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DERMATOPHYTOSIS: INFECTION AND PREVENTION -A REVIEW

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ABSTRACT: The growing impact of infections caused by dermatophytes i.e. *Trichophyton*, *Microsporum* and *Epidermophyton* is not upto the mark in their treatments via conventional methods due to resistance, side effects, and high toxicity. Over prescription and overuse of traditional antifungal agents, high side effects, less eco-friendly nature, high manufacturing costs, high management costs etc., have stimulated the research for alternative natural drugs, such as herbal extract, essential oils and some commercially available compounds. This paper reviews the antidermatophytic activity of various commercially available and conventionally available herbals from different plants and their major role in prevention of prevalent strains dermatophytes. The mode of action of dermatophytes for causing dermatophytosis as well as mode and mechanism of action of various antifungal agents (herbals extracts, oils, suspensions and commercially available compounds) have also proposed. *In vitro* susceptibility tests and *in vivo* models used in antidermatophytic assays as well as the mechanism of action of dermatophytes are involved under the perspective of the potential use of herbals as antifungal agents in the clinical treatment of resistance strains responsible for dermatophytosis.

INTRODUCTION: Superficial fungal infections caused by dermatophytes have increased during the last decades, particularly among high risk patients [1]. The prevalence of these fungal infections have opened to level in last few years that skin mycoses now affect more than 20% populations of the world [2]. Dermatophytes, include *Trichophyton, Microsporum* and *Epidermophyton*, are responsible for major skin infections, sometimes acquiring lifetime risk.

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They are a group of keratinophilic fungi that can infect keratinized tissues of human and animals such as skin, hair and nails causing dermatophytoses. These infections are also a major grounds for morbidity-associated superficial mycoses, with recurrent relapses and often refractory to therap [3]. Although conventional antifungal drugs are available (azoles, allylamines, and morpholine derivates) for curing of dermatophytosis.

An increasing resistance to these conventional compounds can result in treatment failure. Moreover, the effective life span of classical antifungals is in fact inadequate due to their repeated use as antifungal and immunosuppressive drugs as well as in organ transplantation, lymphomas and HIV secondary infections. Recently, research in aromatic and medicinal plants, and particularly their extracts and essential oils, has attracted many investigators. Essential oils have traditionally been used during centuries for their antifungal propert [4]. More recently, several studies have shown evidence of the huge potential of these natural products as antifungal agents [5-10] justifying their current use in a number of pharmaceutical, food and cosmetic products. Therefore, it is not astonishing that essential oils are one of the most talented groups of natural products, for the development of broad-spectrum, cheaper and safer antifungal agents.

Various techniques are available to evaluate the *in vitro* antidermatophytic activity of essential oils. The agar-based disk diffusion, broth micro-dilution, and vapor phase tests are the mostly used. Also *in vivo* models have been created in order to access efficiency of *in vitro* results. Notwithstanding, the widespread use of essential oils by humans and the large evidence, in recent studies, of their potential as complementary or alternative options for prophylaxis and treatments of dermatophytosis, their exact mechanism of action, remains scantily understood. This paper reviews the current knowledge concerning the antidermatophytic activity of essential oils belonging to family.

Dermatophytes and dermatophytosis:

Dermatophytes may be classified as geophilic, zoophilic and antropophilic on the basis of their main habitat or host. The first group is abundant in soils and is normally associated with decomposing keratinous structures such as hair, feathers, fur, and horns. On the other hand, zoophilic and antropophilic fungi have a more specific distribution and infect animals and humans, respectively [11]. Species of the genera *Trichophyton*, *Microsporum* and *Epidermophyton* (Fig. 1) are responsible for common infections in the skin and appendages, generally called dermatophytosis or ringworm infections [11, 12]. These fungi colonize keratinized human or animal tissues causing an infection that may vary from mild to very intense. The range of severity depends upon several factors including the host reaction to the metabolic products produced by fungi, the virulence of the infecting strain, the site of infection (tissue keratinization), and also environmental factors [13, 14]. The infections are highly prevalent due to the large number of reservoirs (skin, hair, nails), the readiness of transmission from one host to another, and to the high resistance of the strains to adverse environmental conditions. Antropophilic dermatophytes generally coexist in equilibrium on the skin and normally cause only mild irritation. Thus, dermatophytic infections are usually noninvasive, but in immunocompromised patients they can rapidly progress to life-threatening disseminated infections.

