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Review Article

ROLE OF HERBAL ANTIFUNGAL AGENTS FOR THE MANAGEMENT OF FUNGAL DISEASES: A SYSTEMATIC REVIEW

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ABSTRACT

Nowadays, fungal infection of skin is one of the most common dermatological problems worldwide. It has been investigated that 40 million people suffer from fungal infections. Superficial and subcutaneous fungal infections affect the skin, keratinous tissues, and mucous membranes. The dermatophytic infections, superficial candidiasis of the mouth, skin, or genital tract and infections due to *Malassezia*, such as pityriasis versicolor and *Malassezia* folliculitis are the main afflicting conditions. Systemic fungal infections may be caused by either an opportunistic organism that infects an at-risk host or may be associated with a more invasive organism or may be endemic to a specific geographical area. The most frequently encountered pathogens are *Candida albicans* and *Aspergillus* spp. but other fungi such as non-*albicans Candida* spp. are increasingly important in causing systemic fungal infections. There are numerous antifungal agents used clinically to treat fungal infections, i.e., azoles, allylamines, echinocandins, griseofulvin, and flucytosine. The course to modern treatment has not been without its problems and complications, particularly the drug resistances. Phytochemistry of various plant species has indicated that the phytochemicals could be a better source of medicine as compared to synthetically produced drugs. Natural medicines from a plant origin are still used as therapeutic agents, especially for treating bacterial, fungal, viral, protozoal, helminthic infections, etc. This review focuses on the use of plant constituents to prevent fungal infections caused by various pathogens. Hence, it will be proved beneficial for the drug industries.

Keywords: Fungal infection, Dermatophyte, Pityriasis versicolor, Pathogens, Endemic, Natural medicines.

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INTRODUCTION

The humans live in peaceful coexistence with the surrounding microorganisms but an infection may emerge from the surrounding microorganisms when the defense system is damaged or the concentration of pathogens reach an exceptionally high density whereas infectious disease is a condition in which the infecting agents do elicit a response of the body, which leads to clinically manifest signs and symptoms. Bacteria, viruses, parasites, fungi, prions, worms, and helminths have all been involved in causing infectious diseases. A few decades ago, an infection caused by bacteria was the most feared and as the strategies to control bacterial infections in patients improved, but nowadays, fungi are the most hazardous pathogens [1].

Fungi exist in two basic forms: Yeasts and molds. Yeasts are typically single, small, and oval cells, whereas mold colonies consist of filamentous strands called hyphae. Some fungi are dimorphic, exists either as yeasts or molds depending on the external environment such as temperature [2,3]. Fungi are ubiquitous within the environment; however, only a few species are routinely found associated with humans who are capable of causing disease. A handful of fungi that is responsible for causing disease in healthy individuals are considered as true pathogens, (*Histoplasma* and *Paracoccidioides*), while the majority of fungi causing disease primarily in immuno-suppressed individuals are often classified as opportunistic pathogens (*Candida* and *Cryptococcus*) [4]. However, it is obvious that some opportunistic fungal pathogens also cause disease in otherwise healthy individuals (*Candida vaginitis* or *Cryptococcus gattii* outbreaks) [5,6]. Invasive fungal infections are characterized by high morbidity and mortality, although these infections are now more frequent they are still difficult to diagnose, prevent, and treat. [7]

For a systemic effect, the intravenous or oral route is mainly used to treat topical fungal infection. However, it causes many side effects, including gastric irritation, diarrhea, nausea, vomiting and stomach pain, headache, fever, renal impairment, and anemia. Hence, the topical drug delivery is the most suitable routes for the administration of drugs that undergo first-pass metabolism. It is generally effective against fungal infections [8]. By spreading and rubbing ointments, creams, and gels applied directly to an external body surface for topical administration of drugs to the skin. For the therapeutic effect, the drug must permeate and diffuse across the skin [9,10]. The rate and extent of transport depend on the drug molecular properties and the characteristic of the biologic tissue. Advantages of the topical treatment of fungal infections include targeting the site of infection; increase the efficacy of treatment, reduction in the risk of systemic side effects, and to increase the patient compliance [11].

