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A COMPREHENSIVE REVIEW: THE ROLE OF HERBS IN MANAGEMENT OFFUNGAL INFECTION

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Abstract:
This comprehensive examination highlights the intricate relationship between humans and fungi, emphasising the prevalence of fungal infections when the body's defenses are compromised. Fungi, vital components of ecosystems, implicate certain species in severe human diseases that require immediate treatment. The text categorises fungal infections into superficial, subcutaneous, and systemic mycoses, detailing their transmission routes and characteristics. Furthermore, it discusses the antifungal potential of various herbal remedies such as aloe vera, garlic, neem, turmeric, peppermint, and bitter gourd, which contain bioactive compounds that exhibit significant antifungal activity. Each plant's mechanisms of action are critically reviewed, revealing their roles in disrupting fungal cell integrity, inhibiting biofilm formation, and enhancing immune response. This exploration of herbal antifungals not only underscores their importance in traditional medicine but also suggests their potential as alternative treatments amid rising antifungal resistance.

Keywords: MANAGEMENT OF FUNGAL INFECTION

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Introduction

Humans and the microbes that surround them coexist peacefully; an infection only arises when the body's defenses are compromised or the concentration of pathogens reaches an abnormally high level. The majority of infections go undetected, but occasionally the agents that cause the body to react, resulting in signs and symptoms that are clinically evident. This condition is called an infectious disease[1]. Infectious diseases have been linked to bacteria, viruses, parasites, fungus, worms, and helminthes. A variety of fungus may parasitise humans, animals, plants, and other organisms. Besides the rice blast fungus, Dutch elm disease, and chestnut blight, plant infectious fungi can also cause damage and losses to agriculture and forestry[2].Some different fungi may cause serious diseases in humans, many of which can be fatal if left untreated.These include aspergillosis, candidosis, coccidioidomycosis, cryptococcosis,

histoplasmosis, mycetomas, mucormycosis, and paracoccidioidomycosis. Local infections like ringworm and athlete's foot can be brought on by the so-called dermatophytic and keratinophilic fungi, which can also affect the skin, nails, hair, and eyes. Allergies can also be caused by fungi from many taxonomic groups, and fungus spores can induce allergic reactions[3].

Parasites exist in two essential shapes: yeasts and moulds. Yeasts are regularly single, little, oval cells,though form colonies comprise of filamentous strands called hyphae. A few organisms are dimorphic, existing as either yeasts or moulds depending on the outside environment. A few species, in any case, are adventitious pathogens in people, causing shallow, subcutaneous or systemic contamination.Most parasites causing systemic contamination do so by coordinate inward breath into the lung or byintrusion of a wound location. Others, such as Candidaalbicans, are commensal occupants of the gastrointestinal tract and skin, which beneath certain conditions may multiply and relocate into the systemic circulation, for illustration, when presentedinto the body through restorative gadgets such as vascularcatheters[4].

Fungi, as a characteristic feature, are eukaryotes that are heterotrophic and have structures that can be either unicellular or multicellular, and are surrounded by a rigid cell wall made up of glucans and cellulose. The main sterol found in their cell membranes is ergosterol. They acquire their nutrients through extracellular digestion, utilizing enzymes and secreted acids to break down complex substrates into simple molecules. As a result, they play crucial roles in various ecosystems by recycling carbon and nitrogen from complex organic sources. Fungi reproduce through asexual, parasexual, or sexual means and historically, they were classified based on the morphological characteristics of their sexual (teleomorphs) and asexual forms (anamorphs)[5].

Several herbal plants like **neem**, **aleovera**, **turmeric**, **mentha**, **Bitter gourd** etc. Contains metabolites which works as the anti-fungal.

The term Aleovera comes from the Arabic word “Alloeh,” which translates to “shining bitter substance,” while the term ‘Vera’ originates from Latin, meaning “true”[6]. The Liliacea family includes the cactus-like plant known as Aloevera. Aloevera gel is a mucilaginous colorless gel, secreted by the parenchymatous cells of fresh Aloevera leaves[7]. Aloe Vera has long been utilized for healing skin wounds (such as burns, cuts, insect bites, and eczema) and digestive issues due to its anti-inflammatory, antimicrobial, and healing abilities[8].

