skin diseases.

1. Introduction

Skin anomalies are the most common of all the diseases. It affects individuals irrespective of their region, culture, age and affects anywhere between 30 to 70% of the global population. According to the Global Burden of Disease project (2013) carried out at Institutes of Health Metrics, skin diseases are one of the major epidemiological burdens across the globe. It is reported that skin diseases have risen by 46.8% since 1990 making it fourth in rank responsible for most of the diseases (Giesey et al., 2021; Flohr and Hay, 2021). The top three predominant skin diseases are fungal diseases, acne and skin carcinoma (Hay et al., 2014). The worldwide prevalence of eczema has remained consistent. In fact, it is seen that skin diseases start affecting individuals at one yearand the predicament continues to 70 years and above, when conditions such as eczema and pruritis prevail (Fig. 1). Evidences have been found that skin diseases such as psoriasis are also associated with increasing incidence of cardiovascular complications (Hu and Lan, 2017).

With the increasing prevalence, dermatological treatments have been included on the List of Essential Medicines by WHO (Laing et al., 2003). It severely affects the quality of life of individuals. Diseases such as acne, dermatitis and melasma affect the confidence of the patients leading to anxiety, effect on work and even depression (Jobanputra and Bachmann, 2000). Reports have shown women and children are particularly affected by dermatological conditions. It severely affects their clothing choice and self-esteem, inclining them to social phobias and mental health. In underdeveloped nations, conditions where people are living in smaller spaces can further aggravate the situation, leading to transmission of communicable skin diseases. Even in developed countries, the socioeconomic burden cannot be ignored. In US alone, the cost of the treatment was approximately 86 billion USD per year (Seth et al., 2017). In countries where, healthcare expenditure is borne by the individuals, it can significantly contribute to economic burden.

Various international policies have been framed with the intention to improve dermatological care by training healthcare professionals and providing medications at cost effective rates. However, it has been seen that most of the individuals in economically weaker societies approach traditional healers for their treatment. Traditional systems of medicine have been used since time immemorial for the treatment of various ailments and skin diseases has been one of them. Although, essential oils have received a lot of attention in cosmetic industry and extensive information is available with regard to their pharmacological properties, but there is not much information

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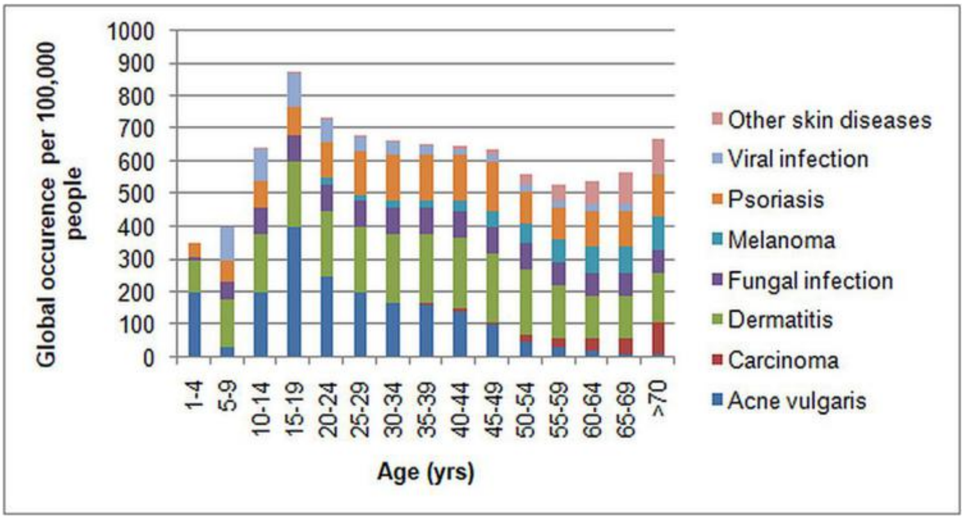


Fig. 1. Depiction of the global occurrence of different dermatological disorders in populations of different age groups (created from Global Burden of Disease project, 2013).

available on their role in the treatment of dermatological disorders. Therefore, this manuscript was prepared with the intention to compile the potential of different essential oils in the prevention/treatment of skin disorders. Additionally, their mechanism in the treatment of major dermal diseases has also been summarized.

In order to understand the biological roles of essential oils, it is imperative that the author makes himself/herself familiar with the barrier properties of the skin and the mechanisms which are involved in the disruption of this organ.

2. The barrier property of skin

The skin is the largest organ in the human body and covers the body surface, accounting for around 15% of the total body weight and having a surface area of 1.5−2m^2 (Tobin 2017). It provides a protective interface between the external environment and an individual's tissues, preventing water and electrolyte loss, reducing chemical penetration, regulating body temperature, and protecting against pathogenic microorganisms, ultraviolet radiation, and even dehydration. The three layers of the skin are the epidermis, dermis, and hypodermis, with each layer playing a specific function in the skin. The outermost layer of the skin is the epidermis which fulfils most of the barrier functions of the skin and is predominantly made up of cells, mostly 95% keratinocytes. The remaining 5% is made up of melanocytes, Merkel cells and Langerhans cells. The stratum basale followed by stratum spinosum, stratum granulosum, stratum lucidum (not present in thin skin), and the uppermost stratum corneum are the layers that run from the epidermis' deepest section to the skin's surface (de Macedo and Freitas, 2021). The epidermis is mostly composed of lipids namely phospholipids, free fatty acids, cholesterol and ceramides which forms a brick-mortar barrier responsible for skin barrier efficacy. Additionally, the skin has a moisture retention capability which is facilitated by the presence of natural moisturizing factor (NMF) in corneocytes located in the stratum corneum (SC). Some of the NMFs present are urea, amino acids, lactic acid, glycosaminoglycans etc. The filaggrin proteins which are present in intercellular lipids are also responsible for hydration. Furthermore, filaggrins are broken down in the upper SC which releases free amino acids to act as NMF (Vaughn et al., 2018). The basement membrane which is produced by keratinocytes and the dermal fibroblasts amalgamates the dermal-epidermal junction. It provides strength for the hold of the dermis to the epidermis and also prevents the entry of chemicals and cells. The dermis layer is tough fibroelastic tissue that nourishes, supports and helps in binding of epidermis with hypodermis.The hypodermis, which lies under the dermis is the deepest layer of the skin, that contains blood vessels and nerves. This layer is essential for the temperature control of the skin and the body, and contains approximately 80% of all body fat in non-obese people (Tobin 2017).

3. Skin anomalies

Skin is the vital body organ that is associated with numerous diseases affecting all age groups from the neonates to the elderly. Skin may lose its barrier property due to endogenous and exogenous factors. The symptoms and severity of skin issues vary widely. They can be short-term or long-term, painful or not, trivial or life-threatening. Infections and disorders like psoriasis, eczema, acne, and fungal infection place a huge strain on healthcare system and have a negative impact on patients' quality of life.

3.1. Eczema/ atopic dermatitis

Atopic dermatitis (AD), or eczema, is an inflammatory skin condition. It is a chronic disease which persists throughout the patient's life and significantly affects the quality of life of individuals around the world, especially in developed countries. It affects approximately 15 to 20% of children and 2.1 to 4.9% of adults globally (Habeshian and Cohen, 2020). The characteristics of AD include dry skin, lesions and inflamed skin with visible oozing, or weeping. The development of AD is based on a number of factors either genetic or environmental, that induce altered skin barrier and/or affect the cell-mediated immune responses. Barrier defects are caused by a variety of factors, including filaggrin (FLG) mutations, chemical exposure, microorganisms, low temperature, and low humidity (Dursun et al., 2019). External antigens stimulate the production of interleukins (IL) IL-4, IL-5, and IL-13, mediated through type-2 helper cells (Th-2) and also support immunoglobulin (IgE) mediated hypersensitivity reactions. Excessive use of preservatives, harsh detergents and fragrances, can alter the pH of the skin, and can change the enzymatic activity leading to inflammation. Both the innate and adaptive immune pathways can also be triggered by environmental pollutants. The presence of a single organism, *S. aureus* also plays an important role in AD. Other species include Streptococcus pyogenes and yeasts like *Malassezia sp*., can directly trigger skin inflammation. In Japan, *M. restricta* and *M. globosa*strains were found in almost 90% of individuals affected by AD and *M. dermatitis*, a novel species, was also isolated in smaller amounts (Dréno 2017).