Moreover, some zoophilic and geophilic dermatophytes are responsible for quite severe inflammatory reactions due mainly to delayed hypersensitivity responses to fungi proteases. In addition, in recent years, infections have increased considerably among pediatric and geriatric populations [15, 16]. Cutaneous dermatophytosis are usually documented by their scaly patches, with central clearing and sharply demarcated, annular, erythematous, sometimes presenting vesicles, blisters and pustules [11].

Nevertheless, in many cases, its analysis is not clinically obvious, requiring mycological analyses, such as direct microscopic observations, fungi isolation and culture, biochemical and physiological tests [17]. In addition, in some cases, it is very difficult to discriminate dermatophytosis from other clinical conditions that also reveal similar symptoms. For example, *Tinea corporis* may mimic other skin infections such as nummular eczema, subacute cutaneous lupus erythematosus, pustular psoriasis, subcorneal pustular dermatosis, dermatitis, herpes simplex and varicella zoster virus infections [18] (**Fig.1**).

Taking into account treatment costs, duration and side effects of conventional agents, an accurate diagnosis is essential to define which treatments must be applied [17]. Classification of human dermatophytosis based on tissue keratinisation at the site of infection, as suggested by scientists [19]. The sites of infection, as well as the common name of the infection, and the species concerned are also indicated. Dermatophytosis is also very common among pets and livestock, yet exceptional in wild animals. Besides the high contagiousness among animal communities and the difficulties in applying effective control measures, long duration of the infection and high costs of treatments are other factors impairing a successful struggle against this disease.

Also of great anxiety is the ability of zoophilic dermatophytes to be transmitted to humans, hence causing serious public health problems. Among the zoophilic species most commonly involved in these infections are *Trichophyton mentagrophytes*, *Trichophyton rubrum* [20]. Infection of dermatophytosis includes various topical abnormalities *Tinea pedis, T. mannum, T. corporis* and *T. cruris*, T. *unguium T. capitis* **(Fig. 2)**. Freshly, echinocandins have also been used but only for systemic *Candida* and *Aspergillus* infections [21, 22].