The neem tree [*Azadirachta Indica*], an evergreen in most tropical countries, belongs to the Meliaceae family of mahogany trees. Native to India and Burma, it is one of two species in the genus *Azadirachta* that grow in tropical and semi-tropical climates. This tree grows quickly, reaching an average height of 15-20 meters but rarely reaching 35-40 meters[9]. Neem leaves have antibacterial qualities, they may be utilized to reduce bacterial contamination in the air. Neem seeds have also been utilized in traditional medicine to cure infections, particularly those that affect the ears and eyes[10].

Curcuma longa, the scientific name for turmeric, is a member of the ginger family, *Zingiberaceae*. The tall, perennial plant Curcuma longa has underground rhizomes that are primarily oval, ablong, pyriform, and short-branched[11]. It has been used to treat ringworm, tinea, rash, itching, and skin conditions. The rhizome of the perennial herb turmeric is thick, ellipsoid-ovate, and contains an orange cortex. The rhizomes are used medicinally because of their volatile oil, which has antifungal and carminative effects, and their yellow curcuminoids, which have anti-inflammatory and anti-oxidant qualities. Turmeric volatile oil contains turmerone, atlantone, and zingiberone as active ingredients[12].

Peppermint, or Mentha × *Piperita L*., is a member of the *Lamiaceae* family and is native to the Mediterranean. It is a hybrid mint that is grown all over the world and is a mix between spearmint and water mint. Additionally, the essential oil (EO) has biological action against a wide range of species, including as bacteria, nematodes, fungus, and insect pests[13].

TYPES OF FUNGAL INFECTION

The external source of fungal diseases in people is the environment, and they are caught via ingesting, inhalation, or traumatic implantation. Depending on where the infection first occurred, fungal infections can be divided into many

major categories. This makes the level of parasitic adaptability of the various fungal groups very evident, and the manner the site is impacted is linked to the method the fungus enters the host[28].

1. THE SUPERFICIAL MYCOSES

These infections only affect the mucous membranes, the skin's outermost layers, and the hair and nails. The two main illnesses in this category are superficial types of candidosis and dermatophyses. Despite affecting millions of people globally, these illnesses are easily detected and typically have good treatment outcomes[28]. The specifics of superficial infections are covered elsewhere, but they are prevalent in all settings. However, local climate conditions like heat and humidity might encourage the growth of Malassezia infections or dermatophytosis. Although the exact causes of this enhanced vulnerability are unknown, circumstances that increase the surface Pco2 concentration in the outer layers of the epidermis are probably going to increase the likelihood of dermatophyte hyphe invasion. This may also result in tinea pedis and tinea cruris[29].Tinea pedis, often known as athlete's foot, is a condition that causes scaling and maceration between the toes, especially in the fourth interdigital area, along with itching. This condition may be brought on by dermatophytes, gram-negative bacteria, erythrasma, or Candida species. The space between the toes can be either dry or moist in dermatophyte infections, and it can be vesicular in certain infections, especially those brought on by T. interdigitale. Involvement of the dorsum of the foot or the sole may occur. The commonest cause is T. rubrum.Host resistance to dermatophytosis depends on several innate and acquired immunologic factors. These include increased epidermal turnover and locally produced peptides such as β defensins and fatty acids. Acquired immunity is mediated through T lymphocyte (Th1) cytokines such as interleukin (IL)-17, although its effectiveness is reduced in non-inflammatory infections—for example, the soles of the feet and tinea imbricata[30].