3.2. Psoriasis

Psoriasis affects approximately 1−3% of the general population worldwide. It is a chronic skin condition which is controlled by disturbed immune responses within the skin. Plaque psoriasis (further referred to as Psoriasis Vulgaris) is the most common type of psoriasis which accounts for more than 80% − 90% of psoriasis cases (Rendon and Schäkel, 2019). It is characterized by silver scales, red patches on most parts of the skin often associated with itching. Itching occurs daily in around 75% of psoriasis patients and lasts for a long time. In addition, when the severity of psoriasis worsens, not only itch but also pain or a burning sensation may develop. Psoriasis is found in men, but it has previously been demonstrated to be more common and severe in women. Many abnormalities, such as aberrant keratinocyte growth and immune cell infiltration in the dermis and epidermis, have been documented, involving both the innate and adaptive immune systems, with dendritic cells and T cells, amongst other cells, playing major roles. It is believed that damaged keratinocytes secrete antimicrobial peptides (AMPs) such as LL37, β-defensins, S100 etc. LL37 binds to DNA from damaged cells and stimulates toll-like receptor 9 (TLR9) in plasmacytoid dendritic cells (pDC), a specialised subset of dendritic cells. These cells secrete type I interferon (IFN) such as IFN-α, IFN-β which further promotes maturation of myeloid dendritic cells (mDC). mDC cells promote differentiation of Th1 and Th17 cells as well as production of IFN-γ and Il-17. Further, when LL37 binds to RNA of damaged cells, stimulation of pDCs is observed through TLR7. It also promotes mDC maturation through TLR8 and subsequently release of TNF-α, IL-23 and IL-12 (Komiya et al., 2020). Studies have suggested inflammatory signals such as TNF-α, IFN-γ etc. are responsible for psoriatic inflammation and adaptive immune response through T-cells is accountable for maintenance of psoriasis. Interleukins and binding of LL37 to DNA stimulate keratinocyte proliferation (Rendon and Schäkel, 2019).

3.3. Acne

Acne vulgaris is a very common skin condition which affects people of all age groups. Globally, approximately 85% of people are affected by the disease (Tan and Bhate, 2015). It is characterized by lesions of both types; inflammatory and non-inflammatory, blackheads, whiteheads, open and closed comedones, papules, pustules, nodules, and cysts. Acne is associated with scars that can persist over a lifetime and have long-lasting psychosocial effects. Acne, as well as the post-inflammatory hyperpigmentation that results from it, is associated with depression, social isolation, and suicide ideation. Heredity, hormones, nutrition, pollutants, climatic conditions, and other bacterial species are the factors that are responsible for the development of acne, either alone or in combination (Cong et al., 2019). Increased sebum production, which is the main source of nutrients for *P. acnes*, is a major contributing factor in the development of acne. *P. acnes* bacteria produce propionic acid and acetic acid, which leads to the conversion of sebaceous triglycerides into fatty acids and causes inflammation of the follicular wall and surrounding dermis. Although *P. acne* is important for normal skin microbiota, it is also found predominating in acne affected skin. Several mechanisms which modulate the pathophysiology of acne are postulated. *P. acnes* enhances the sebum secretion by increasing the activity of diacylglycerol acyltransferase enzyme present in skin. Further, the bacteria also break down triglycerides and oxidize squalene found in sebum which triggers comedogenesis. *P. acnes* also binds to TLR-2 and TLR-4 on the surface of keratinocytes and stimulates monocytes to release interferons, interleukins, TNF-α, cytokins and β-defensins leading to inflammation (Xu and Li, 2019).

Another causative bacteria involved in pathogenesis of acne is *S. epidermidis*, an anaerobic microorganism that produces a fatty acid modifying enzyme that forms cholesterol in the skin by fatty acid esterification. *S. aureus*, a gram positive rod-shaped bacteria, produces extracellular enzymes such as lipases, proteases, hyaluronidases, and collagenase by invading the skin. These enzymes cause tissue injury and spread the pathogen into the deeper tissues. The capsular polysaccharides and pore-forming toxins produced by *S. agalactiae* are important factors in the development of *P. acnes* (Claudel et al., 2019).

3.4. Fungal infection

The incidence of superficial fungal infections is increasing nowadays and they are more common in individuals with immunocompromised conditions such as AIDS. Fungi are parasitic microorganisms which can cause both superficial and deep infections which invade the internal organs. Depending on the level of tissue penetration, skin fungal infections are classified as superficial, cutaneous, or subcutaneous. Cutaneous fungal infection that affects keratinized structures is caused by specific filamentous fungi named dermatomycetes like the genera *Trichophyton, Epidermophyton*, and *Microsporum*. The causative organisms for cutaneous fungal infections are various *tinea* spp. such as var. *faciei,* var. *barbae,* var. *capitis*, and var. *manuum* (Hainer, 2003). The mode of transmission is human contact with infected persons, animals, soil, and fomites. Furthermore, subcutaneous fungal infection caused by *Sporothrixs chenckii* and *Candida albicans*, occurs when a fungal infection spreads to the subcutaneous region (Gunaydin et al., 2020).

3.5. Skin ageing

Skin ageing is a natural process that depends on both internal and external factors, leading to cumulative changes in skin structure, function, and appearance. Aged skin is differentiated with low levels of lipids, NMF and water content. According to some experts, most of the effects are caused by extrinsic factors, and only 3% of ageing factors have the intrinsic background (Zhang and Duan, 2018). Gender, ethnicity, and genetic variations are the most important intrinsic factors of ageing. Ageing due to intrinsic factors is a physiological process that leads to dry, wrinkled skin with fine lines. The proliferation of basal cells is reduced, which results in a thin epidermal layer, and there is an inevitably diminished contact surface area between dermis and epidermis. Consequently, the supply of nutrition to the epidermis is also lessened, further aggravating basal cell proliferation (keratinocytes, fibroblasts, and melanocytes). On the other hand, ageing due to external factors such as exposure to UV radiations, environmental pollutants and toxins, smoking, is distinguished by deep wrinkles and hyperpigmentation. About80% of facial ageing, referred to as photoaging is caused by exposure to UV radiation (Bocheva et al., 2019).

3.6. Melasma

Melasma is a common acquired hyperpigmentary disorder that has a high prevalence in females and people with darker skin. The clinical signs which are usually asymptomatic include light to dark brown spots with irregular bodies, known as hyperpigmentation. The aetiology and pathogenesis of melasma are unknown, however, it is thought to be caused by a combination of factors such as UV and even visible light exposure, heredity, hormonal impacts, pregnancy, thyroid dysfunction, cosmetics, and medications. On histological examination, the skin shows signs of pigmentation in the epidermis and/or dermis, enlarged melanocytes and increased melanosomes (Ogbechie-Godec and Elbuluk, 2017). Recent research suggests that melasma is not only a melanocyte disease but also a photoaging skin problem. Growth-differentiation factor-15 (GDF-15) which is a type of transforming growth factor-β (TGF-β), is also a contributing factor of melasma and induces vascular proliferation. These findings suggest that mast cells play a significant role in the development of photoaging and hyperpigmentation. Several cytokines such as IL-1α, IL-6, secreted from sebocytes have been shown to have a paracrine effect on epidermal melanocytes (Kwon et al., 2019). Recently, it has been shown that the shorter wavelengths of visible lightmore specifically, blue light, also induces hyperpigmentation. Visible light penetrates the dermis layer and skin appendages, and in combination with UVA1 radiation, affects the dermis component and ultimately leads to the development of melasma lesions (Passeron and Picardo, 2018).

3.7. Seborrhoeic dermatitis

Seborrhoeic dermatitis is a skin disorder which is believed to be affected by *Malassezia sp*. The fungal species consumes skin triglycerides as food, and the metabolism products such as oleic acid creates barrier disruption and stimulates inflammatory responses. It tiggers a cascade of events leading to increased production of IFN-γ, interleukins, TNF-α etc. (Deangelis et al. 2007). The disease is also elicited by extreme weather conditions or stress, although other predisposing factors may also be involved. Further, reports have revealed bacterial colonization of *Staphylococcus aureus* may also contribute to seborrhoeic dermatitis (Park et al., 2017). Sebum plays an important role in the epidermal barrier. Malassezia exhibits inability to synthesize lipids, and therefore feeds on sebum lipids which is another contributing factor to aetiology of seborrhoeic dermatitis (Xu et al., 2007). Recent evidence suggests epidermal barrier disruption due to change in thickness of SC, integrity of tight junctions and composition of lamellar lipids provides favourable environment for colonization of Malassezia (Yokouchi and Kubo, 2018).