There are numerous antifungal agents used clinically to treat fungal infections and can be broadly classified into five major classes, i.e., azoles, allylamines, echinocandins, griseofulvin, and flucytosine [12]. Although the course to modern treatment has not been without its problems and complications, particularly the drug resistances which have not had a major impact on the currently used antifungals with the exception of superficial Candidiasis infections; however, azole resistance is well recognized. The rise of *Candida auris* as a pathogen, which is resistant to multidrug is a further worry although it has not had a major impact on skin infection, superficial carriage is well documented [13-16].

Therefore, the discovery of novel antifungals is severely needed. Phytochemistry of various plant species has indicated that the phytochemicals could be a better source of medicine as compared to synthetically produced drugs. The use of plants as medicine goes back to early man. These traditional medicines based on medicinal plants have been used for centuries. Therefore, one approach that has been used for the discovery of antimicrobial agents is the evaluation of plant extracts [17].

TYPES OF FUNGAL INFECTIONS

Topical/superficial disease caused by fungal pathogens

Superficial fungal infections occur in the outermost layers of the skin, nails, hair, and mucous membranes [18].

Dermatophytosis

Dermatophyte fungi are organisms that digest keratin [19]. Dermatophytes infect the stratum corneum of the epidermis and keratinized tissues derived from it, such as hair or nail. *Trichophyton* spp., *Microsporum* spp., and *Epidermophyton* spp. are responsible for most of the superficial fungal infections, although the causative agents can be some yeast and some non dermatophyte molds [20].

Tinea pedis

Tinea pedis is a dermatophyte infection of the foot, affecting particularly the toes and sole caused mainly by *Trichophyton rubrum, Trichophyton mentagrophytes,* and *Epidermophyton floccosum* pathogens. This infection affects l5–30% of the population [21] and is the most common dermatophyte fungal disease that occurs in man [22]. Individuals with tinea pedis may be susceptible to secondary bacterial infection with, for example, Group A *streptococcus* [23].

Tinea corporis

Two major causative organisms causing tinea corporis are *T. rubrum, T. mentagrophytes* affecting neck, trunk, and the extremities. The classic tinea corporis lesion is a sharply defined circular lesion with erythema, scaling, and small blisters or pustules at the border. The lesion is usually <5 cm in diameter. The fungus is often transmitted from domestic animals, such as cats, dogs, hamsters, and guinea pigs to humans [21].

Tinea capitis

The predominant causative agent of this infection is *Trichophyton tonsurans* and mainly causes disease in childhood, presenting with alopecia and scaling on the scalp [24,25].

Tinea unguium or onychomycosis (nails)

T. rubrum and *T. mentagrophytes* dermatophytes are the principal causes of onychomycosis, accounting approximately for 90% of toenail infections and 50% of fingernail infections [26-28].

Superficial candidiasis

Superficial candidiasis infections are usually caused by *Candida albicans,* and this organism is a common commensal in the mouth, vagina, and gastrointestinal tract in healthy individuals. The prevalence of carriage is greater in hospitalized patients and those who are immuno-compromised.

Oropharyngeal candidiasis (oral thrush)

It has typical symptoms and signs of soreness and white patches on an erythematous background (plaque type). An erythematous variety exists; this does not have plaques, but sore areas of erythema are typical. Acute or chronic infection can occur in immuno-compromised individuals. Other predisposing factors include antibiotic therapy and dentures.

Vaginal candidiasis (vaginal thrush)

Vaginal candidiasis is a common infection, with clinical appearances similar to those of oropharyngeal disease, plus vaginal discharge. Pruritus can also occur, and recurrent episodes are common. Women with vaginal thrush seldom have underlying predisposing factors.