2. SUBCUTANEOUS MYCOSES

A diverse collection of fungal infections known as subcutaneous mycoses arise at the site of transcutaneous trauma. The progression of infection is gradual as the etiologic agent endures and adjusts to the unfavourable host tissue environment. Sporotrichosis, chromoblastomycosis, mycetoma, lobomycosis, rhinosporidiosis, subcutaneous zygomycosis, and subcutaneous phaeohyphomycosis[31] are the most prevalent subcutaneous fungal diseases that are frequently found in soil, leaves, and organic matter. Their high morbidity is mostly induced by traumatic injection with thorns or any other object infected with these fungus. Although they are found in many tropical and subtropical nations, reports of them are most frequently found in Africa, Central and South America, and India[32].

3. SYSTEMIC MYCOSES

Fungi that infiltrate the body through an internal organ or a deep focus, such the lungs, digestive tract, or paranasal sinuses, are the source of systemic mycoses. Blood infections have the ability to spread, leading to disseminated diseases that frequently affect the skin. The two forms of systemic mycoses include endemic respiratory infections (histoplasmosis, blastomycosis, coccidioidomycosis, paracoccidioidomycosis, and cryptococcosis) and opportunistic mycoses (systemic candidiasis, aspergillosis, and systemic mucormycosis)[34].Species of Schizomycetes and Deuteromycetes are the main culprits for systemic mycotic infections. Coccidioides immitis, Cryptococcus neoformans, Blastomyces dermatitidis, Actinomyces israelii, Nocardia asteroides, and Histo-P plasma capsulatum are frequently among them. The Schizomycetes, namely A. israelii and N. asteroides, are categorised as higher bacteria, and infections with these species are only referred to be mycotic infections by custom and habit. In the natural mouth cavity, A. israelii sustains a saprophytic development. These fungi are free-living saprophytes in the human environment[33].

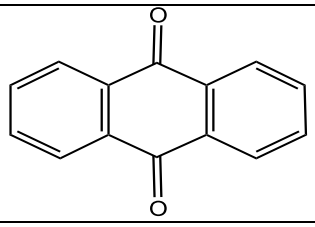
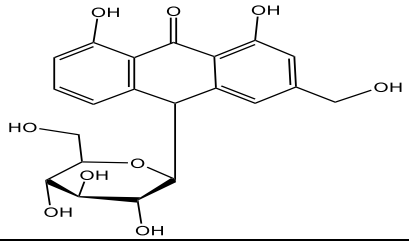
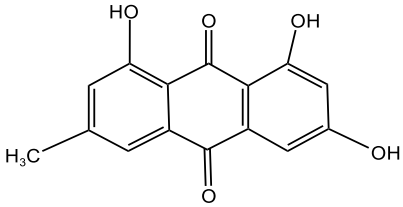
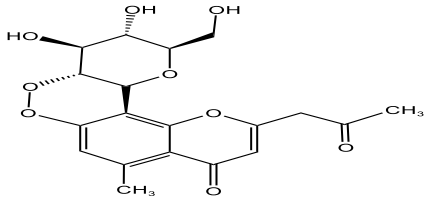
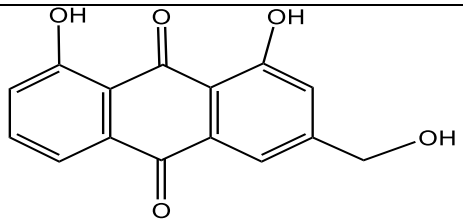
ANTIFUNGAL ACTIVITY OF HERBAL PLANTS

ALEOVERA

Globally, more than 250 species of aloe are cultivated. Commercial cultivation is limited to two species: *Aloe arborescens* and *Aloe barbadensis Miller*. Grown in warm, tropical climates, aloe plants cannot withstand cold conditions, such as those seen during winters[14]. This medicinal herb has been used historically to treat skin conditions like as burns, wounds, and anti-inflammatory processes. Moreover, Aloe vera has shown other therapeutic properties