3.8. Skin cancer

It is an abnormal growth of skin cells that can be categorized on the basis of the cell type affected. Basal and squamous cells are the most affected and the disease is termed as basal and squamous cell carcinoma respectively. When melanocytes are affected, then it is termed as melanoma. Unlike, basal cell carcinomas, squamous cell carcinoma are invasive and dangerous if not treated at an early stage. Melanoma, on the other hand is the most malignant and fatal form of skin cancer. It appears in the form of black, brown, blue, pink, white or red patches. In general, skin carcinomas are caused by excessive exposure to UV radiations or sun bathing. Following UV exposure, particularly UVB, progression of inflammation is observed, where keratinocytes and macrophages are stimulated to release TNF-α, TGF-β, IFN-γ which promotes type 2 T helper cells leading to ineffective phagocytosis (Kreul et al., 2012). Simultaneously, dendritic cells stimulate IL-22 and TGF-β1 pathway and contribute to tumour progression (Daaboul et al., 2018). Natural killer cells act as a defence against tumour cells by selective recognition and targeting through killer receptors. However, the tumour microenvironment tends to down regulate these receptors (Bomfim et al., 2016).

3.9. Skin complications in COVID-19

With the emergence of the COVID-19 pandemic, the use of personal protective equipment (PPE) has been on the rise. Extended usage of goggles, face masks and gloves have led to dermatological manifestations such as itching and burning. Clinical signs such as contact dermatitis and acne have been reported lately (Darlenski and Tsankov, 2020). Long-term use of hats has led to manifestation of seborrhoeic dermatitis. Excessive use of disinfectants has contributed to skin drying which further contributes to eczema. Additionally, frequent washing of hands has been encouraged which also leads to drying (Darlenski and Tsankov, 2020). Therefore, it can be said that in the present era, COVID-19 has only aggravated the occurrence of skin disorders making it one of the most prominent human disease worldwide.

4. Challenges in the treatment of skin disorders

The treatment of skin problems comprises of targeting the causative factors by administering therapies topically or orally. Topical treatments of retinoids, antimicrobials, and comedolytic agents are generally preferred. For more severe forms of infection, oral treatments of antimicrobials, anticancers and hormonal agents are given. Nonetheless, the route of administration depends on a number of factors such as the age of the patient, convenience, site of infection and the severity of the disease. However, it cannot be ignored that oral therapy is associated with numerous adverse reactions such as hepatic toxicity, drug-drug interactions etc. (Homayun et al., 2019). Methotrexate despite being cost effective, exhibits side effects such as leucopenia, elevation of liver transaminases and nausea. It also has the potential to cause teratotoxicity (Wilsdon et al., 2019). Cyclosporin also shows hypertension, hepatotoxicity, nephrotoxicity and non-melanoma skin cancer (Paul et al., 2003). Because of the potential side effects it is usually recommended as short-term intermittent therapy. Similarly, retinoids which are vitamin A analogues, also shows side effects such as cheilitis and some adverse effects such as conjunctivitis, hepatitis and tertaogenicity. Phosphodiesterase-4 inhibitor, apremilast is another synthetic drug which acts by regulating the inflammatory response. Although, routine examination of hemotological parameters is not required, it demonstrates common side effects such as nausea, diarrhoea, upper respiratory tract infections, nasopharyngitis. Keeping in mind, the difficulties faced in these therapies, biologicals such as monoclonal antibodies (Infliximab, Certolizumab etc.) and fusion proteins were introduced. These drugs show adverse events such as increased chances of tuberculosis (TB), cancer, hemotological disorders and multiple sclerosis. Although the success rate is higher for severe forms of infections when treated with biologicals, they need to be administered as a subcutaneous injection (Martins et al., 2020). Some other drugs which are routinely used for treatment of skin diseases also exhibit adverse reactions/side effects which cannot be overlooked (Table 1). Phototherapy, although seemingly a good option for the treatment of severe forms of acne, melasma and psoriasis, has various problems such as frequent visits and expensive treatments (Martins et al., 2020). A burgeoning issue is the development of resistance against drugs used for the treatment of dermatological disorders associated with microbial infections and much success has not been achieved in this area. Essential oils have shown potential in this regard (Becerril et al., 2012) and can be a feasible option.

5. Potential of essential oils in skin disorders

According to World Health Organization, medicinal plants could be the best source of drugs. Almost 80% of the population in developing countries rely on pre-existing knowledge of herbal medicines for the treatment of various diseases (Ekor 2014). Natural medicine has attracted considerable attention due to several advantages such as cost effectiveness, lesser side-effects, better patient acceptability owing to long history of use. Besides, there are evidences that natural products play an important role in the treatment of many diseases that are almost difficult to treat with other medicinal systems. Therefore, herbal medicine is being considered for the treatment of many dermatological disorders ranging from simple itching to severe forms of cancer (Tabassum and Hamdani, 2014).

Essential oils (EOs) are an essential component of the plants and have been used widely in cosmetic, fragrance and pharmaceutical industry. They are volatile substances naturally produced by plants, which gives them plant a distinguished smell or taste. The components present in EOs are produced in cytoplasm and plastids of plant

Table 1
The different topical drugs available for dermatological disorders and the challenges associated with them.

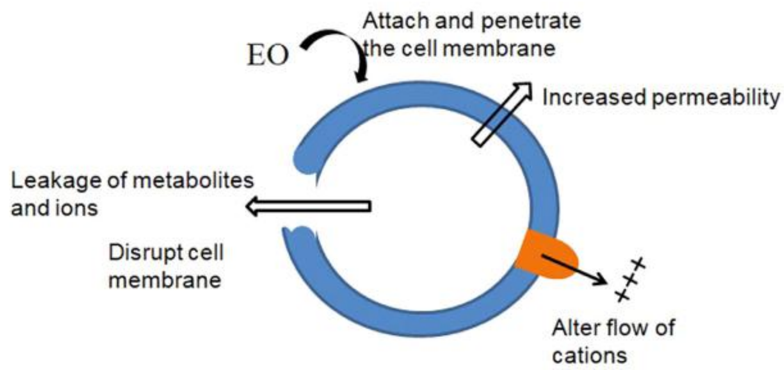
Treatment	Mechanism of action	Challenges	Reference
Topical corticosteroids	Suppress neutrophils, monocytes, lymphocytes, Langerhans cells, interleukins, TNF and granulocyte-monocyte colony stimulating factor (GM-CSF).	hypopigmentation, striae, acne, and skin atrophy	Rendon et al. 2019
Topical calcineurin inhibitors	inhibit cutaneous T cell activation and proliferation, epidermal barrier repair actions	Burning, pruritus, cost prohibitive	Habeshian and Cohen, 2020
Topical vitamin D analogues	bind to vitamin D receptors on T cells and keratinocytes to block keratinocyte proliferation and boost keratinocyte differentiation	Burning, irritation	Afifi et al. 2005
Topical retinoids	keratolytic, anti-comedogenic, and anti-inflammatory.	Burning, irritation, eczema, blister	Thielitz et al. 2008
Salicylic acid	Keratolytic	Irritation	Madan et al. 2014
Antioxidants	neutralizing ROS	Gastrointestinal disturbances, kidney stones	Salehi et al. 2018
Immunosuppressants			
Azathioprine	Disturbed DNA synthesis in T-cells	nausea, vomiting, headache, hepatotoxicity and leukopenia	LiverTox
Methotrexate	Blocks DNA and RNA synthesis and affects T-cell functions	myelosuppression, hepatotoxicity, and pulmonary fibrosis	Karadag et al. 2015
Mycophenolate mofetil	Inhibits biosynthesis of purine and influences T and B cell functions	headaches, GI upset, leukopenia	Varnell et al. 2017
Ciclosporin	inhibits T-cell-dependant immune responses	Nephrotoxicity and hypertension	Carle et al. 2003
Biologics			
Secukinumab	Down regulationTh17 and Th22 cytokines	Patient inconvenient due to subcutaneous injections	Usach et al. 2019
Fezakinumab	Anti-IL-22 mAb		
Ustekinumab	IL-12/IL-23p40 antagonist		
Emolizumab	anti−IL 31R mAb		
JAK inhibitors			
Baricitinib	selective inhibitor of JAK1 and JAK2	Nausea, Indigestion, diarrhoea.	Kremer et al. 2012
Tofacitinib	selective JAK1 and JAK3 inhibitor	Headaches, Upper respiratory tract infection, Increased cholesterol levels	
Phosphodiesterase inhibitors			
Crisaborole	phosphodiesterase-4 (PDE 4) inhibitors, PDE 4breaks down c-AMP which is responsible for down regulation of proinflammatory cytokines and upregulates anti-inflammatory cytokine	GI side effects, irritation and burning at the application site	Li et al. 2018
Apremilast	-do-	diarrhoea, vomiting, and depression	Li et al. 2018
Macrolides	Inhibits bacterial protein synthesis	Bacterial resistance	Kwiatkowska et al. 2012
Azole antifungals	Inhibition of synthesis and degradation of ergosterol in the fungal cell	Hepatotoxicity, gynaecomastia, alopecia, decreased libido, hypokalemia, hyponatremia	Benitez et al. 2019
Polyenes	bind to sterol ergosterol causing electrolyte and cytoplasmic material leakage	fever, chills, nausea, headache, hypotensions	Campoy and Adrio, 2017
Echinocandins	inhibit the enzyme β−1,3-glucan synthase which synthesizes glucan components in fungal cell wall	nausea, vomiting, bilirubinemia	Patil and Majumdar, 2017
Nucleoside analogs	disrupts fungal RNA, DNA, and protein synthesis	nephrotoxicity, myopathy, pancreatitis	Khungar and Han, 2010