Candidiasis of the skin

Candidiasis of the skin is often confined to body folds, including the inter-digital spaces of the hands or feet. Typically, small satellite pustules lie distal to the periphery of the rim of the rash. Chronic paronychia (nail fold infections) can be caused by *Candida.*

Malassezia infection

Malassezia spp. are common surface commensals of greasy skin includes scalp, chest, and they are associated with pityriasis versicolor, seborrheic dermatitis, and folliculitis [29].

Pityriasis versicolor

Pityriasis versicolor is a scaly, hypo- or hyper-pigmented rash on the trunk which is found common in tropical regions and the patches can resemble vitiligo, but the presence of scaling is typical.

Seborrheic dermatitis

Seborrheic dermatitis is a common scaly condition affecting the face, the front of the chest, and the scalp. Severe seborrheic dermatitis is particularly common in patients with AIDS or chronic neurological Parkinson's disease.

Malassezia folliculitis

Malassezia folliculitis is an itchy, follicular rash on the upper back and shoulders that can resemble acne [30].

Subcutaneous infection

Although subcutaneous mycoses can disseminate, they are usually limited to the dermis and subcutaneous tissues.

Sporotrichosis

Sporotrichosis is caused by the dimorphic fungus *Sporothrix schenckii* and is the most prevalent subcutaneous infection [31]. The fungus is found in soil, vegetation and usually causes disease in farmers or gardeners, especially those who tend roses. It is a localized cutaneous or subcutaneous lesion, which may spread via the lymphatic system and form further lesions. Lymphocutaneous sporotrichosis is a non-life-threatening disease [32].

Chromoblastomycosis

Chromoblastomycosis is a chronic cutaneous or subcutaneous fungal infection caused by members of the Dematiaceae family including *Fonsecaea pedrosoi*, *Cladosporium carrionii*, *Fonsecaea compacta*, *Phialophora verrucosa,* and *Rhinocladiella aquaspersa* and found in wood, vegetable debris, and soil [33]. Symptoms are raised, crusted lesions of the skin.

Chronic mucocutaneous candidiasis

Chronic mucocutaneous candidiasis is a rare syndrome consisting of chronic infection of mucous membranes usually by *C. albicans*, which may extend to the skin and nails. The condition is associated with impaired cell-mediated responses to *Candida*, although the underlying defect remains poorly understood [34,35]. Various manifestations including white fissured lesions; hyperkeratotic, granulomatous and vegetating lesions, autosomal recessive trait associated with endocrine disorders, for example, hypoparathyroidism.

Systemic fungal infections

Systemic fungal infections can be divided into two distinct groups: The endemic or dimorphic mycoses. These infections are caused by true pathogenic fungi as compared with the opportunistic mold and yeast infections that are saprophytes, which only will invade an immuno-compromised host [36,37]. Such infections are life-threatening and are associated with high rates of death. Solid organ transplant recipients who take immunosuppressive medications to limit the risk of rejection also have an increased susceptibility to systemic fungal infections [2,3].

Opportunistic pathogens

Invasive candidiasis

At present, *Candida* spp. rank as the fourth most frequent cause of nosocomial bloodstream infections [38,39]. Nosocomial candidiasis may be either endogenous which is acquired through previous colonization of the mouth, gastrointestinal tract, vagina or skin or by exogenous which is acquired by cross-infection from another patient or healthcare worker [40]. *C. albicans* is the most frequently isolated species, causing 48–60% of bloodstream fungal infections [38,41,42]. However, a change in the pattern of *Candida*-related disease has been resulting in the emergence of a number of important non-*albicans Candida* spp., such as *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis,* and *Candida glabrata* [38,41,43]. This epidemiological change has major clinical implications by some non-*albicans Candida* spp. and has higher complication and death rates than *C. albicans* infections, and some species are resistant to antifungal agents [44,45].