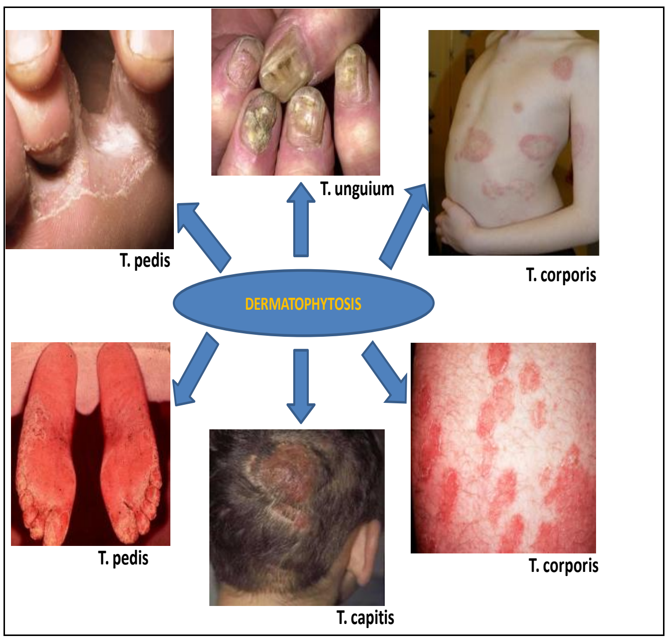

FIG.1: VARIOUS SYMPTOMS OF DERMATOPHYTOSIS

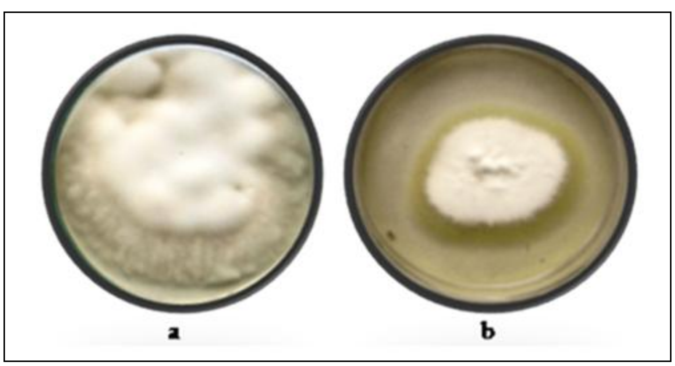

FIG. 2: CULTURES OF DERMATOPHYTES, A. *TRICHOPHYTON MENTAGROPHYTES*, B. *TRICHOPHYTON RUBRUM*,

Superficial mycosis (e.g. *Tinea pedis, T. mannum, T. corporis and T. cruris*) usually react to topical antifungals [3, 11, 23]. Among all the three genera of dermatophytes, *Trichophyton* is most prevalent strain responsible for dermatophytosis. The most common agents are azoles (eg. clotrimazole, miconazole, econazole, oxiconazole, tioconazole) and allylamines, (e.g. terbinafine and naftifine). Morpholine derivates such as amorolfine and butenafine have been also used [3]. With topical medication, primarily mild skin reactions may occur at the site of application [24]. For patients displaying wide areas of infection or in cases of severe or constant infections, oral therapy should be considered and the same is true for infections caused by *T. unguium* and *T. capitis*, where itraconazole, fluconazole, griseofulvin, and ketoconazole are the subjected antifungals to be used [3, 23].

Some antifungals are inhibitors of enzymes involved in the metabolism of other drugs. For example, it is well known that itraconazole inhibits cytochrome (CYP) 3A4 and, therefore, should not be administrated to patients receiving triazolam, oral midazolam, lovastatin, simvastatin, quinidine or pimozide. Other example is fluconazole which inhibits both CYP 2C9 and CYP 3A4. Thus, cautions should be taken in patients getting phenytoin, warfarin, cyclosporine, and oral sulfonylurea hypoglycemic agents.

Another example is terbinafine a drug that interacts with CYP 1A2 and must not be administered to patients treated with warfarin, nortriptyline or theophylline [26-28]. Also, gastrointestinal interactions may occur with drugs or substances that affect gastric acidity. For example, antacids, histamine-2 receptor blockers, proton pump inhibitors and oral didanosine decrease the absorption of capsule formulations of itraconazole while coca-cola may significantly increase it [28]. Bearing in mind to aforementioned grounds it can be concluded that the success of dermatophytosis treatments depends not only of the knowledge of the disease but also of other factors such as clinical pattern and strictness of the infection, causative agent, and possible drug interactions with attendant medications as well as patient's preference [29].

Essential oils:
Essential oils are natural composite mixtures of terpenic and non-terpenic compounds. Commonly, monoterpenes and sesquiterpenes as well as their oxygenated derivatives are the major constituents but phenylpropanoids, fatty acids and their esters may also occur [30]. These secondary metabolites can be found in various plant organs (flowers, fruits, seeds, leaves, stems, and roots) being produced and stored in different secretory structures. The type of structure (secretory cells, osmophores, secretory cavities, secretory ducts, glandular trichomes or epidermal cells) is closely related to the plant family [31].

Anatomical details of these structures are also very relevant to the market value of aromatic plants since they allow the verification of authenticity, detection of substitutions and/or adulterations [32].They play important roles as signaling agents namely in the defense of plants against microorganisms, insects, and herbivores, as attractants of pollinators, and in allelopathic interactions [30, 33]. Aromatic plants and their essential oils have traditionally been used since the distant past for their biological properties (bactericidal, fungicidal, virucidal, insecticidal), as well as for cosmetic and medicinal applications [30, 34]. In recent years, research on aromatic plants has attracted many researchers and *in vitro* screening programs, based on ethno-botanical approaches, proved to be very competent in validating traditional uses and providing new ways in the search for active compounds [35]. Nowadays many essential oils are commercially valued in the pharmaceutical, food, sanitary, cosmetic, and perfume industries [30].

The largest global markets for medicinal and aromatic plants are China, France, Germany, Italy, Japan, Spain, United Kingdom and United States of America [36]. Several methodologies can be employed to extract these oils from plants. However, with reference to the International Standard Organization on Essential Oils [37] they must be obtained exclusively by distillation of plant material using water, steam or dry distillation or by expression. The obtained oils are characterized as volatile liquids, presenting a strong odour, rarely colored, soluble in organic solvents and insoluble in water. Both wild field-growing and cultivated plants can be used to extract essential oils or other secondary metabolites. On the other hand, for ecological reasons, the gathering of large amounts of plants growing in the wild must be avoided since this can harm the species and reduce biodiversity.