cells and stored in glands, resin conduits and secretory cavities. EOs are usually present as liquid in different parts of plant. EOs contains a mixture of various components which if present in higher concentration (20−70%) are regarded as major component, otherwise categorized as minor if present in trace amounts. However, it is reported that the composition of EO is controlled by a number of factors such as geographical place, harvesting time, maturity, part of the plant, variation in species, processing and storage conditions. Each EO is a complex mixture of more volatile compounds such as terpenes and terpenoids. Terpenes, the largest group of components in essential oils, are mixtures of several isoprenes which are essentially C5 units. Additionally, terpenes also contain monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), eg.farnesenes; triterpenes (C30), and tetraterpenes (C40). Monoterpenes and sesquiterpenes are categorized as major components responsible for most of the pharmacological activities (Herman and Herman, 2015).

Plants synthesize EO for their antifungal, antibacterial property as well as protect them from insect invasion. It is because of these properties, EO are regarded as effective remedies against bacteria, fungi, or virus infection, inflammatory skin conditions such as acne and dermatitis. In addition, they have been found to be effective as anti-ageing agents, anti-inflammatory and wound healing treatments (Lin et al., 2018). The use of EO for general skin maintenance has a long history of use which is well known. It is noteworthy that EO are produced by more than 17,500 species of plants across the globe but only about 300 of them are commercialized (Wińska et al., 2019). This stresses that EOs have a lot of potential for the treatment of various dermatological diseases.

5.1. Essential oils as antimicrobials

The pharmacological activity of EOs depends on the type and concentration of components and the functional groups present on the moieties. Their lipophilic nature is responsible for easy penetration through the cell membranes of the microbes (Fig. 2a). It is reported that the components in EOs allows them to attach to the cell membranes and facilitates penetration allowing death of the microbes. Further it is reported that EOs also affect the permeability of cell membranes leading to leakage of cell contents (Wińska et al., 2019). Loss of vital components such as electrolytes, proteins and sugars can lead to destruction of cells. Additionally, some authors have reported that EOs can change the direction of flow of cations like H^+ and K^+, which can alter the pH, composition of the cells and thus their activity (Tongnuanchan and Benjakul, 2014). An interesting observation is the ability of certain EO such as *elaleuca cajuputi, Thymus vulgaris, Cinnamomum verum, Lavandula Angustifolia*, to fight microbial resistance strains. For instance, lavender EO is found to be active against methicillin and gentamycin resistant *S.aureus* strains responsible for most of the topical diseases (De Rapper et al. 2013). Similarly *Eucalyptus globules* and *Melaleuca cajuputi* EOs are effective against



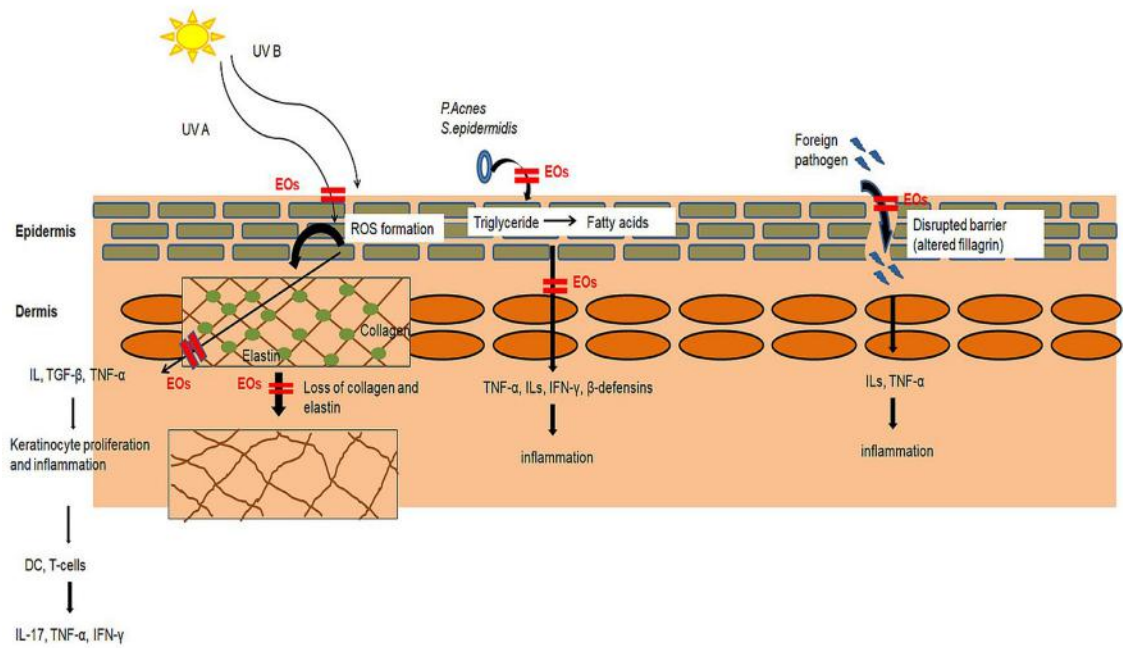


Fig. 2. **(a)** The different mechanisms demonstrating antimicrobial activity of Essential oils. (**b**) A snapshot of the role of essential oils in different dermatological disorders; psoriasis/cancer, ageing, acne, eczema/dermatitis (from left to right). EO; essential oil, DC; dendritic cells, ROS; reactive oxygen species.

methicillin resistant *S.aureus* at MIC 10 mg/ml and 5 mg/ml respectively (Hamoud et al., 2012). *Melaleuca alternifolia* EO is active against mupirocin resistant *S.aureus* at MIC 0.5% (Carson et al., 1995) while *Thymus vulgaris* EO acts against multidrug resistant *S.aureus* at MIC 1.3 mg/ml (Van Vuuren and Viljoen, 2006). EO of *Thymus vulgaris, Cinnamomum verum, Origanum vulgare, Mentha piperita* are effective against azole and polyene resistant *C. albicans* strains (D'agostino et al., 2019).

5.2. Essential oils as anti-ageing agents

Ageing, although a natural phenomenon, is also triggered by UV exposure which leads to degenerative changes such as loss of elasticity, thinning of epidermis, dryness and wrinkling of skin. UV exposure induces the formation of free radicals which synergistically contributes to loss of cellular functions and ageing (Fig. 2b). Morphologically ageing can be characterized by loss of collagen and elastin fibres in the extracellular matrix in the dermis and lack of support within the epidermal layers (Xiong et al., 2018). The enzymes elastase and collagenase are responsible for degradation of matrix fibres. Synthetic chemicals only act to restore the hydration in the skin which repairs the defects and blemishes superficially. EOs are regarded as true anti-ageing agents as evidences have been found that they increase the synthesis of collagen and elastin (Table 2). Some EOs from *Alpinia zerumbet, Calendula officinalis, Crocus sativus* etc. have also been found to increase the synthesis of hyaluronidase (Tu et al. 2015; Lohani et al. 2019; Madan et al. 2018), an enzyme which promotes formation of hyaluronidin. Hyaluronidin contributes to moisture and viscoelasticity in the skin (Jegasothy et al., 2014). *Panax ginseng* EO has been popularly used as anti-ageing agent. The active component ginsenosides present in this EO is believed to stimulate microcirculation, provide moisturization and alleviate wrinkles. It also acts as free radical scavenger which gives it an antioxidant activity. The *in-vitro* studies carried out are usually compared with a standard anti-ageing compound, epigallocatechin gallate which inhibits elastase, collagenase and hyaluronidase at IC_{50} values of 10.29, 1.56 and 12.71 μg/ml respectively. Therefore, natural agents which demonstrate these activities above the reference IC_{50} values are regarded as true anti-ageing agents (Xiong et al., 2018).

The skin pigment, melanin has an important function in pigmentation. Skin disorders such as melasma and freckles occur due to excessive production and accumulation of melanin. The synthesis of melanin is regulated by an enzyme tyrosinase, which controls the initial steps of melanin formation (Kim et al., 2012). Studies have suggested inhibition of tyrosinase can play an important role in hyperpigmentation disorders and ageing (Azmi et al., 2014).

