

## Novel leads from herbal drugs for infectious skin diseases

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Infectious diseases, particularly skin and mucosal infections, are common in most of the tribal inhabitants due to lack of sanitation, potable water and awareness of hygienic food habits. Skin diseases like wounds, furuncles, sepsis, atopic dermatitis, cellulitis, gas gangrene, acne, candidiasis can be caused by a variety of the microbes. Plants produce a diverse range of bioactive molecules, making them rich sources of different types of medicine. Many hundreds of medicinal plant species worldwide are used in the traditional medicine as treatment for skin diseases caused by bacteria and fungi. In the present study different solvent extracts of *Asteracantha longifolia* Nees., *Daemia extensa* R. Br., *Euphorbia hirta* L., *Euphorbia tirucalli* L., *Euphorbia nerrifolia* L., *Haliotropium indicum* L., *Morus alba* L., *Pithecellobium dulce* (Roxb.) Benth., *Trichodesma indicum* R. Br., *Curcuma amada* L. and *Curcuma longa* L. were evaluated for their antimicrobial activity against some skin diseases causing bacteria and fungi using agar well diffusion method. The plant extracts showed potent activity against microorganisms and confirmed the folkloric claims as an antimicrobial agent for treating skin infections.

**Keywords:** Skin diseases; antimicrobial activity; medicinal plants; herbal drugs

### 1. Structure and function of the skin

The skin is the largest organ of the human body, both in terms of surface area and weight. It accounts for 15% of total body weight. It serves as an important environmental interface providing a protective envelope that is crucial for homeostasis. On the other hand, the skin is a major target for toxic insult by a broad spectrum of physical (UV radiation) and chemical (xenobiotic) agents that are capable of altering its structure and function [1]. Skin acts as a physical barrier and prevents harmful substances and microorganisms from entering the body. It protects body tissues and the network of muscles, bones, nerves and blood vessels against injury. It also controls the loss of fluids like blood and water, helps regulate body temperature through perspiration, and protects from the sun's damaging ultraviolet rays. The skin consists of three layers. The epidermis or outer layer is made up of mostly dead cells with a protein called keratin. This makes the layer waterproof and is responsible for protection against the environment. The dermis or middle layer is made up of living cells. It also has blood vessels and nerves that run through it and is primarily responsible for structure and support. The subcutaneous fat layer is primarily responsible for insulation and shock absorbency. It also contains structure like sweat glands, sebaceous glands, hair and hair follicles. Sebaceous glands secrete an oily substance called sebum and are found over the entire surface of the body except for the palms, soles and dorsum of the feet. Sebum protects hair and skin, and keeps them from becoming dry, brittle, and cracked. It also inhibits the growth of microorganisms on skin.

### 2. Diseases of the skin

Infectious diseases, particularly skin and mucosal infections, are common in most of the tribal inhabitants due to lack of sanitation, potable water and awareness of hygienic food habits [2]. It has been estimated that skin diseases account for 34% of all occupational diseases. As the primary interface between the body and external environment, the skin provides the first line of defense against broad injury by microbial and chemical agents. And many more factors other than trauma and primary skin disease have been identified as contributory to skin infections and these include immune deficiency diseases, diabetes mellitus and systemic or topical use of steroids [3]. The most damaging consequence of disruption to the skin is invasion by pathogenic microorganisms [4]. Skin diseases can be caused by a variety of the microbes and the skin is a haven for many microbes. In skin and soft tissue infections, the commonest bacterial agents are *Staphylococcus aureus*, *Streptococcus pyogenes* (Group A haemolytic streptococcus), *Clostridium perfringens* and the bacteriodes group. Others are *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Neisseria gonorrhoea*, *Pasturella tulurensis*, *Bacillus anthracis* and *Pseudomonas aeruginosa*. The common fungi which cause skin infections are *Candida albicans*, *Candida neoformans*, *Epidermophyton floccosum*, *Trichophyton tonsurans*, *Melassezia furfur*, etc.