Therefore, concentration should be shifted towards the development of effective protocols for plant proliferation in order to produce a large quantity of plants from which chemicals of interest can be extracted thus preventing the exploitation of wild populations [38]. These approaches allow large-scale propagation in controlled conditions in any time of the year, hence avoiding damage of natural populations [39-41]. The production of essential oils in plants is under diverse physiological, biochemical, metabolic and genetic regulation [42] and generally shows a unpredictable chemical composition due to both intrinsic (sexual, seasonal, ontogenetic, and genetic variations) and extrinsic (ecological and environmental variations) factors [43, 44].

Antidermatophytic activity of essential oils:
Several studies have been available confirming the effect of essential oils and their major compounds on dermatophytic fungi (*Trichophyton*, *Microsporum* and *Epidermophyton*). The most active oils was *Thymus serpyllum*, *Thymus vulgaris*, *Lavandula latifolia*, *L. angustifolia*. Since this method is performed in sealed conditions and due to difficulties in applying this *in vivo*, the authors suggested that both potent vapor activity and potent contact activity of the oils would be necessary for anti-infectious therapy [5]. The *in vitro* antifungal activity of several commercial Essential oils against clinical strains isolated phase method. *Thymus vulgaris* and *Eugenia caryophyllata* (*Syzigium aromaticum*) oils were the best fungi inhibitors due to the presence of phenolic compounds, namely thymol, carvacrol and eugenol [6]. Moreover, the antidermatophytic activity of species of *Ocimum* oil was also evaluated using the agar diffusion method.

Recently, several essential oils were assayed for their antidermatophytic activity, using a microdilution broth test. Synergistic therapy of available antifungal drugs with essential oil has also been assessed [45, 46]. However, regarding dermatophytes, a small number of studies are known. Shin and Lim [47] evaluated the combination of *Pelargonium graveolens* essential oil and its main compounds (citronellal and geraniol) with ketoconazole, against *Tricophyton* spp.

The antifungal activity of ketoconazole was significantly enhanced with the natural compounds and its minimal effective dose was also reduced, hence minimizing possible side-effects. Prun and Shin [48] evaluated the synergism between *Allium* spp. Oils and ketoconazole using both a checkerboard titer and disk diffusion tests. A significant synergism between *A. sativum* oil and also allicin with this antifungal drug was demonstrated. Khan and Amhad [49] explored the combinational effect of several active essential oils and their main compounds with fluconazole against a clinical isolate of *T. rubrum.* The maximum level of synergism was found between cinnamaldehyde and fluconazole. This compound was able to reduce MIC of fluconazole up to 8-fold and reduce its own MIC up to 32-fold. Also the essential oil of *Syzigium aromaticum* showed the highest reduction of MIC (up to 128-fold) in combination with fluconazole.

Mechanism of action Essential oils on dermatophytes:

The comprehension of both the mode and mechanism of action of essential oil is important to ensure their usefulness in therapeutic practices. Although these agents have been extensively screened for their antifungal activity, interaction between the oils and microorganisms, which is lately responsible for its activity, is weakly explored. Regarding the few studies on this matter, *Candida* spp. and *Aspergillus* spp. have been the species mostly used [50] and, therefore, very few information is available for dermatophytes. The main studies on the evaluation of mode and mechanism of action of essential oil on dermatophytes are summarized below.

Pinto *et al.* (1998) evaluated the ergosterol content of *T. rubrum* and exhibited that 0.08 μL/mL of *Thymus pulegioides* oil was able to reduce ergosterol content [51]. A mechanism of action based on impairment of the biosynthesis of ergosterol was recommended as also occurs with conventional azole antifungal drugs [52]. Pereira *et al.* [53] through scanning electron microscopic observations showed that essential oil were able to damage the cell membrane and cell wall in a dose and time dependent manner. Park *et al.* [54] analysed the mechanism of action of eugenol, a main compound in *Syzygium aromaticum* oil.

Modifications in *T. mentagrophytes* hiphae ultrastructure were observed, namely destruction of inner mitochondrial membranes and cell wall as well as expansion of endoplasmic reticulum near cell membranes, suggesting a mechanism of action through changes in fungal cell structure, particularly at the membrane level. Bajpai *et al.* [55] performed a spore germination assay using several *T. rubrum* and *M. canis* strains as well as one strain of *T. mentagrophytes*. Several oils from lamiaceae was used and showed a strong detrimental effect on all the strains tested. Also another study of the oil was performed on *T. rubrum*, showing a time-dependent kinetic inhibition of this fungus.