Table 2
A snapshot of essential oils from various sources along with their potential in different dermatological disorders.

Essential oil	Component responsible for pharmacological activity	Pharmacological activity	Dermatological disorder	Reference
Abies koreana	Bornyl acetate, limonene	Antimicrobial against *S. epidermidis, P.acnes*	Acne	Yoon et al. 2009
	Bornyl ester, camphene, α-pinene	Antimicrobial against *C.albicans*	Fungal infection	Lee and Hong, 2009
Achillea millefolium	Eucalyptol, camphor, α-terpineol	Antimicrobial against *C.albicans*	Fungal infection	Candan et al. 2003
Alpinia zerumbet	γ-terpinene, cineole, *p*-cymene, sabinene, terpinen-4-ol	inhibit collagenase, tyrosinase, hyaluronidase, and elastase, free radical scavenger, antioxidant	Ageing, melasma	Tu et al. 2015
Anthemis aciphylla	α-Pinene, Terpinen-4-ol	Antimicrobial against *S. epidermidis*	Acne	Hüsnü et al. 2006
Anthemis nobilis	Not known	Antimicrobial against *P.acnes*	Acne	Zu et al. 2010
	2-Methylbutyl-2-methyl propanoic acid, limonene, 3-methylpentyl-2-butenoic acid, isobutyl isobutyrate	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
Angelica archangelica	α-Phellandrene, α-pinene, β-phellandrene, $\delta-3$-carene	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
Artemisia sp.				
var. *dracunculus*	Estragole	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
var. *sieberi*	α thujone, β thujone	Antimicrobial against *M.furfur, M. slooffiae, M. obtusa*	Eczema, dermatitis, psoriasis	Khosravi et al. 2016
Boswellia sp.	α-Pinene, myrcene, limonene, α-thujene, p-cymene, β-pinene	Antimicrobial against *C.albicans*	Fungal infection	van Vuuren et al. 2014
Cananga odorata	Bicyclosesquiphellandrene, β-farnesene, Benzyl acetate, linalool, methyl benzoate	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
Calendula officinalis	trans$-\beta-$ocimene, dihydrotagetone	Free radical scavenger, antioxidant	Ageing	Lohani et al. 2019
Cinnamomum sp.				
Var. zeylanicum	Cinnamaldehyde	Antimicrobial against *S. epidermidis*	Acne	Nuryastuti et al. 2009
	Not known	*P.acnes*	Acne	Zu et al. 2010
	trans-Cinnamaldehyde, eugenol	Antimicrobial against *C.albicans*	Fungal infection	Giordani et al. 2006
	Cinnamaldehyde, eugenol	Antimicrobial against *M.furfur*	AD, psoriasis	Pooja et al. 2013
Citrus aurantium	Limonene, *E*-nerolidol, terpineol	Antimicrobial against *S. epidermidis*	Acne	Hsouna et al. 2013
	Linalyl acetate, linalool	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
	D-limonene	Anti-oxidant, anti-inflammatory, chemopreventive	Cancer	Liu et al. 2015
Citrus medica	Not known	Antimicrobial against *P.acnes*	Acne	Zu et al. 2010
	Not known	Antimicrobial against *C.albicans*	Fungal infection	Nasir et al. 2015
Commiphora myrrha	(*E*)-β-Ocimene, furanoeudesma-1,3-diene	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
Coriandrum sativum	Not known	Antimicrobial against *P.acnes*	Acne	Luangnarumitchai et al. 2007
	Decanal, 1-decanol, 2-dodecenol	Antimicrobial against *C.albicans*	Fungal infection	Furletti et al. 2011
Crocus sativus	Safranal, crocin	Anticollagenase, anti-hyaluronidase, antioxidant	Ageing, melasma	Madan et al. 2018
Curcuma longa	Not known	Antimicrobial against *P.acnes*	Acne	Luangnarumitchai et al. 2007
Cupressus sempervirens	α-Pinene, 3- carene, cedrol, terpinolene and sabinene	Antimelanoma via growth inhibitory effect	Chemopreventive	Cardile et al. 2009
Cymbopogon citrates	Not known	Antimicrobial against *P.acnes*	Acne	Luangnarumitchai et al. 2007
	Geranial, β-myrcene, Z-citral	Antimicrobial against *C.albicans*	Fungal infection	Tarek et al. 2014
Daucus carota	Carotol, β-Bisabolene, α-Pinene, Geranyl acetate	Antimicrobial against *C.albicans*	Fungal infection	Maxia et al. 2009
	$\beta-2$-himachalen-6-ol	Chemopreventive	Cancer	Daaboul et al., 2018
Eucalyptus globules	1,8-Cineol	Antimicrobial against *S. epidermidis, C.albicans*	Acne, Fungal infection	Hamoud et al., 2012
	p-Cymene, terpinene	*P.acnes, UV-B induced cancer*	Acne, Cancer	Lee et al. 2017
Erigeron bonariensis	trans-α-Farnesene, isolongifolene-5-ol, α-maaliene, berkheyaradulen, α-muurolene	Inhibit collagenase, elastase, and hyaluronidase Inhibit tyrosinase	Ageing, melasma	Elgamal et al. 2021
Foeniculum vulgare	(*E*)-anethole, limonene, fenchone	Antimicrobial against *S. epidermidis*	Acne	Mota et al. 2015
	trans-Anethole, DL-limonene, carvone	Antimicrobial against *C.albicans*	Fungal infection	Tarek et al. 2014
Illicium anisatum	Eucalyptol	Anti-elastase, anticollagenase, inhibit NO and PGE2 levels	Ageing, anti-inflammatory,	Kim et al. 2009
Jasminum grandiflora	Not known	Antimicrobial against *P.acnes*	Acne	Zu et al. 2010
Juniperi aetheroleum	α-Pinene, β-pinene, sabinene	Antimicrobial against *S. epidermidis, C.albicans*	Acne, Fungal infection	Hamoud et al., 2012

(*continued*)

Table 2 (*Continued*)