A broad panel of microbial pathogens are associated with various skin infections. The Gram positive Staphylococci and Streptococci are causing wound infections, furuncles, carbuncles, abscesses, impetigo and erysipelas. The Gram positive Corynebacteria are part of the physiological skin flora. However, Corynebacteria may cause opportunistic skin infections in immunosuppressed patients. The Gram negative *Escherichia coli* are part of the physiological intestinal flora. However, outside the intestine they may cause wound infection and sepsis. Anaerobic Gram negative rods may cause skin infections under certain circumstances, i.e. in immunocompromised subjects. The yeast *Candida albicans*

and *Candida krusei* may occur in low frequency on skin and mucous membranes without causing symptoms. As opportunistic pathogens they may overgrow the normal flora and cause skin diseases like impetigo and candidiasis in diabetics, adipose and immunodeficient subjects [5].

*Pseudomonas*, Gram negative rod is a frequent pathogen of wound infections. *Pseudomonas aeruginosa* is the most prevalent burn patient's pathogen capable of causing life-threatening illnesses [6]. This bacterium can cause clinically significant infections such as wound and burns infections, giving rise to blue-green pus [7]. Some infections like hot tub folliculitis or nail infection may be mild but others can be fatal without prompt treatment [8]. *Pseudomonas aeruginosa* is able to infect different parts of the body. Several factors like the ability to stick on the cells, minimal food requirements, resistance to many antibiotics, production of proteins that damage tissue, protective outer coat make it a strong opponent. Some diseases caused by fungi include candidiasis, ringworms, athlete's foot, tinea pedis, sporotrichosis, blastomycosis and others not with distinctly specified conditions. Some skin diseases caused by microorganisms are listed in Table 1 and some photographs are shown in Fig. 1.

### 2.1. Modes of transmission

Infectious agents may be transmitted either through direct or indirect contact. Direct contact occurs when an individual is infected by contact with the reservoir, for example, by touching an infected person, ingesting infected meat, or bitten by an infected animal or insect. Transmission by direct contact also includes inhaling the infectious agent in droplets emitted by sneezing or coughing and contracting the infectious agent through intimate sexual contact. Indirect contact occurs when a pathogen can withstand the environment outside its host for a long period of time before infecting another individual. Inanimate objects that are contaminated by direct contact with the reservoir may be the indirect contact for a susceptible individual. Ingesting food and beverages contaminated by contact with a disease reservoir is another example of disease transmission by indirect contact.

## 3. Natural drug therapy for microbial skin diseases

The search for newer source of antibiotics is a global challenge preoccupying research institutions, pharmaceutical companies and academia, since many infectious agents are becoming resistant to synthetic drugs [9]. One way to prevent antibiotic resistance of pathogenic species is by using new compounds that are not based on existing synthetic antimicrobial agents. Problem of resistance, environmental degradation and pollution associated with irrational use of orthodox medicines have necessitated renewed interest in nature as a source of effective and safer alternatives in the management of human infections [10]. During the last decade the pace of development of new antimicrobial drugs has slow down while the prevalence of resistance has increase astronomically.

In developing countries, the World Health Organization (WHO) estimates that about three quarters of the populations relies on plant based preparations used in their traditional medicinal system and as the basic needs for human primary health care. Plants produce a diverse range of bioactive molecules, making them rich sources of different types of medicine [11]. Natural products, either as pure compounds or as standardized plant extracts, provide unmatched availability of chemical diversity [12]. Several plants containing volatile oils, polyphenols and alkaloids as active constituents are utilized as popular folk medicines, while others gained popularity in the form of finished products collectively named phytomedicines [13].

Plants have always been the principal form of medicine throughout the world, as people strive to stay healthy in the face of chronic stress and pollution, and to treat illness with medicines that work in count with the body's own defense. Plant derived products can be exploited with sustainable, comparative and competitive advantage. These include reduced cost, less dangerous, more effective and readily available [14]. Tribal healers in most of the countries, frequently use herbal medicine to treat cut wounds, skin infection, swelling, aging, eczema and gastric ulcer [15]. The different parts of plants used for skin diseases contain some active principles or components that are antimicrobial and nutritive in function [16].