Table 1: Classification of medicinal plants according to the bioactive compounds present in the plant for antifungal activity

S. No.	Bioactive compounds	Plant	The chemical constituent for antifungal activity
1	Polyphenols		
1.1		*Baseonema acuminatum*	Three phenolic compounds, 1-galloyl-β-D-glucopyranosyl-(1->4)-β-D galactopyranoside, 2-methoxy-5-(1',2',3'-trihydroxypropyl) phenyl-1-*O*-(6"-galloyl)-β-D-glucopyranoside and 2-methoxy-5-hydroxymethyl-phenyl-1- *O*-(6"-galloyl)-β-D-glucopyranoside together were reported for antifungal activity against *Candida albicans* [82]
1.2		*Cuban propolis*	A novel polyisoprenylated benzophenone showed significant antimicrobial and antifungal activities against a variety of bacteria and yeasts [83]
1.3		*Garcinia mangostana*	Geranylated biphenyl derivative 3-hydroxy-4-geranyl-5 methoxybiphenyl has strong antifungal and a number of other biological activities [84]
1.4		*Isolona cauliflora* and *Monodora angolensis*	Some of the prenylindoles had antifungal and antimalarial activities [85]
1.5		*Lycium chinense*	Dihydro-*N*-caffeoyltyramine, *trans*-*N*feruloyloctopamine, trans-*N* caffeoyltyramine, and *cis*-*N*-caffeoyltyramine reported to have anti-fungal activity [86]
1.6		*Toronia toru*	4-Hydroxyphenyl-6-O-[(3R)-3,4- dihydroxy-2-methylenebutanoyl]-D-glucopyranoside has the main antimicrobial component of the crude extract [87]
2.	Flavonoids		
2.1		*Artemisia giraldii*	The flavones hispidulin and belamcanidin were shown to inhibit the growth of the broad range of human pathogenic fungi [88]
2.2		*Aquilegia vulgaris*	4-methoxy-5,7-dihydroxyflavone 6-Cglucoside (isocytisoside) showed activity against the mold *Aspergillus niger* [89]
2.3		*Adina cordifolia*	A flavon 3,4',5,7-tetraacetyl quercetin exihibited moderate antifungal activity against *Aspergillus fumigatus* and *Cryptococcus neoformans* [90]
2.4		*Hildegardia barteri*	An isoflavone, 2-hydroxy maackiain was observed to have antifungal activity [91]
2.5		*Malus sylvestris*	Flavonoid derivative phloretin has antifungal properties [92]
2.6		*Piper solmsianum*	The four compounds eupomatenoid-3, eupomatenoid-5, conocarpan, and orientin exhibited antifungal action against all the dermatophytes tested [93]
2.7		*Selaginella tamariscina*	Amentoflavone exhibited potent antifungal activity [94]
3	Coumarins		
3.1		*Clausena excavate*	Clausenidin, dentatin, nor-dentatin, and carbazole derivatives, and clauszoline J showed antimycotic activity [95]
3.2		*Melia azedarach*	Hydroxycoumarin scopoleti reported to be antifungal against *Fusarium verticillioides* [96]
3.3		*Senecio poepigii*	A bioactive eremophilanolide, 1-tigloyloxy-8bH,10bH-eremophil- 7 (11)-en-8a, 12-olide showed antifungal properties [97]
3.4		*Tordylium apulum*	An antifungal dihydrofuranocoumarin, 20(S),30(R)-20-acetoxyisopropyl- 30-acetoxy-20,30-dihydroangelicin, were reported [98]
4	Quinones		
4.1		*Annona squamosa*	A compound, 11-hydroxy-16-hentriacontanone was reported for its antifungal potential [99]
4.2		*Kigelia pinnata*	The naphthoquinones kigelinone, isopinnatal, dihydro-a-lapachone were reported for antifungal activity [100]
4.3		*Rubia tinctorum* and *Rhamnus frangula*	Alizarin and emodin are the major anthraquinone aglycones for antifungal activity [101]
5	Saponoins		
5.1		*Phytolacca tetramera*	Phytolaccosides B and showed antifungal activities against a panel of human pathogenic opportunistic fungi [102]
5.2		*Sansevieria ehrenbergii*	Three spirostanol saponins designated sansevierin A, sansevistatin 1, and sansevistatin 2 and three steroidal exhibited antimicrobial activities, particularly against the pathogenic fungi *Candida albicans and Candida neoformans* [103]
5.3		*Smilax medica*	Spirostanol steroidal saponins together with the smilagenin 3-O-b-Dglucopyranoside and disporoside A exhibited antifungal activity against the human pathogenic yeasts *Candida albicans, Candida glabrata,* and *Candida tropicalis* [104]
5.4		*Ypsilandra thebetica*	Recently, steroidal saponins ypsilandroside B, ypsilandroside A, isoypsilandroside A, isoypsilandroside B, and isoypsilandrogaine were reported for antimicrobial activities [105]
6	Xanthones		
6.1		*Calophyllum caledonicum*	Caledonixanthone E was reported for strong antifungal activity [106]
6.2		*Cudrania fruticosa*	Isoprenylated xanthone, cudrafrutixanthone which showed antifungal activity against *Candida albicans* [107]
6.3		*Monnina obtusifolia*	1,3,6- Trihydroxy-2,5 dimethoxyxanthone was reported to have the antifungal potential [108]
6.4		*Securidaca longepedunculata*	The dichloromethane yielded 1,7-dihydroxy- 4-methoxyxanthone, which exhibited antibacterial activity against *Staphylococcus aureus* and antifungal activity against *Aspergillus niger*, *Aspergillus fumigatus*, and a *Penicillium* species [109]