A time-killing dependent assay on *T. rubrum* IOA-9 to compare the ability of potent essential oil and active compounds with fluconazole carried out. Finally, Transmission Electron Microscopy (TEM) was used to distinguish ultastructural changes in the existence of cinnamaldehyde. Alterations included lysis of cell wall and plasma membranes, endoplasmic reticulum expansion near cell membrane, excessive vacuolization, disintegration of mitochondria, plasma membranes, cell walls, and nuclear and cytoplasmic contents, abnormal distribution of polysaccharides and leakage of cytoplasmic contents.

Generally, the most active antifungal compounds of essential oil are mainly phenolic terpenes such as carvacrol and thymol. These compounds proved to be able to attack cell walls and membranes, affecting the permeability and release of intracellular constituents, as well as several invasive targets, allowing all together embarrassment of fungal infection [56].

Many herbal compunds have also shown fungicidal activity against dermatophyte strains. Overall it concludes that the antimicrobial and better bioavailability of herbal extracts as well as essential oils is not due to a single mechanism of action but may result from the effect of different compounds on several cell targets via different modes and mechanisms [57-58].

It has been reported that proteolytic activity is suppressed in *T. rubrum*, among other factors, by the availability of free aminoacids, and that proteases with optimal activity in acidic pH are important virulence factors of dermatophytes. A model has been proposed in regulation of proteolytic enzymes by neutral pH during the infectious process of dermatophytosis (**Fig. 3**). These works suggest that development in keratin and the consequent degration of this protein are somehow regulated by the gene, interfering with the secretion of proteases with optimal activity in alkaline pH. Moreover, pH signaling and monitoring pathways could be considered dermatophyte virulence factors, allowing the development and maintenance of the infection.

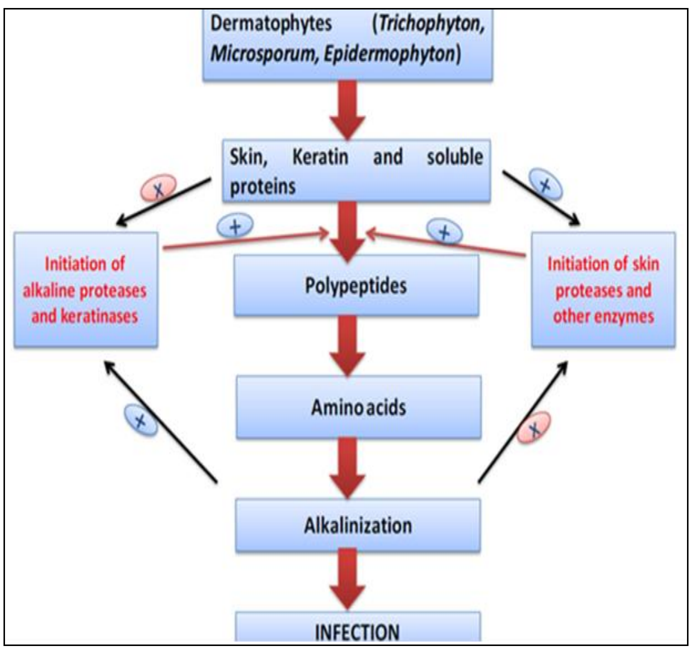

FIG. 3: MODEL FOR THE NEUTRAL pH REGULATION OF PROTEOLYTIC ENZYMES SECRETED BY DERMATOPHYTES.

CONCLUSIONS: Essential oils have proved, in several *in vitro* assays, to be useful alternatives to conventional antifungal agents having azole groups for the treatment of dermatophytosis. Moreover, it reflects that resistance may occur with their use since multiple mutations are required to overcome all the distinct antifungal actions of each and all of the oils constituents. Conversely, to guarantee their safety, further toxicity studies need to be performed as well as assays to clarify the mechanism of action and possible connections with other antibiotics. The optimization of formulations, the organization of optimal concentrations for clinical applications and the search for possible side-effects are together research lines that need to be explored.