Medicinal plants have been used in traditional treatment of skin diseases worldwide. *Acalypha wilkesiana* is a common ornamental plant in southern Nigeria used as a herbal remedy for the treatment of undefined skin infections in children [17]. Iranian traditional medicine (ITM), uses plants in the treatment of burns, dermatophytes and infectious diseases or as an antiseptic and anti-inflammatory agents [18]. Plants and its phytoconstituents are used to treat fungal infections particularly candidiasis such as oropharyngeal candidiasis, vulvovaginal candidiasis and others such as spirotrichosis, chromoblastomycosis, etc. [19]. South African plant *Dodonaea viscosa* Var. *angustifolia*, leaves and twigs extracts is traditionally used as a gargle for oral candidiasis [20]. Septilin, an Ayurvedic herbal formulation, is used extensively as an immunomodulator and has also been employed in the treatment of various skin infections [21]. Benjamen et al. [22] and Abatan [23] reported that leaf juice and decoctions of *Senna alata* are used in the treatment of ringworm and other skin diseases. Other herbs known to be used for treatment of skin infections include *Quisqualis indica*, *Cormelina benghalensis*, *Amaranthus spinosus*, *Ramunculus scleratus*, *Cassia alata* [24].

**Table 1** Some skin diseases caused by microorganisms

Diseases	Organisms	Entry site	Symptoms	Mode of Transmission
Impetigo	<i>S. pyogenes</i> , <i>S. aureus</i>	Skin around the nose and mouth	Vesicles on skin, fever, rash, diarrhea, itching, weakness	Direct contact with lesions or with nasal carriers
Carbuncle	<i>S. aureus</i>	Hair follicles	Painful, hard, red lump with multiple opening discharging pus	Squeezing the carbuncle, cutting it open without medical supervision can spread
Wounds	<i>S. aureus</i> , <i>S. Pyogenes</i> , <i>P. aeruginosa</i>	Skin	Redness, pain, swelling, raised temperature, fever	Direct contact, airborne dispersal
Atopic dermatitis	<i>S. aureus</i>	Armpits, hair and scalp	Large pimples, skin becomes red, flaky and very itchy	Direct contact
Boils	Staphylococcus Species	Broken skin, sweat glands, hair follicles	Lump filled with pus	At places where people congregate or share facilities. sports locker rooms are high potential for contraction of the contagion
Toxic shock syndrome	<i>S. aureus</i> , <i>S. pyogenes</i>	Surgical incisions	Fever, vomiting, diarrhea, muscle aches, low blood pressure and a rash that peels	Through infected boil, insect bite, in women who are on their period and using a tampon
Cellulitis	Streptococcus species, <i>E. coli</i> , <i>P. mirabilis</i> , <i>H. influenza</i>	Small breaks in the epidermis	Redness, pain, tenderness, fever and chills	Direct contact with person who has a purulent lesion
“Flesh-eating” disease	<i>S. pyogenes</i> , <i>V. vulnificus</i> , <i>C. perfringens</i> , <i>B. fragilis</i>	Infected area of the skin	Severe pain, swelling, fever, skin become tense and discolored, shock and death occurs if not immediately treated	Via wounds, cuts or be introduced into the tissue by injection drug use.
“Hot tub” folliculitis	<i>P. aeruginosa</i>	Hair follicles	Skin become itchy, bumpy, red rash, bumps may become filled with pus	From warm, wet areas
Gas gangrene	<i>C. perfringens</i>	Muscle tissue	Blisters with gas bubbles, skin becomes inflamed with a pale to brownish-red and very painful swelling, increased heart rate	Open fractures, frostbite, contaminated needle is used to inject an illegal drug into a muscle
Acne	<i>P. acnes</i> , <i>P. granulosum</i> , <i>S. epidermidis</i> , <i>M. furfur</i>	Sebaceous follicles	Inflammatory lesions originating with accumulations of sebum that rupture a hair follicle, ice pick scars, box car scars	Block the openings of sebaceous glands, stimulates bacteria to multiply and cause surrounding tissues to become inflamed.
Candidiasis	Candida species	Skin and mucosal membranes	Tiny, pus filled lesions in the surrounding skin, itching and burning	Through contaminated faeces, litter and dirty drinkers
Tinea versicolor	<i>P. orbiculare</i> , <i>P. ovale</i> , <i>M. furfur</i>	Skin	Light brown or white patches on the skin, rashes on the trunk	Warm and humid environment
Athlete’s foot and Ringworm	<i>T. rubrum</i> , <i>E. floccosum</i>	Skin	Red, raised lesions on and around the toes and soles of the feet	Directly from person to person or by contact with the objects used by infected person.
Sporotrichosis	<i>S. schenckii</i>	Skin	Red, pink, or purple small painless bump	Unbroken skin after contact with hay or moss carrying the mold
Blastomycosis	<i>B. dermatitidis</i>	Nose	Pus-filled lesions and multiple abscesses	Inhalation of the fungus from its natural soil habitat