Essential oil	Component responsible for pharmacological activity	Pharmacological activity	Dermatological disorder	Reference
Juniperus communis	α-Pinene, β-pinene	Antimicrobial against *P.acne, C. albicans*	Acne, Fungal infection	Hamoud et al., 2012
Kunzea ericoides	α-Pinene, p-cymene	Antimicrobial against *S. epidermidis, P.acnes, C.albicans*	Acne, Fungal infection	van Vuuren et al. 2014
Lavandula sp.				
Var. angustifolia	Linalool, linalyl acetate	Antimicrobial against *S. epidermidis, P.acnes, C.albicans*	Acne, Fungal infection	Luangnarumitchai et al. 2007
	Linalool, linalyl acetate	Reduce Th-1 specific TNF-α and IL-1β	Psoriasis	Rai et al. 2020
Var. stoechas	α-Fenchone, 1,8-cineole, camphor	Antimicrobial against *S. epidermidis, P.acnes, C.albicans*	Acne, Fungal infection	Kirmizibekmez et al. 2009
Leptospermum scoparium	(−)-(E)-Calamenene, leptospermon	Antimicrobial against *S. epidermidis, C.albicans*	Acne, Fungal infection	van Vuuren et al. 2014
	Eudesma-4(14),11-diene, α-selinene, (E)-methyl cinnamate	Antimicrobial against *P.acnes*		
Melaleuca sp.				
Var. alternifolia	α-Terpinene, γ-terpinene, terpinen-4-ol, 1,8-Cineole	Antimicrobial against *S. epidermidis*	Acne	Christoph et al. 2000
	terpinen-4-ol, γ-terpinene	Antimicrobial against *C.albicans*	Fungal infection	
Var. leucadendrun	1,8 cineole, p-cymene, linalool	Antimicrobial against *M.furfur*	Eczema, dermatitis, psoriasis	Pooja et al. 2013
	1,8-cineol, viridiflorol	Free radical scavenger	Anti-oxidant	Pino et al. 2010
Mentha sp.				
Var. piperita	1,8-Cineol, menthone, menthol	Antimicrobial against *S. epidermidis, P.acnes, C.albicans*	Acne, Fungal infection	Hamoud et al., 2012
Var. spicata	Not known	Antimicrobial against *P.acnes, C. albicans*	Acne, Fungal infection	Zu et al. 2010
	Carvone, limonene	Antimicrobial against *M.furfur, M. sympodialis, M. globosa, M. restricta*	Eczema, dermatitis, psoriasis	Khosravi et al. 2016
Ocimum sp.				
Var. americanum	Neral, geraniol, methyl chavicol	Antimicrobial against *P.acnes*	Acne	Viyoch et al. 2006
Var. basilicum	Linalool, methyl chavicol	Antimicrobial against *S. epidermidis*	Acne	Opalchenova and Obreshkova, 2003
	Linalool, 1,8-Cineole, anethole	Antimicrobial against *C.albicans*	Fungal infection	Vieira et al. 2014
Var. kilimandscharicum	Camphor, limonene, camphene	Antimicrobial against *M.furfur*	Eczema, dermatitis, psoriasis	Pooja et al. 2013
Origanum sp.				
Var. microphyllum	Carvacrol, Terpin-4-ol, thymol	Antimicrobial against *S. epidermidis*	Acne	Sökmen et al. 2004
Var. vulgare	Cymene, cymenol	Antimicrobial against *C.albicans*	Fungal infection	-do-
	thymol, α terpinene, α cymene	Antimicrobial against *M.furfur*	Eczema, dermatitis	Vinciguerra et al. 2018
	Carvacrol	Inhibit collagenase, elastase, and hyaluronidase	Ageing	Laothaweerungsawat et al. 2020
Piper nigrum	Not known	Antimicrobial against *P.acnes*	Acne	Luangnarumitchai et al. 2007
	β-Caryophyllene, limonene	Antimicrobial against *C.albicans*	Fungal infection	de Rapper et al. 2013
Pinus pinaster	α-Pinene	Free radical scavenger, hydroxyl reducing agent	Antioxidant, anti-inflammatory	Tümen et al. 2018
Pelargonium graveolens	Citronellol, geraniol	Free radical scavenger	Anti-oxidant, Ageing	Lohani et al. 2019
Plectranthus amboinicus	Carvocrol, thymol, caryophyllene	Anti-melanoma via inhibition of tumour nodule	Chemo preventive	Manjamalai and Grace, 2013
Pluchea dioscoridis	β-Caryophyllene, α-Maaliene, Berkheyaradulen	Inhibit collagenase, elastase, hyaluronidase, tyrosinase	Ageing, melasma	Elgamal et al. 2021
Pituranthos tortuosus	Sabinene, αpinene, limonene, and terpinen-4-ol	Downregulate tumour growth factors, apoptosis	Chemo preventive	Krifa et al. 2016
Premna odorata	β-Caryophyllene	anti-collagenase, anti-elastase and anti-hyaluronidase	Ageing	Altyar et al. 2020
Rosa centifolia	Not known	Antimicrobial against *P.acnes*	Acne	Zu et al. 2000
Rosmarinus officinalis	1,8-Cineole, α-pinene, camphor, camphene	Antimicrobial against *S. epidermidis, C.albicans*	Acne, Fungal infection	Jiang et al. 2011
Salvia sp.				
Var. bracteata	Caryophyllene oxide	Antimicrobial against *S. epidermidis*	Acne	Cardile et al. 2009
Var.eremophila	Borneol, α-pinene, bornyl acetate	Antimicrobial against *S. epidermidis*	Acne	Ebrahimabadi et al. 2010
Var. rubifolia	γ-Muurolene γ-Muurolene, α-pinene, thujone, p-cymene	Anti-melanoma via growth inhibitory activity	Cancer	Cardile et al. 2009
Santalum album	α-santalol	Reduce levels of 5-lipoxygenase, IL-17 and PDE-4, inhibit tyrosinase levels	Anti-inflammatory, psoriasis, dermatitis, ageing	Moy and Levenson, 2017
Syzygium aromaticum	Eugenol, β-caryophyllene, 2-methoxy-4-[2-*propenyl*]phenol acetate	Antimicrobial against *S. epidermidis*	Acne	Fu et al. 2007
	DL-Limonene	Antimicrobial against *S. epidermidis*	Acne	-do-

(*continued*)

Table 2 (*Continued*)

Essential oil	Component responsible for pharmacological activity	Pharmacological activity	Dermatological disorder	Reference
Thymus sp.				
Var.herba-barona	Thymol, carvacrol, p-Cymene	Antimicrobial against *C.albicans*	Fungal infection	Oh et al. 2009
Var. kotschyanus	thymol, carvacrol	Antimicrobial against *M.furfur, M.globosa, M. restricta*	Eczema, dermatitis	Khosravi et al. 2016
Tridax procumbens	α-Pinene, ß-pinene, phellandrene, sabinene	Anti-melanoma	Chemo preventive	Manjamalai et al. 2012
Zingiber officinale	Not known	Antimicrobial against *P.acne, C. albicans*	Acne	Zu et al. 2010
Zornia brasiliensis	Germacrene, humulene, farnesene	Inhibit tumour growth	Chemo preventive	Costa et al. 2015

5.3. Essential oils as antioxidants

Solar radiation is the main reason for excessive production of reactive oxygen species which triggers oxidative stress. A cascade of events including interaction of reactive oxygen species (ROS) with lipids, DNA and other cellular components results in loss of biological functions and cell death. ROS also indirectly activates enzymes, collagenase and elastase which promote skin ageing. Melanogenesis, the process of melanin formation, reportedly also produces ROS in melanocytes (Jiratchayamaethasakul et al., 2020). Therefore**,** sequestration of these events by the use of an antioxidant can be effective strategy to delay skin ageing and melanogenesis.

5.4. Essential oils as anti-psoriatics

EOs from a number of plant species such as *Azadirachta indica, Aloe barbadensis, Fucus vescicolosus, Glycyrrhiza glabra, Hypericum perforatum, Pilocarpus jaborandi* have been reported to have anti-psoriatic effects (Amenta et al., 2000)**.** Although their mechanism of action is not clear, it is postulated that their anti-inflammatory activities (Fig. 2b) studied by different oedema models may have some contribution in the treatment of psoriasis. In another study by El-Gammal (El-Gammal et al., 2018), a combination of *Propolis* and *Aloe vera* were applied topically to patients to determine the anti-psoriatic potential. It was found that caffeic acid-phenethyl ester found in propolis has anti-inflammatory and anti-oxidant properties via inhibition of release of prostaglandins and leukotrienes. Aloesin found in *Aloe vera* prevents the release of interleukins which substantiates its role in psoriasis. Some other EOs having anti-psoriatic activity is depicted in Table 2.

5.5. Essential oils in dermatitis/eczema

Although, studies on EOs with special focus on diseases such as eczema, dermatitis were not found, studies have claimed that EOs which exhibit anti-inflammatory activity and/or inhibit the activity of *M. furfur* can be postulated to have anti-psoriatic property (Fig. 2b). *Avena sativa* extract was found to inhibit the production of interleukins, expression of phospholipase A_2 and cyclooxygenase which demonstrate its anti-inflammatory activity (Aries et al., 2005)**.** A study conducted by Kim (Kim et al., 2010) showed that *A. vera* gel decreased the levels of IL-5 and IL-10 which suggest its possible role in the treatment of AD. The curcumin found in Curcuma longa has proven to have strong anti-inflammatory and anti-oxidant activity, and the authors have suggested its possible use in inflammation related to eczema (Aggarwal et al., 2007)**.** A clinical study was conducted wherein cream containing extracts of *Matricaria chamomilla* were used in eczema patients and it was found to provide similar relief as steroidal creams (Aertgeerts et al., 1985)**.**

5.6. Essential oils as anti-cancer agents

The anti-carcinogenecity of EOs has been well explored previously (Pavithra et al., 2019)**.** It is reported that plant EOs consist of both chemopreventive as well as chemotherapeutic activity. *In-vivo* studies have demonstrated the potential of Turmeric and sandalwood EOs which shows that it significantly inhibits cytochrome P450 enzymes and TPA-induced ornithine decarboxylase respectively suggesting their anti-carcinoma activity (Liju et al., 2014; Dwivedi and Zhang, 1999)**.** Topical application of perillyl alcohol found in many plant species such as lemon grass, spearmint, caraway etc. have shown potential in UV-B induced skin carcinoma (Barthelman et al., 1998)**.** Cytotoxic activity of EOs obtained from *Platycladus orientalis, Prangos asperula, Salvia rubifolia, Tridax procumbens and Plectranthus amboinicus* have shown promising potential (Pavithra et al., 2019)**.**

Table 3
Some commercial essential oil based products used in various dermatological disorders.