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REFERENCES:

1. Achterman RR, White TC: Dermatophyte virulence factors: identifying and analyzing genes that may contribute to chronic or acute skin infections. Int. J. Microbiol. 2012; 8.
2. Arif T, Mandal TK, Dabur R: Natural products: antifungal agents derived from plants. In: Tiwari VK, ed. Opportunity, Challenge and Scope of Natural Products in Medicinal Chemistry. India: Research Signpost. 2011; 283-311.
3. Harvey A, Stoppler MC: Fungal Nails (Onychomycosis, Tinea unguium); 2011, www.medicinenet.com.
4. Qidwai A, Pandey M, Shukla SK, Kumar R, Pandey A, Dikshit A. Antibacterial activity of *Mentha piperita* and *Citrus limetta* against *Propionibacterium acnes* (anaerobic bacteria). IJPSR. 2016, 7(7): 2917-2924.
5. Laham NA, Abdelateef N, Naieem M: Dermatophytosis Among Out patients in Gaza, Particularly Tinea capitis. J. Al Azhar Univ. Gaza (Natural Sciences). 2011; (13),17-30.
6. Mihali CV, Buruiana A, Turcus V, Covaci A, Ardelean A: Comparative studies of morphology and ultra-structure in two common species of dermatophytes: *Microsporum canis* and *Microsporum gypseum*. Annals of RSCB. 2012; (17), 85-89.
7. Mikaili A, Chalabi M, Ghashghaie A, Mostafaie A: Immunization against bovine dermatophytosis with live *Trichophyton verrucosum*. Afr. J. Microbiol. Res. 2012; 6(23), 4950-4953.
8. Sharma A, Chandra S, Sharma M:. Difference in keratinase activity of dermatophytes at different environmental conditions is an attribute of adaptation to parasitism. Mycoses. 2012; 55(5), 410-415.
9. Sharma A, Sharma V, Kumawat TK, Seth R: A Review on Antidermatophytic Efficiency of Plant Essential Oils. Int. J. Pure Appl. Biosci. 2014; 2(6), 265-278.
10. Sharma R, Swati: Effect of Keratin Substrates on the Growth of Keratinophilic Fungi. J. Acad. Ind. Res. 2012; 1(4), 170-172.
11. Lima B, López S, Luna L, Agüero MB, Aragón L, Tapia A, Zacchino S, López ML, Zygadlo J, Feresin GE: Essential oils of medicinal plants from the Central Andes of Argentina: chemical composition, and antifungal,

antibacterial, and insect-repellent activities. *Chemistry & Biodiversity*. 2011; (8), 924-936.