(Contd....)

Table 1: ***(Continued)***

S. No.	Bioactive compounds	Plant	The chemical constituent for antifungal activity
7	Alkaloids		
7.1		*Aniba panurensis*	6,8-didec-(1Z)-enyl-5,7-dimethyl-2,3-dihydro-1H-indolizinium from *Aniba panurensis* demonstrated the activity against drug-resistant strains of *Candida albicans* [110]
7.2		*Corydalis longipes*	The alkaloids N-methylhydrasteine hydroxylactam and 1-methoxyberberine chloride from *Corydalis longipes* showed high efficacy individually [111]
7.3		*Datura metel*	Recently, an alkaloid, 2-(3,4-dimethyl-2,5-dihydro-1H-pyrrol-2-yl)-1-methylethyl pentanoate , has been isolated from the plant *Datura metel* and showed *in vitro* as well as *in vivo* activities against *Aspergillus* and *Candida* species [112]
7.4		*Epinetrum villosum*	Cocsoline, a bisbenzylisoquinoline alkaloid from the *Epinetrum villosum* displayed antifungal activities [113]
7.5		*Melochia odorata*	Frangulanine, a cyclic peptide alkaloid, and waltherione A, a quinolinone alkaloid from leaves of *Melochia odorata*, were reported to exhibit antifungal activities against a broad spectrum of pathogenic fungi [114]
7.6		*Zanthoxylum chiloperone* var. angustifolium	Canthin-6-one and 5-methoxy-canthin-6-one of *Zanthoxylum chiloperone* var. angustifolium exhibited antifungal activity against *Candida albicans, Aspergillus fumigatus* and *Trichophyton mentagrophytes* [115]
8	Terpenoids and essential oil		
8.1		*Delphinium denudatum*	The roots of yield 8-acetylheterophyllisine, panicutine, and 3-hydroxy-2-methyl-4H-pyran-4-one which have shown antifungal activity against a number of human pathogenic fungi [116]
8.2		*Litsea cubeba*	The essential oil from the leaves of have α–*cis*-ocimene, 3,7-dimethyl-1,6-octadien-3-ol and ntransnerolidol had manifest antifungal activities with minimal inhibitory concentration between 0.03 and 0.4 μL/mL for utilized pathogenic fungi and 1.0–2.0 μL/mL for molds [117]
8.3		*Polyalthia longifolia*	The diterpenoids 16ahydroxy-cleroda-3,13 (14)-Z-diene-15,16-olide and 16-oxo-cleroda-3,13 (14)-Ediene-15-oic acid isolated from the hexane extract of the seeds demonstrated significant antifungal activity [118]
8.4		*Vernonanthura tweedieana*	The afforded one antifungal active sesquiterpene, 6-cinnamoyloxy-1-hydroxyeudesm-4-en-3- one [119]
9	Polypeptides		
9.1		*Cicer arietinum*	A peptide designated cicerarin showed antifungal activity [120]
9.2		Black pumpkin	A novel antifungal peptide, cucurmoschin, inhibited mycelial growth in the fungi [121]
9.3		*Basella rubra*	Two novel antifungal peptides, designated alpha- and betabasrubrins, respectively. [122]