**Fig. 1** Some skin diseases caused by microorganisms.

In search for novel leads from herbal drugs against stubborn skin diseases caused by microorganisms some plants which are traditionally claimed to be used in the treatment of skin diseases were screened for their potential as antimicrobial agents. The plants screened for antibacterial and antifungal activity are *Asteracantha longifolia*, *Curcuma amada*, *Curcuma longa*, *Daemia extensa*, *Euphorbia hirta*, *Euphorbia tirucalli*, *Euphorbia nerrifolia*, *Heliotropium indicum*, *Morus alba*, *Pithecellobium dulce* and *Trichedesma indicum*.

#### 4. Antimicrobial activity

The eleven plants belonging to the families Acanthaceae, Asclepiadaceae, Boraginaceae, Euphorbiaceae, Fabaceae, Moraceae and Zingiberaceae were evaluated for their antimicrobial potential. The antimicrobial activity was done by agar well diffusion method [25, 26] against two Gram positive bacteria (*Staphylococcus aureus* ATCC25923 and

*Bacillus subtilis* ATCC6633), two Gram negative bacteria (*Pseudomonas aeruginosa* NCIM2719 and *Escherichia coli* ATCC25922) and four fungi (*Candida albicans* ATCC2091, *Candida tropicalis* ATCC4563, *Candida neoformans* NCIM3542 and *Cryptococcus leueteolus* NCIM 3238).

## 5. Results and discussion

The result of antimicrobial activity of selected plant extracts are shown in table 2. The dried plant powder was first defatted with petroleum ether and then individually extracted with toluene, ethyl acetate and methanol. All the extracts exhibited variable degree of antibacterial and antifungal activity. The rhizome and peels of *C. amada* and *C. longa* presented strongest activity against Gram positive bacteria and fungi; however they were not active against Gram negative bacteria. The reason for the difference in sensitivity between Gram positive and Gram negative might be ascribed to the differences in morphological constitutions between these microorganisms. However, all the four extracts of all the plants except rhizome and peels of *C. longa* and *C. amada* showed activity also against Gram negative bacteria (*E. coli* and *P. aeruginosa*). Antimicrobial activity of methanol extract of these plants has been reported [27]. The results indicate the potential usefulness of the rhizome and peels of *C. longa* and *C. amada* as antimicrobial agents. The extensive use of these herbal drugs by the local people in treating various types of skin disorders might therefore be justified by their antimicrobial activities against different strains of bacteria and fungi, which are known to be responsible for causing various skin diseases.

**Table 2** Antimicrobial activity of different solvent extracts of some medicinal plants against skin diseases causing bacteria and fungi

Plant	Bacteria (Zone of inhibition in mm)															
	<i>Staphylococcus aureus</i>				<i>Bacillus subtilis</i>				<i>Pseudomonas aeruginosa</i>				<i>Escherichia coli</i>			
	PEE	TOE	EAE	MEE	PEE	TOE	EAE	MEE	PEE	TOE	EAE	MEE	PEE	TOE	EAE	MEE
<i>A. longifolia</i>	10.0	9.0	9.5	11.5	-	9.5	9.5	9.0	9.5	9.5	9.0	9.0	11.0	10.5	10.5	9.5
<i>D. extensa</i>	9.5	9.0	9.5	-	12.5	10.0	9.5	13.0	9.0	9.0	9.5	11.5	10.0	9.5	11.5	11.0
<i>E. hirta</i>	10.0	11.0	11.5	12.0	9.0	9.0	9.0	9.0	12.0	11.0	11.5	12.0	11.0	11.0	11.0	12.0
<i>E. tirucalli</i>	-	9.5	11.5	11.0	-	9.5	9.5	9.0	10.0	11.5	11.5	14.0	10.5	10.0	11.5	12.0
<i>E. nerrifolia</i>	-	-	10.0	10.0	-	-	9.5	9.5	9.5	9.0	9.5	10.0	10.0	10.0	11.5	12.0
<i>H indicum</i>	9.0	9.5	9.5	10.0	10.0	10.5	10.5	9.0	9.0	9.0	9.5	10.0	10.0	10.0	10.0	11.0
<i>M. alba</i>	9.5	-	9.0	9.0	9.5	9.0	9.5	-	9.0	9.5	9.0	9.5	10.0	9.5	9.0	9.5
<i>P. dulce</i>	9.5	10.0	9.0	-	9.5	-	9.5	9.5	10.0	9.5	10.0	9.5	10.0	10.0	10.0	10.0
<i>T. indicum</i>	-	9.5	-	13.0	9.0	11.0	9.0	-	9.5	9.5	10.0	9.0	11.0	11.0	10.0	10.0
<i>C. amada</i> (Rhizome)	13.0	14.0	14.0	12.5	15.0	15.0	15.0	14.0	-	-	-	-	-	-	-	-
<i>C. amada</i> (Peels)	13.0	14.0	14.5	13.5	15.0	16.0	16.0	16.0	-	-	-	-	-	-	-	-
<i>C. longa</i> (Rhizome)	-	11.5	11.0	10.5	10.0	12.0	11.5	12.0	-	-	-	-	-	-	-	-
<i>C. longa</i> (Peels)	-	9.0	10.5	10.5	10.5	11.5	11.0	11.0	-	-	-	-	-	-	-	-