12. Sharma V, Kumawat TK, Sharma A, Seth R, Chandra S: Distribution and Prevalence of Dermatophytes in Semi-Arid Region of India. Adv. Microbiol. 2015; (5), 93-106.
13. Suklampoo L, Thawai C, Weethong R, Champathong W, Wongwongsee W: Antimicrobial Activities of Crude Extracts from Pomelo Peel of Khao-nahm-peung and Khao-paen Varieties. KMITL Sci. Tech. J. 2012; 12 (1), 55-61.
14. Gupta S, Agrawal P, Rajawat R, Gupta S: Prevalence of dermatophytic infection and determining sensitivity of diagnostic procedures international journal of pharmacy and pharmaceutical sciences. 2014; 6 (3), 0975-1491.
15. Kumar V, Bhatia, Sharma PC: Epidemiological studies on Dermatophytosis in human patients in Himachal Pradesh. 2014; 3(1), 134.
16. Humera QF, Ansari , Mizbah B, Patel J, Siddiqui AW: Epidemiology and *In-Vitro* Antifungal Susceptibility Testing of Dermatophytes. International Journal of Advanced Research (2014); 2(2), 553-560.
17. Doddamani PV, Harshan KH, Kanta RC, Gangane R, Sunil KB: Isolation Identification and Prevelance of Dermatophytes People‘s Journal of Scientific Research. 2013; 6(2).
18. Kumaran G, Jeya M: Clinico-Mycological Profile of Dermatophytic Infections. Int J Pharm Bio Sci. 2014; 5(2)1-5.
19. Surendran KAK, Ramesh M, Rekha B, Boloor B, Nandakishore A: Clinical and Mycological Study of Dermatophytic Infections. Indian J Dermatol. 2014; 59(3), 262-267.
20. Kainthola A, Gaur P, Dobhal A, Sundriya S: Prevalence of Dermatophytoses in Rural Population of Garhwal Himalayan Region, Uttarakhand, International Research Journal of Medical Sciences. 2014; 2(8), 9-12.
21. Kumar R, Shukla SK, Pandey A, Srivastava SK, Dikshit A. Copper oxide nanoparticles: an antidermatophytic agent for *Trichophyton* spp. Nanotechnol Rev 2015; 4(5): 401–409.
22. Partha PM, Nandan K, Dey S: Clinico-Mycological Profile of Dermatophytosis in Patients Attending a Tertiary Care Hospital in Eastern Bihar. India‖. Journal of Evolution of Medical and Dental Sciences. 2014; 3(29), 8263-8269. doi: 10.14260/jemds/20.
23. Lecha M, Effendy I, Feuilhade d, Chauvin M, Di Chiacchio N, Baran R: Treatment options –development of consensus guidelines. Journal of the European Academy of Dermatology and Venereology. 2005; (19), 25-33.
24. Lakshmipathy DT, Kannabiran K: Review on Dermatomycosis: Pathogenesis and Treatment. Nat. Sci. 2010; 2(7), 726-731.
25. Gupta AK, Chow M, Daniel CR, Aly R: Treatment of Tinea pedis. Dermatologic clinics. 2003; (21), 431-462.
26. Andriole VT: Current and future antifungal therapy: New targets for antifungal agents. Journal of Antimicrobial Chemotherapy. 1994; (44), 151-162.
27. Del Rosso JQ: Currrent managment of onychomycosis and dermatomycoses. Current Infectious Disease Reports. 2000; (2), 438-445.
28. Gupta AK, Katz HI, Shear NH: Drug interactions with itraconazole, fluconazole and terbinafine and their management. Journal of the American Academy of Dermatology. 1999; (41), 237-249.
29. Del Rosso JQ, Gupta AK: Drug interactions update. Focus on oral antifungal agents. Today’s Ther Trends. 2000; (18), 181-188.
30. Gupta AK, Ryder JE, Skinner AR: Treatment of onychomycosis: Pros and cons of antifungal agents. Journal of Cutaneous Medicine and Surgery. 2004; (8), 25-30.
31. Bakkali F, Averbeck S, Averbeck D, Idaomar M: Biological effects of essential oils–A review. Food and Chemical Toxicology. 2008; (46), 446-475.
32. Upton R, Graff A, Jolliffe G, Länger R, Williamson E: American Herbal Pharmacopoeia: Botanical Pharmacognosy -Microscopic Characterization of Botanical Medicines. New York, USA: CRC Press. 2011.
33. Ghasemi PA, Fatahi VM, Craker L, Shirmardi H: Chemical composition and bioactivity of essential oils of Hypericum helianthemoides, Hypericum perforatum and Hypericum scabrum. Pharm. Biol. 2014; 52(2), 175-81.
34. Houel E, Rodrigues AMS, Jahn-Oyac A, Bessiere JM, Eparvier V, Deharo E, Stien D: In vitro antidermatophytic activity of Otacanthus azureus (Linden) Ronse essential oil alone and in combination with azoles. J. Appl. Microbiol. 2013; (116), 288-294.
35. Hussain AI, Efstratiou E, Moore JE, Singh-Nee N, Poonam: Antimicrobial activity of Callendula officinalis petal extracts against fungi, as well as gram-negative and gram-positive clinical pathogens. Complement. Ther. Clin. Pract. 2012; 18(3), 173-6.
36. Alviano DS, Alviano CS: Plant extracts: search for new alternatives to treat microbial diseases. Current Pharmaceutical Biotechnology. 2009; (10), 106-121.
37. Askew MF: IENICA’s Essential Oils Market Information Booklet. Central Science Laboratory: IENICA copyright. 2004.
38. Elaissi A, Salah KBH, Mabrouk S, Larbi KM, Chemli R, HarzallahSkhiri F: Antibacterial activity and chemical composition of 20 Eucalyptus species’ essential oils. Food Chem. 2011; (129):1427-1434.
39. Kumar P, Mishra S, Malik A, Satya S: Compositional analysis and insecticidal activity of Eucalyptus globules (family: Myrtaceae) essential oil against housefl y (Muscadomestica). Acta Tropica 2012; (122), 212-218.
40. Canter PH, Thomas H, Ernst E: Bringing medicinal plants into cultivation: opportunities and challenges for biotechnology. Trends in Biotechnology. 2005; (23),180-185.
41. Debnath M, Malik CP, Bisen PS: Micropropagation: a tool for the production of high quality plant-based medicines. Current Pharmaceutical Biotechnology. 2006; (7), 33-49.
42. Chaturvedi HC, Jain M, Kidwai NR: Cloning of medicinal plants through tissue culture-a review. Indian Journal of Experimental Biology. 2007; (45), 937-948.
43. Sigurgeirsson B, Baran R: The prevalence of onychomycosis in the global population-A literature study. J Eur Acad Dermatol Venereol. 2014; (28),1480-1491.
44. Gupta AK, Paquet M, Simpson FC: Therapies for the treatment of onychomycosis. Clin Dermatol. 2013; (31), 544-554
45. Angioni A, Barra A, Coroneo V, Dessi S, Cabras P: Chemical composition, seasonal variability, and antifungal activity of *Lavandula stoechas* L. ssp. *stoechas* essential oils from stem/leaves and flowers. Journal of Agricultural and Food Chemistry. 2006; (54), 4364-4370.
46. Ghannoum M: Azole resistance in dermatophytes: Prevalence and mechanism of action. J Am Acad Dermatol. 2015; (72), AB133.
47. Shin S, Lim S: Antifungal effects of herbal essential oils alone and in combination with ketoconazole against *Trichophyton* spp. Journal of Applied Microbiology. 2004; (97), 1289-1296.