Invasive aspergillosis

Aspergillus spp. is ubiquitous, occurring most frequently in soil, water, and decaying vegetation. Most *Aspergillus* infections are acquired through the respiratory tract inhalation and are associated with hospital construction work or contaminated ventilation systems. Infections may also be acquired from plants or certain foods such as pepper. Sign and symptoms include: Unremitting fever and pulmonary infiltrates during antibiotic therapy, chest pain, pleural rub, pleural effusion, and hemoptysis. Computed tomography scan shows characteristic halo and air crescent signs while radiography reveals single or multifocal lesions [46].

Cryptococcus

Cryptococcal infection usually results from the inhalation of *Cryptococcus neoformans*, which is found primarily in soil contaminated by pigeon or chicken excreta. *Cryptococcus* has a particular affinity for the central nervous system, resulting in *Cryptococcal meningitis*, and is one of the most significant life-threatening fungal infections associated with HIV [47]. Cryptococcal infection may also be seen in non-immuno-compromised individuals [48] and patients with impaired cell-mediated immunity, for example, that undergoing solid organ transplantation [49].

Zygomycosis

Fungal infections from the class Mucorales (*Mucor, Absidia*, and *Rhizopus*) are seen increasingly in immune-compromised hosts [50]. Mucorales infections are typically an airborne disease, initiated in the upper or lower airways and have clinical symptoms similar to those of aspergillosis [51-53].

Other invasive infections

Rarer opportunistic pathogens that have emerged during recent years include *Penicillium marneffei*, *Fusarium* spp., *Malassezia* spp., *Trichosporon* spp., *Saccharomyces cerevisiae,* and *Blastoschizomyces capitatus* [54-57]. Invasive infection by *Malassezia furfur*, a commensal yeast normally associated with the superficial fungal infection. Tinea versicolor has also increased in frequency in recent years and is associated with parenteral nutrition [58].

Endemic pathogens

Systemic endemic mycoses include a group of dimorphic fungi that are found in distinct geographical regions [59].

Blastomycosis

Blastomycosis is the dimorphic fungi caused by the pathogens *Blastomyces dermatitidis and Blastomyces gilchristii*, which are found in humid soil containing decaying vegetation or decomposed wood and are associated with freshwater drainage basins [60]. It is reported mainly in North America and in Africa but occasionally has also been reported in Central and South America, Mexico, India, and the Middle East [61].

Histoplasmosis

Histoplasmosis caused by the dimorphic fungus *Histoplasma capsulatum* is found worldwide, but particularly in North, Central, and South America. Depending on the immune status of the host and the infectious dose, the clinical manifestations vary. In immunocompetent persons, the disease is usually asymptomatic or manifests as an acute respiratory illness that is self-limiting, whereas in immuno-compromised persons, it can result in severe illness with progressive pulmonary disease or disseminated infection. Symptoms are usually mild, but due to heavy exposure of fungus in individuals may cause fever, chills, headache, myalgia, anorexia, cough, and chest pain [62-64].

Coccidioidomycosis

It is endemic in the southwestern parts of the USA (California, Arizona, New Mexico, Utah, and Nevada) and parts of Central and South America (Mexico, Brazil, and Argentina) and caused by the dimorphic fungi *Coccidioides immitis and Coccidioides posadasii*. The most common clinical manifestations are chest pain, cough, fever, weight loss, and fatigue, often associated with dermatological manifestations including erythema nodosum or erythema multiforme and rheumatological manifestations including myalgia and arthralgia. The disease can also spread from the lungs hematogenously to bones, joints, skin, and the central nervous system [65-71].