Dermatological disorder/ Activity	Essential oil/ Source	Brand name
Acne	*Citrus aurantium* (subsp. *Bigaradia), Melaleuca alternifolia, Cinnamonum* sp.	Soul Tree
Acne	*Melaleuca alternifolia, Salvia sclarea*	Dot and key
Acne	*Melaleuca alternifolia, Persea americana*	House of beauty
Ageing	*Santalum album, Crocus sativus, Glycyrrhiza glabra, Rubia cordifolia*	Kama Ayurveda
Antibacterial, antioxidant	*Mentha* sp.	Organic by nature
Anti-inflammatory, antibacterial	*Melaleuca alternifolia, Salvia rosmarinus, Cannabis sativa*	Brillaire
Dryness	*Psoralea corylifolia*	Auli
Eczema/ Dermatitis/ Psoriasis	*Holarrhena pubescens, Curcuma longa, Centella asiatica, Glycyrrhiza glabra, Azadirachta Indica, Capsicum annuum*	Bio Resurge
Fungal infection	Not disclosed	Bioayurveda
Fungal infection	*Melaleuca alternifolia*, medium chain triglycerides from undisclosed source	Sea el
Melasma	*Curcuma longa, Juniperus communis*	Vedaearth
Melasma	*Rosmarinus officinalis, Citrus Medica* (subsp. *Limonum)*	Aroma magic
Pigmentation/Melasma	*Helichrysum* sp.*, Rosa canina*	Organic by nature
Psoriasis/ Fungal infection/ Ageing	*Aloe Vera, Indigofera tinctoria, Wrightia tinctoria*	Dr. JRK
Wrinkles	*Prunus domestica, Punica granatum*	Organic by nature

6. Future prospects

It is seen that EOs have a predominant role in the treatment of different dermatological disorders. Their lipophilic nature makes them viable candidates for topical delivery. It can be seen that EOs have been widely used for cosmetic/superficial dermatological manifestations and their commercial applicability has been discussed in Table 3. However, topical application of EOs is another challenge which is often overlooked. EOs when administered as such in the form of oils or as conventional topical formulations may show signs of skin irritation, erythma and burning. Another problem is their high volatility because of which their sufficient skin retention is not possible. Additionally, stability is also an issue due to rapid decomposition when exposed to light, humidity or oxygen. Furthermore, certain components like terpenoids exhibit hypersensitivity reactions identical to allergic contact dermatitis (Koyama and Heinbockel, 2020). Therefore, to realize the full potential of EOs, encapsulation into a suitable delivery system such as micro/nano carrier systems can be a feasible strategy. This will not only improve the shelf-life of EO but also improve the patient acceptability while minimizing side effects.

7. Conclusion

The present review was prepared with the intention to summarize the potential of EO obtained from different sources in the treatment of diverse dermatological disorders. In spite of their vast pharmacological activities, EOs are not accepted by clinicians. Their encapsulation into a suitable delivery system can improve their acceptability. This will help the formulation scientists and the clinicians to develop suitable formulation strategies for the prevention and cure of skin diseases.

Declaration of Competing Interest

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References

Aertgeerts, P., Albring, M., Klaschka, F., Nasemann, T., Patzelt-Wenczler, R., Rauhut, K., Weigl, B., 1985. Comparative testing of Kamillosan cream and steroidal (0.25% hydrocortisone, 0.75% fluocortin butyl ester) and non-steroidal (5% bufexamac) dermatologic agents in maintenance therapy of eczematous diseases. Z. Hautkr. 60, 270–277.
Aggarwal, B.B., Sundaram, C., Malani, N., Ichikawa, H., 2007. Curcumin: the Indian solid gold. Adv. Exp. Med. Biol. 595, 1–75.
Amenta, R., Camarda, L., Di Stefano, V., Lentini, F., Venza, F., 2000. Traditional medicine as a source of new therapeutic agents against psoriasis. Fitoterapia 71, S13–S20.
Aries, M.F., Vaissiere, C., Pinelli, E., Pipy, B., Charveron, M., 2005. Avenarhealba® inhibits A23187-stimulated arachidonic acid mobilization, eicosanoid release, and cPLA2 expression in human keratinocytes: potential in cutaneous inflammatory disorders. Biolog. Pharmaceut. Bull. 28, 601–606.
Azmi, N., Hashim, P., Hashim, D.M., Halimoon, N., Majid, N.M.N., 2014. Anti−elastase, anti−tyrosinase and matrix metalloproteinase−1 inhibitory activity of earthworm extracts as potential new anti−aging agent. Asian Pac. J. Trop. Biomed. 4, S348–S352.
Barthelman, M., Chen, W., Gensler, H.L., Huang, C., Dong, Z., Bowden, G.T., 1998. Inhibitory effects of perillyl alcohol on UVB-induced murine skin cancer and AP-1 transactivation. Cancer Res. 58, 711–716.
Becerril, R., Nerin, C., Gomez-Lus, R., 2012. Evaluation of bacterial resistance to essential oils and antibiotics after exposure to oregano and cinnamon essential oils. Foodborne Pathog. Dis. 9, 699–705.
Bocheva, G., Slominski, R.M., Slominski, A.T., 2019. Neuroendocrine aspects of skin aging. Int. J. Mol. Sci. 20, 2798.
Bomfim, L.M., Menezes, L.R., Rodrigues, A.C.B., Dias, R.B., Gurgel Rocha, C.A., Soares, M.B., Neto, A.F., Nascimento, M.P., Campos, A.F., Silva, L.C.E., Costa, E.V., 2016. Antitumour activity of the microencapsulation of Annona vepretorum essential oil. Basic Clin. Pharmacol. Toxicol. 118, 208–213.
Carson, C.F., Cookson, B.D., Farrelly, H.D., Riley, T.V., 1995. Susceptibility of methicillin-resistant Staphylococcus aureus to the essential oil of Melaleuca alternifolia. J. Antimicrob. Chemother. 35, 421–424.
Claudel, J.P., Auffret, N., Leccia, M.T., Poli, F., Corvec, S., Dréno, B., 2019. Staphylococcus epidermidis: a potential new player in the physiopathology of acne? Dermatology 235, 287–294.
Cong, T.X., Hao, D., Wen, X., Li, X.H., He, G., Jiang, X., 2019. From pathogenesis of acne vulgaris to anti-acne agents. Arch. Dermatol. Res. 311, 337–349.
D'agostino, M., Tesse, N., Frippiat, J.P., Machouart, M., Debourgogne, A., 2019. Essential oils and their natural active compounds presenting antifungal properties. Molecules 24, 3713.
Daaboul, H.E., Dagher, C., Taleb, R.I., Bodman-Smith, K., Shebaby, W.N., El-Sibai, M., Mroueh, M.A., Daher, C.F., 2018. The chemotherapeutic effect of β-2-himachalen-6-ol in chemically induced skin tumorigenesis. Biomed. Pharmacother. 103, 443–452.
Darlenski, R., Tsankov, N., 2020. COVID-19 pandemic and the skin: what should dermatologists know? Clin. Dermatol. 38 (6), 785–787.
DeAngelis, Y.M., Saunders, C.W., Johnstone, K.R., Reeder, N.L., Coleman, C.G., Kaczvinsky, Jr., J.R., Gale, C., Walter, R., Mekel, M., Lacey, M.P., Keough, T.W., 2007. Isolation and expression of a Malassezia globosa lipase gene, LIP1. J. Investigat. Dermatol. 127, 2138–2146.
Dréno, B., 2017. What is new in the pathophysiology of acne, an overview. J. Eur. Acad. Dermatol. Venereol. 31, 8–12.
Dursun, R., Daye, M., Durmaz, K., 2019. Acne and rosacea: what's new for treatment? Dermatol. Ther. 32 (5), e13020.
Dwivedi, C., Zhang, Y., 1999. Sandalwood oil prevents skin tumour development in CD1 mice. Eur. J. Canc. Prevent. 8, 449–455.
Ekor, M., 2014. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Front. Neurol. 4, 1–10.
El-Gammal, A., Di Nardo, V., Daaboul, F., Tchernev, G., Wollina, U., Lotti, J., Lotti, T., 2018. Is there a place for local natural treatment of psoriasis? Open Access Maced. J. Med. Sci. 6, 839.
Flohr, C., Hay, R., 2021. Putting the burden of skin diseases on the global map. Brit. J. Dermatol. 184, 189–190.
Giesey, R.L., Mehrmal, S., Uppal, P., Delost, G., 2021. The global burden of skin and subcutaneous disease: a longitudinal analysis from the global burden of disease study from 1990-2017. SKIN J. Cutan. Med. 5, 125–136.
Gunaydin, S.D., Arikan-Akdagli, S., Akova, M., 2020. Fungal infections of the skin and soft tissue. Curr. Opin. Infect. Dis. 33, 130–136.
Habeshian, K.A., Cohen, B.A., 2020. Current issues in the treatment of acne vulgaris. Pediatrics 145, S225–S230.
Hainer, B.L., 2003. Dermatophyte infections. Am. Fam. Physician 67 (1), 101–109.
Hamoud, R., Sporer, F., Reichling, J., Wink, M., 2012. Antimicrobial activity of a traditionally used complex essential oil distillate (Olbas® Tropfen) in comparison to its individual essential oil ingredients. Phytomedicine 19 (11), 969–976.
Hay, R.J., Johns, N.E., Williams, H.C., Bolliger, I.W., Dellavalle, R.P., Margolis, D.J., Marks, R., Naldi, L., Weinstock, M.A., Wulf, S.K., Michaud, C., 2014. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. J. Investig. Dermatol. 134, 1527–1534.
Herman, A., Herman, A.P., 2015. Essential oils and their constituents as skin penetration enhancer for transdermal drug delivery: a review. J. Pharm. Pharmacol. 67, 473–485.
Homayun, B., Lin, X., Choi, H.J., 2019. Challenges and recent progress in oral drug delivery systems for biopharmaceuticals. Pharmaceutics 11, 1–29.
Hu, S.C.S., Lan, C.C.E., 2017. Psoriasis and cardiovascular comorbidities: focusing on severe vascular events, cardiovascular risk factors and implications for treatment. Int. J. Mol. Sci. 18, 2211.
Jegasothy, S.M., Zabolotniaia, V., Bielfeldt, S., 2014. Efficacy of a new topical nano-hyaluronic acid in humans. J. Clin. Aesth. Dermatol. 7, 27–29.
Jiratchayamaethasakul, C., Ding, Y., Hwang, O., Im, S.T., Jang, Y., Myung, S.W., Lee, J.M., Kim, H.S., Ko, S.C., Lee, S.H., 2020. In vitro screening of elastase, collagenase, hyaluronidase, and tyrosinase inhibitory and antioxidant activities of 22 halophyte plant extracts for novel cosmeceuticals. Fish Aquat. Sci. 23, 1–9.
Jobanputra, R., Bachmann, M., 2000. The effect of skin diseases on quality of life in patients from different social and ethnic groups in Cape Town, South Africa. Int. J. Dermatol. 39, 826–831.
Kim, H.E., Ishihara, A., Lee, S.G., 2012. The effects of caffeoylserotonin on inhibition of melanogenesis through the downregulation of MITF via the reduction of intracellular cAMP and acceleration of ERK activation in B16 murine melanoma cells. BMB Rep. 45, 724–729.
Kim, J., seok Lee, I., Park, S., Choue, R., 2010. Effects of Scutellariae radix and Aloe vera gel extracts on immunoglobulin E and cytokine levels in atopic dermatitis NC/Nga mice. J. Ethnopharmacol. 132, 529–532.
Komiya, E., Tominaga, M., Kamata, Y., Suga, Y., Takamori, K., 2020. Molecular and cellular mechanisms of Itch in Psoriasis. Int. J. Mol. Sci. 21, 8406.
Koyama, S., Heinbockel, T., 2020. The effects of essential oils and terpenes in relation to their routes of intake and application. Int. J. Mol. Sci. 21, 1–36.
Kreul, S.M., Havighurst, T., Kim, K., Mendonça, E.A., Wood, G.S., Snow, S., Borich, A., Verma, A., Bailey, H.H., 2012. A phase III skin cancer chemoprevention study of DFMO: long-term follow-up of skin cancer events and toxicity. Cancer Prevent. Res. 5, 1368–1374.
Kwon, S.H., Na, J.I., Choi, J.Y., Park, K.C., 2019. Melasma: updates and perspectives. Exp. Dermatol. 28, 704–708.
Laing, R., Waning, B., Gray, A., Ford, N., Hoen, E.T., 2003. 25 years of the WHO essential medicines lists: progress and challenges. Lancet 361, 1723–1729.
Lin, T.K., Zhong, L., Santiago, J.L., 2018. Anti-inflammatory and skin barrier effects of topical applications of some plant oils. Int. J. Mol. Sci. 19, 70.
Liju, V.B., Jeena, K., Kuttan, R., 2014. Chemopreventive activity of turmeric essential oil and possible mechanisms of action. Asian Pac. J. Cancer Prevent. 15, 6575–6580.