including anticancer, antioxidant, antidiabetic, and anti-hyperlipidemia. Aloevera contains more than 75 different compounds, including vitamins (vitamin A, C, E, and B12), enzymes (i.e., amylase, catalase, and peroxidase), minerals (i.e., zinc, copper, selenium, and calcium), sugars (monosaccharides such as mannose-6-phosphate and polysaccharides such as glucomannans), anthraquinones (aloin and emodin), fatty acids (i.e., lupeol and campesterol), hormones (auxins and gibberellins), and others (i.e., salicylic acid, lignin, and saponins)[8]. A. vera gel have high moleculer weight compounds which demonstrate benificial effect. Lactine like proteins, polysacchrides and postagladins, Manos-6phosphate shows a role in the healing of wound, bradykinin-degrading glycoproteins may shows anti inflamatory effect. For antiviral properties anthraquinones have been studied from various plants[6].

Antifungal Bioactive Compoundsof*Aloe barbadensis Miller* –

COMPOUND NAME	PARTS OF PLANT	MOLECULAR FORMULA	STRUCTURE
Anthraquinones	Roots, Rhizomes, Fruits, and Flowers	$C_{14}H_8O_2$	
Aloin	Leaf	$C_{21}H_{20}O_9$	
Emodin	Root and Leaf	$(C_{12}H_{22}O_{11})n$	
Aloesin	Leaf	$C_{21}H_{22}O_{10}$	
Aloe emodin	Root and leaf	$C_{15}H_{10}O_5$	

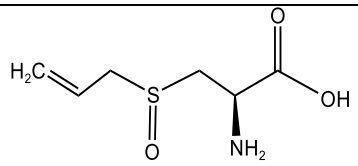
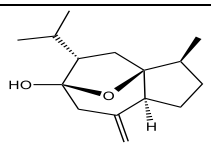
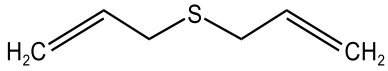
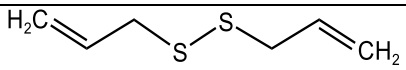
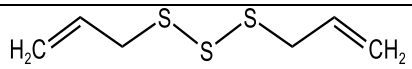
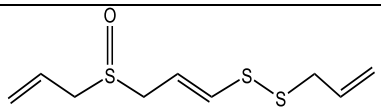
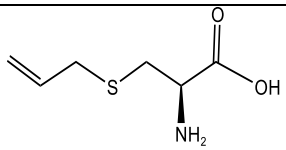
(Table-1) (Ref–50)

GARLIC

Allium Sativum (Garlic) is a member of the Liliaceae family. *Allium Sativum* contains therapeutic, curative, and medicinal properties[13]. *Allium Sativum* oil (Garlic oil) has been demonstrated to possess potent antifungal and anti-inflammatory properties. The two most prevalent volatile sulfur-containing substances in garlic oil are diallyldisulphide (DDS) and diallyltrisulfide (DTS)[15]. It has been used for a long time all over the world. As a major culinary spice plant, garlic has a vital function in both preventing and controlling disease; in fact, it can heal a number of illnesses.It has long been used to combat human infections[16]. Garlic contains organosulfur compounds, particularly

allicin, which are strong antibacterial agents with a wide range of biological actions against viruses, fungi, bacteria (both Gram-positive and Gram-negative), and protozoa[17]. Garlic extract has been shown to have a protective impact against in-vivo fungal infections and toexhibit an in-vitro growth suppression effect against a variety of yeasts, including Candida spp., and fungi, including Coccidioides immitis[18].Garlic's sulphur content and bioflavonoids, such as quercetin and cyanidin, are also said to be very beneficial in avoiding infections and illnesses. It has been discovered that garlic's active ingredients, such as allistatin I and allistatin II, are potent anti-Staphylococcus and anti-E. coli bacteria[35].