  

Plant	Fungi (Zone of inhibition in mm)															
	<i>Candida tropicalis</i>				<i>Candida albicans</i>				<i>Candida neoformans</i>				<i>Cryptococcus leueteolus</i>			
	PEE	TOE	EAE	MEE	PEE	TOE	EAE	MEE	PEE	TOE	EAE	MEE	PEE	TOE	EAE	MEE
<i>A. longifolia</i>	9.5	9.5	-	-	-	-	-	-	-	-	-	-	10	-	-	-
<i>D. extensa</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>E. hirta</i>	-	-	-	-	-	-	-	-	10.0	10.0	10.5	-	-	-	10.0	
<i>E. tirucalli</i>	9.5	9.0	9.0	9.5	12.5	-	10.0	10.0	10.5	-	-	10.5	-	-	-	10.5
<i>E. nerrifolia</i>	9.0	9.0	10.5	12.0	9.5	9.0	-	-	-	-	-	-	9.0	9.0	9.0	9.0
<i>H indicum</i>	9.0	9.0	9.0	10.0	-	-	-	-	-	-	-	-	9.0	9.0	9.0	9.0
<i>M. alba</i>	11.0	10.5	9.5	12.5	9.5	9.0	9.5	10.5	-	9.0	-	-	9.0	9.0	10.0	10.0
<i>P. dulce</i>	-	10.0	9.0	10.0	9.5	9.0	9.5	10.5	-	9.0	-	9.5	10.0	10.0	10.0	10.0
<i>T. indicum</i>	10.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>C. amada</i> (Rhizome)	10.0	10.0	-	-	-	-	10.0	9.5	9.5	9.5	10.0	-	11.0	12.0	12.0	10.5
<i>C. amada</i> (Peels)	9.5	9.0	10.0	9.0	-	-	-	10.0	10.5	11.0	10.5	-	12.0	12.0	10.5	10.5
<i>C. longa</i> (Rhizome)	-	11.0	11.5	10.5	9.5	9.5	10.5	10.0	-	10.5	10.5	10.75	10.0	11.0	13.0	12.5
<i>C. longa</i> (Peels)	10.0	10.5	9.0	10.0	10.0	11.0	10.0	9.0	-	10.5	9.5	9.5	10.0	12.0	11.0	10.5

-: no activity; PEE: petroleum ether extract; TOE; toluene extract; EAE: ethyl acetate extract; MEE: methanol extract

## 6. Conclusion

The results indicate that scientific studies carried out on medicinal plants having traditional claims of effectiveness might warrant fruitful results. Further studies might aim at the isolation and identification of active substances from the active plant extracts which could also disclose compounds with better therapeutic value. Therefore, ayurvedic knowledge supported by modern science is necessary to isolate, characterise, and standardise the active constituents from herbal source. This combination of traditional and modern knowledge can produce novel drugs for skin diseases caused by microorganisms. Herbs are widely available in the world. The wide spectrum makes them attractive candidates for further research.

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