48. Pyun MS, Shin S: Antifungal effects of the volatile oils from *Allium* plants against *Trichophyton* species and synergism of the oils with ketoconazole. Phytomedicine: International Journal of Phytotherapy & Phytopharmacology. 2006; (13), 394-400.
49. Khan MSA, Amhad I: Antifungal activity of essential oils and their synergy with fluconazole against drug-resistant strains of *Aspergillus fumigatus* and *Trichophyton rubrum*. Applied Microbial and Cell Physiology. 201; (90), 1083-1094.
50. Reichling J, Schnitzler P, Suschke U, Saller R: Essential oils of aromatic plants with antibacterial, antifungal, antiviral and cytotoxic properties. Forsch Komplementmed. 2009; (16), 79-90.
51. Pinto E, Vale-Silva L, Cavaleiro C, Salgueiro L: Antifungal activity of the clove essential oil from *Syzygium aromaticum* on Candida, *Aspergillus* and dermatophyte species. Journal of Medical Microbiology. 2009; (58), 1454-1462.
52. Palmeira OA, Salgueiro L, Palmeira R, Martinez J, Pina C, Queiroz JA, Rodrigues AG: Anti-candida activity of essential oils. Mini Reviews in Medicinal Chemistry. 2009; (9), 1292-1305.
53. Pereira FO, Wanderley PA, Viana FAC, Lima RB, Sousa FB, Lima EO: Growth inhibition and morphological alterations of *Trichophyton rubrum* induced by essential oil from *Cymbopogon winterianus* Jowitt ex Bor. Braz J Microbiol. 2011; (42), 233-242.
54. Park MJ, Gwak KS, Yang I, Choi WS, Jo HJ, Chang JW, Jeung EB, Choi IG: Antifungal activities of the essential oils in *Syzygium aromaticum* (L.) Merr. Et Perry and *Leptospermum petersonii* Bailey and their constituents against various dermatophytes. The Journal of Microbiology. 2007; (45), 460-465.
55. Bajpai VK, Yoon JI, Kang SC: Antifungal potential of essential oil and various organic extracts of *Nandina domestica* Thunb. against skin infectious fungal pathogens. Applied Microbiology and Biotechnology. 2009; (83), 1127-1133.
56. Zimmermam-Franco DC, Bolutari EB, Polonini HC, Carmo AMR, Chaves MGAM, Raposo NRB. Antifungal activity of *Copaifera langsdorffii* Desf oleoresin against Dermatophytes. Molecules. 2013; (18), 12561-12570.
57. Mishra SB, Pandey H, Pandey AC. Nanosuspension of Phylanthus amarus extract for improving oral bioavailability and prevention of paracetamol induced hepatotoxicity in Sprauge- Dawley rats. IOP Publishing, Avt. Nat. Sci: Nanosci. Nanotechnol. 4 (2013) 035007.
58. Gupta R, Ramteke PW, Pandey H, Pandey AC. Nano-structured Herbal Antimicrobials. IJPSR, (2013) 4(6), 2028-2034. doi:10.1088/2043-6262/4/3/035007.

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