Antifungal Bioactive Compounds of *Allium Sativum* (Garlic)-

COMPOUND NAME	PARTS OF PLANT	MOLECULAR FORMULA	STRUCTURE
Allicin	Fruit (Bud or Clove)	$C_6H_{10}OS_2$	
Alliine	Fruit	$C_6H_{11}NO_3S$	
Diallyl sulfide	Fruit	$C_6H_{10}S$	
Diallyl Disulfide	Fruit, Flower and Stem	$C_6H_{10}S_2$	
DiallyTrisulfide	Fruit, Flower and Stem	$C_6H_{10}S_3$	
Ajoene	Fruit, Flower and Stem	$C_9H_{14}OS_3$	
S-allyl-cysteine	Fruit, Stem and Flower	$C_6H_{11}NO_2S$	

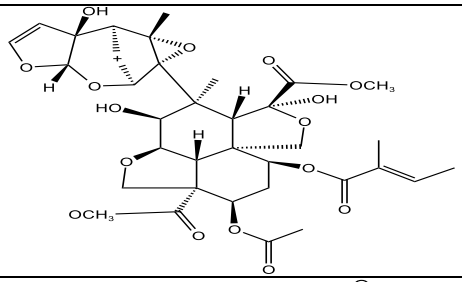
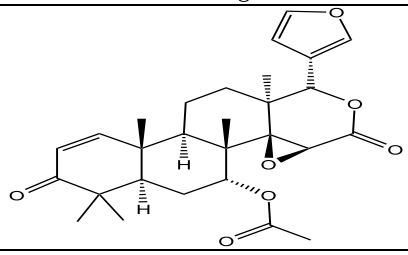
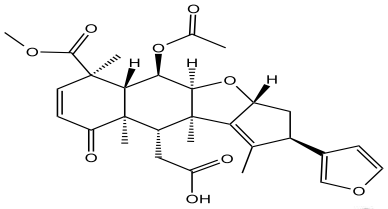
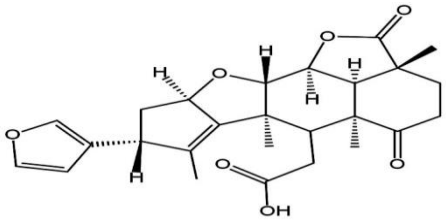
(Table – 2) (Ref – 51, 52)

NEEM

Azadirachta indica A. Juss is the scientific name for neem, which is a member of the tribe Melieae of the Meliaceae family, which is a subfamily of the Meloidae. Neem, sometimes commonly referred to as "Indian lilac" or "Margosa," is readily available in India[21].*A. indica* leaf and seed extracts were examined for antidermatophytic activity and found to be effective against C. albicans and a few dermatophytes, including Trichophytonrubrum, T. violaceaum, Microsporumnanum, and Epidermophytonfloccosum, using the tube dilution technique. Leprosy, ulcers, various forms of metritis, gum and dental issues, and other chronic skin illnesses are all treated with neem seed oil, which is also

believed to be non-mutagenic. Additionally, it works well against opportunistic fungi like Candida species, especially Candida albicans, and is well-known for treating and preventing systemic infections, vaginal candidiasis, and oral thrush[20]. Neem inhibits fungal development through a variety of processes. By interfering with ergosterol production, it damages the fungal cell wall and membrane, resulting in structural instability and cell death[36]. Additionally, neem inhibits biofilm development and spore germination, two processes that are essential to fungal resistance and pathogenicity. Furthermore, by producing reactive oxygen species (ROS), it causes oxidative stress in fungal cells, further harming cellular constituents[37].

Antifungal Bioactive Compounds of *Azadirachta indica*(Neem) –

COMPOUND NAME	PART OF PLANT	MOLECULAR FORMULA	STRUCTURE
Azadirachti	Seed	$C_{35}H_{44}O_{16}$	
Gedunin	Seed and Bark	$C_{28}H_{34}O_7$	
Nimbin	Leaf, Seed and Bark	$C_{30}H_{36}O_9$	
Nimbolide	Leaf and Flower	$C_{27}H_{30}O$	