Paracoccidioidomycosis

Paracoccidioidomycosis is caused by the dimorphic fungi *Paracoccidioides brasiliensis and Paracoccidioides lutzii*. These are found in certain parts of South America, especially not only in Brazil but also in Argentina, Colombia, Ecua dor, Peru, and Venezuela [72,73].

Penicilliosis

In Southeast Asia, penicilliosis is now the third most frequently occurring opportunistic infection in HIV-infected patients. Isolated cases have also been reported in western countries caused by *P. marneffei* [54].

HERBAL ANTIFUNGAL AGENTS

Medicinal plants are of great importance to the health of individuals and communities, and their importance lies in the chemical substances that produce a definite physiological action on the human body. Many of the pharmaceuticals currently available have a long history of use as herbal remedies including opium, aspirin, digitalis, and quinine while their purification and quantification makes them more predictable and chemical processing can sometimes modify their effects in desirable ways. Herbal remedies tend to have a more complex and subtle mix of chemicals and can sometimes offer access to drugs or combinations of drugs that the pharmaceutical industry has not yet exploited. These natural compounds formed the basis of discovering modern drugs [74-76]. Some of the antifungal drugs most recently introduced in clinical practice are echinocandines and sordarines derived from natural products [77,78]. Therefore, there is a need to develop new antifungal agents providing new mechanisms of action, with a broad spectrum of antifungal activity, fewer dose-limiting side effects, and economic [79,80]. Some of the plants having wide fungal activity are listed in Table 1. Which will be proved beneficial for the pharmaceutical industry when formulated. Herbal formulations always have attracted considerable attention due to their good activity and comparatively lesser side effects when compared to synthetic drugs [81].

MARKETED PREPARATIONS

Himalaya V-gel

Himalaya V-gel consists of persian rose, triphala, and cardamom. Himalaya V-gel is indicated for vaginal candidiasis (fungal yeast infection), vaginal trichomoniasis (parasitic vaginal infection), and non-specific bacterial vaginitis.

Himalaya hiora mouth wash

Himalaya hiora mouthwash kills germs, tones gums and refreshes mouth. It contains Meswak, Betel and Bibhitaki. Meswak and (Salvadora persica) tree twigs are popular teeth-cleaning agents, prevent tooth decay, and eliminates toothache and bad breath. Betel (Nagavalli) leaf effectively tackles halitosis, and its mild stimulating properties are beneficial for toothaches. *Belleric myrobalan* (Bibhitaki) is an antimicrobial and antifungal agent that keeps infections at bay.

Purifica 1% vaginal gel

Purifica gel contains *Pueraria mirifica* root extract.

Himalaya wellness acne-n-pimple cream

Himalaya acne-n-pimple cream works wonders with the help of natural ingredients such as Lentil, Silk Cotton Tree, Five-leaved Chaste Tree, Barbados Aloe, and Alum. Lentil's astringent and anti-inflammatory properties help in reducing inflammation associated with acne.

CONCLUSION

Although wide progress has been made in recent decades in medicine, fungal infections are still an unsolved health problem. It is mainly due to the fact that some of the available antifungal drugs cause resistance. The plant kingdom is a rich source of medicinal preparations that offer a wide chemical diversity, making it of huge potential for new drug development. Phytochemistry of various plant species has indicated that the phytochemicals could be a better source of medicine as compared to synthetically produced drugs. Researchers over the last years have developed a variety of chemical structures with antifungal activity based on natural compounds which are in the process of design and development. Thus, the plant kingdom holds a lot of potential which further needs to be explored in depth.

CONTRIBUTION OF AUTHORS

We declare that the work was done by the authors named in the article, and all the liabilities pertaining to claims relating to the content of this article will be borne by the authors. Kusum Kaushik, Shweta Agarwal conceived and designed the study. Kusum Kaushik wrote the manuscript, and all the authors read and approved the manuscript for publication.

CONFLICTS OF INTEREST

No conflicts of interest associated with this article.

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