in: de Macedo, P.M., Freitas, D.F.S., 2021. Superficial Infections of the Skin and Nails. (Eds.) In: Zaragoza, O., Casadevall, A. (Eds.), Encyclopedia of Mycology. Elsevier Inc., New York, pp. 707–718.

Martins, A.M., Ascenso, A., Ribeiro, H.M., Marto, J., 2020. Current and future therapies for psoriasis with a focus on serotonergic drugs. Mol. Neurobiol. 57, 2391–2419.

Ogbechie-Godec, O.A., Elbuluk, N., 2017. Melasma: an up-to-date comprehensive review. Dermatol. Ther. (Heidelb) 7, 305–318.

Park, T., Kim, H.J., Myeong, N.R., Lee, H.G., Kwack, I., Lee, J., Kim, B.J., Sul, W.J., An, S., 2017. Collapse of human scalp microbiome network in dandruff and seborrhoeic dermatitis. Exp. Dermatol. 26, 835–838.

Passeron, T., Picardo, M., 2018. Melasma, a photoaging disorder. Pigment Cell Melanoma Res. 31, 461–465.

Paul, C.F., Ho, V.C., McGeown, C., Christophers, E., Schmidtmann, B., Guillaume, J.C., Lamarque, V., Dubertret, L., 2003. Risk of malignancies in psoriasis patients treated with cyclosporine: a 5 y cohort study. J. Investigat. Dermatol. 120, 211–216.

Pavithra, P.S., Mehta, A., Verma, R.S., 2019. Essential oils: from prevention to treatment of skin cancer. Drug Discov. Today 24, 644–655.

de Rapper, S., Kamatou, G., Viljoen, A., van Vuuren, S., 2013. The in vitro antimicrobial activity of Lavandula angustifolia essential oil in combination with other aromatherapeutic oils. Evid.-Based Complement. Alternat. Med. 2–10.

Rendon, A., Schäkel, K., 2019. Psoriasis pathogenesis and treatment. Int. J. Mol. Sci. 20, 1–28.

Seth, D., Cheldize, K., Brown, D., Freeman, E.E., 2017. Global burden of skin disease: inequities and innovations. Curr. Dermatol. Rep. 6, 204–210.

Tabassum, N., Hamdani, M., 2014. Plants used to treat skin diseases. Pharmacog. Rev. 8, 52–60.

Tan, J.K.L., Bhate, K., 2015. A global perspective on the epidemiology of acne. Brit. J. Dermatol. 172, 3–12.

Tobin, D.J., 2017. Introduction to skin aging. J. Tissue Viabil. 26, 37–46.

Tongnuanchan, P., Benjakul, S., 2014. Essential oils: extraction, bioactivities, and their uses for food preservation. J. Food Sci. 79, R1231–R1249.

Vaughn, A.R., Clark, A.K., Sivamani, R.K., Shi, V.Y., 2018. Natural oils for skin-barrier repair: ancient compounds now backed by modern science. Am. J. Clin. Dermatol. 19, 103–117.

Van Vuuren, S.F., Viljoen, A.M., 2006. A comparative investigation of the antimicrobial properties of indigenous South African aromatic plants with popular commercially available essential oils. J. Essent. Oil Res. 18, 66–71.

Wilsdon, T.D., Whittle, S.L., Thynne, T.R., Mangoni, A.A., 2019. Methotrexate for psoriatic arthritis. Cochr. Datab. System. Rev. 1, 1–108.

Wińska, K., Mączka, W., Łyczko, J., Grabarczyk, M., Czubaszek, A., Szumny, A., 2019. Essential oils as antimicrobial agents—Myth or real alternative? Molecules 24, 2130.

Xiong, L.G., Chen, Y.J., Tong, J.W., Gong, Y.S., Huang, J.A., Liu, Z.H., 2018. Epigallocatechin-3-gallate promotes healthy lifespan through mitohormesis during early-to-mid adulthood in Caenorhabditis elegans. Redox Biol/ 14, 305–315.

Xu, H., Li, H., 2019. Acne, the skin microbiome, and antibiotic treatment. Am. J. Clin. Dermatol. 20, 335–344.

Xu, J., Saunders, C.W., Hu, P., Grant, R.A., Boekhout, T., Kuramae, E.E., Kronstad, J.W., DeAngelis, Y.M., Reeder, N.L., Johnstone, K.R., Leland, M., 2007. Dandruff-associated Malassezia genomes reveal convergent and divergent virulence traits shared with plant and human fungal pathogens. Proceed. Natl. Acad. Sci. 104, 18730–18735.

YokouchiYokouchi, M., Kubo, A., 2018. Maintenance of tight junction barrier integrity in cell turnover and skin diseases. Exp. Dermatol. 27, 876–883.

Zhang, S., Duan, E., 2018. Fighting against Skin Aging: the Way from Bench to Bedside. Cell Transpl. 27, 729–738.