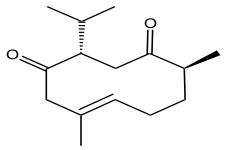
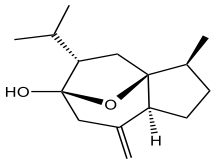
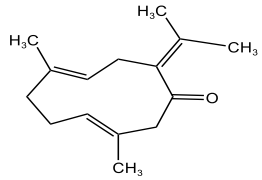
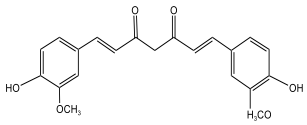
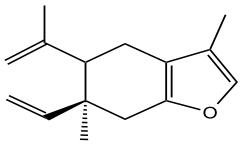
(Table-3) (Ref–53, 54)

TURMERIC

As a member of the *Zingiberaceae* family, *Curcuma longa* (*C. longa*) has drawn a lot of interest for its ability to produce a variety of complex chemicals that are used in medicines and cosmetics as pharmacological agents as well as in food as spices, flavourings, and seasonings. Among *C. longa's* medicinal qualities are its insecticidal, antibacterial, antifungal, antimalarial, antiviral, and antioxidant qualities. *C. longa* has been shown to have poisonous properties against fungi that cause agricultural goods to deteriorate by preventing mycelia from growing[4].By interfering with ergosterol production, curcumin disrupts the integrity of the fungal cell membrane, causing the membrane to become unstable and ultimately resulting in fungal cell death. Furthermore, curcumin compromises the pathogen's structural integrity by inhibiting enzymes involved in the formation of chitin, a crucial part of the fungal cell wall[38]. Turmeric's capacity to lower inflammation and alter immune responses is also essential, especially in cases of systemic or chronic fungal infections, since it lessens the tissue damage brought on by an extended infection.[39]. It has been demonstrated

that curcumin prevents the development of fungal biofilms, which are defence mechanisms that enable fungus to withstand antifungal therapy. Since biofilm development frequently results in persistent infections, this biofilm breakdown is particularly helpful in treating chronic fungal infections[40].

Antifungal Bioactive Compounds of *Curcuma longa*(Turmeric) –

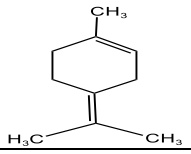
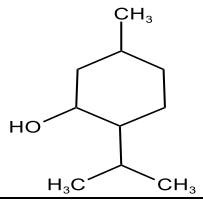
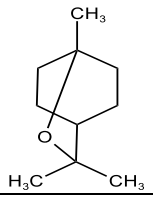
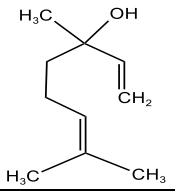
COMPOUND NAME	PART OF PLANT	MOLECULAR FORMULA	STRUCTURE
Curdione	Rhizomes	$C_{15}H_{24}O_2$	
Curcumol	Rhizomes and Root	$C_{15}H_{24}O_2$	
Germacrone	Rhizomes	$C_{15}H_{22}O$	
Curcumin	Rhizomes and Leaf	$C_{21}H_{20}O_6$	
Curzerene	Rhizomes	$C_{15}H_{20}O$	

(Table- 4)(Ref–55)

MENTHA

The primary constituents of *peppermint* (*M. piperita*) oil, menthol and menthone, make it one of the most well-known and often used essential oils. Previous research has demonstrated that the EO and methanolic extracts of herbal components and callus cultures of *M. piperita*[23] have antiviral, antibacterial, antifungal, antibiofilm formation, radioprotective, antioedema, analgesic, and antioxidant properties. *Mentha piperita*, or *peppermint*, and Mentha spicata, or spearmint, are the most widely used species. They both contain strong bioactive substances including rosmarinic acid[41], menthol, and menthone.These substances help mint prevent fungal development, which makes it a natural treatment for fungal infections[42]. The main source of mentha's antifungal properties is its essential oil, which has a high menthol content. It has been demonstrated that menthol damages fungal cell membranes by changing their permeability, which causes cellular contents to seep out and eventually results in cell death[43].Numerous fungal pathogens, such as Candida albicans, which causes common yeast infections, and dermatophytes like Trichophyton rubrum and Microsporum canis, which cause skin diseases like ringworm and athlete's foot, have been demonstrated to be effectively combatted by mint. When administered topically, mint essential oil can treat these surface infections. Mint teas and extracts can also be utilised to treat interior fungal problems[45].

Antifungal Bioactive Compounds of *Mentha piperita* (Mentha) –

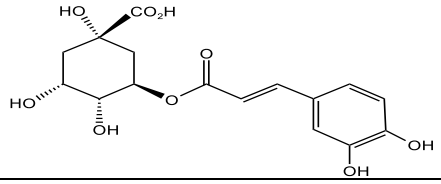
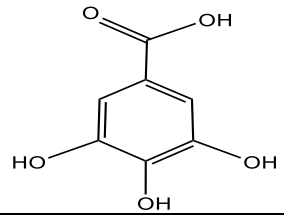
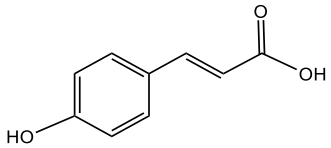
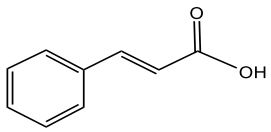
COMPOUND NAME	PART OF PLANT	MOLECULAR FORMULA	STRUCTURE
Terpinolene	Leaf	$C_{10}H_{16}$	
Menthol	Leaf and flower	$C_{10}H_{20}O$	
1,8-Cineole (Eucalyptol)	Leaf	$C_{10}H_{18}O$	
Linalool	Leaf and Flower	$C_{10}H_{18}O$	

(Table- 5) (Ref –56)

BITTER GOURD

The bitter gourd (*Momordica charantia L.*), often called a bitter apple, bitter melon, or balsam pear, is a tropical vine that is a member of the genus Momordica, family Cucubitaceae, and order Cucurbitales. The plant is widely grown in South East Asia, China, and India as a vegetable crop and medicine[26]. The stem, fruits, leaves, and seeds of the entire Momordica charantia plant have therapeutic properties and continue to have medicinal effects[24]. It has been established that *M. charantia*[25] has antibacterial, anticancer, immunotoxic, antiviral, antimutagenic, antifertility, and antidiabetic properties[25]. Momordicin, charantin, and vicine are among the bioactive substances found in the fruit that help fight fungal infections[46]. Bitter gourd causes fungal cell death by interfering with the integrity and production of their cell walls. Additionally, it strengthens the immune system, which aids in the body's more efficient defence against infections[47]. By preventing the development and biofilm formation of Candida albicans, the yeast that causes illnesses such vaginal candidiasis and oral thrush, bitter gourd has demonstrated special potential against this pathogen[25]. Furthermore, it has shown antifungal action against dermatophytes that cause skin diseases including ringworm[48] and athlete's foot, such as Trichophyton rubrum and Microsporum canis. Topical therapies such as extracts or pastes are used to treat skin infections, while bitter gourd juice or dry powder is frequently eaten to treat systemic fungal infections[49].

Antifungal Bioactive Compounds of *Momordica charantia L* (Bitter Gourd) –

COMPOUND NAME	PART OF PLANT	MOLECULAR FORMULA	STRUCTURE
chlorogenic acid	Root	$C_{16}H_{18}O_9$	
Gallic acid	Root	$C_7H_6O_5$	
p-Coumaric Acid	Flower	$C_9H_8O_3$	
Cinnamic acid	Steam and leaf	$C_9H_8O_2$	

(Table - 6) (Ref – 57)

CONCLUSION

The text highlights the antifungal properties of various plants, including neem, turmeric, peppermint, and bitter gourd, emphasizing their effectiveness against a range of fungal pathogens through mechanisms such as disrupting cell membrane integrity and inhibiting biofilm formation. These natural remedies not only demonstrate potential in treating fungal infections but also contribute to overall health benefits, showcasing the importance of plant-based compounds in medicinal applications.

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