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Review Article

Antifungal Property of Medicinal Plants of Vitex Negundo, Acacia Nilotica and Hibiscus Rosa Sinesin

Vaibhav Paymal*, Jaya Kambale, Dr. Nilesh Chougule

Department Of Pharmaceutics, Ashokrao Mane Institute Of Pharmacy, Ambap-416112

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ABSTRACT

The antifungal properties of medicinal plants Vitex negundo, Acacia nilotica, and Hibiscus rosa-sinensis were evaluated for their potential to combat fungal infections. Vitex negundo demonstrated significant antifungal activity against common pathogenic fungi due to its rich phytochemical composition, including flavonoids and alkaloids. Acacia nilotica exhibited notable antifungal effects, particularly against dermatophytes and yeasts, owing to the presence of tannins and saponins. Hibiscus rosa-sinensis showed promising antifungal properties as well, attributed to its anthocyanin and flavonoid content. The results suggest that these plants could serve as potential sources of natural antifungal agents, offering a sustainable alternative to synthetic antifungal drugs. Further studies are required to isolate the active compounds and evaluate their mechanisms of action.

INTRODUCTION

Aspergillosis, dermatophytosis, systemic mycoses, and candidiasis are among the fungal infections that have become a serious global health concern. The use of broad-spectrum antibiotics, immune-suppression, and an increase in the number of people with weakened immune systems have all contributed to the growth in the prevalence of fungal infections.[1] As a result, the increase in antifungal resistance has high-lighted how urgent it is to identify substitute and efficient treatment approaches. For millennia, traditional

medicine has employed medicinal plants to treat a variety of illnesses, including fungal infections. Research are interested in investigating these plants' potential as natural antifungal medicines because of the wide variety of bioactive chemicals they contain.[2] In order to shed light on the mechanisms of action and possible clinical applications of medicinal plants' antifungal activities, this thorough study attempts to compile and evaluate the most recent scientific data[3]. Humans and the microorganisms around them coexist peacefully, but when an immune system is

***Corresponding Author:** Vaibhav Paymal

Address: Department Of Pharmaceutics, Ashokrao Mane Institute Of Pharmacy, Ambap-416112.

Email ✉: vaibhavpaymal8may@gmail.com

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compromised or the pathogen concentration reaches an unusually high density, an infection may arise from the microorganisms; on the other hand, infectious disease refers to a condition in which the infecting agents do cause the body to react, resulting in signs and symptoms that are clinically manifest. In various diseases can arise from a variety of sources, including bacteria, viruses, parasites, fungus, prions, worms, and helminths. A few decades ago, the most dreaded infection was one brought on by bacteria. However, as patient management techniques for bacterial infections advanced, fungi emerged as the most dangerous pathogens.[4] A main or secondary infection brought on by the *Candida* species is called candidiasis.[5] The mouth, throat, skin, vagina, fingers, nails, trachea, lung, or gastro-intestinal system may be the only areas where an infection occurs. *Candida* species can induce invasive candidiasis (IC), which includes deep-seated tissue infections and blood-derived infections (candidemia), when there is significant immune system impairment.[6–7] Over the past three decades, antimicrobial agent resistance has grown to be a global issue. Every year, Almost 2 million Americans contract bacterial and fungal infections; of these, 65% of patients are drug-resistant. [8–9] Around 3,000,000, 250,000, 700,000, and 223, 100 cases of invasive aspergillosis, invasive candidiasis, and cryptococcal meningitis are among AIDS patients have been reported globally in recent estimates.[10]

METHOD

A thorough search of the literature was carried out utilizing reliable academic data bases such as Web of Science, PubMed, and Scopus. Among the search terms were "antifungal," "phytochemicals," "medicinal plants," and "mechanism of action." To guarantee the inclusion of current knowledge, only peer-reviewed publications released between 2010 and 2023 were taken into consideration.

Investigating medicinal plants' antifungal effectiveness against different fungal infections was the main goal of the chosen studies. To evaluate the reliability of the results, the study's methods—such as animal models, time-kill assays, and minimum inhibitory concentration (MIC) assays—were also looked at.

Medicinal Plant And Their Antifungal Properties

A medicinal plant in this review has a detailed description that includes information on its constituents (Table 1) and antifungal qualities.

Vitex Negundo (Nirgundi)

Growing to as small tree, *Vitex negundo* Linn. Belonging to family Verbenaceae is a fragrant, woody shrub. It typically has quadrangular branches with tri- or penta-foliate leaves, which give birth to bluish-purple flowers in branched to cymes. It is found in wastelands, mixed open forests, Afghanistan, India, Pakistan, Sri Lanka, Thailand, Malaysia, eastern Africa, and Madagascar. It grows best in humid environments or beside water channels. Certain regions of Asia, Europe, North America, and the West Indies cultivate it for commercial purposes.[11]

Synonym of plant in Sanskrit: Indrani, Nilanigundi, Nila Pushpa, Nirgundi, Nirgundika, Renuka, Sephalika, Shephali, Shvetasurasa, Sindhooka, Sindhuvaran. In Hindi: Mewri, Nengar, Ningori, Nirgandi, Nirgunda, Nisinda, Panikisambhalu, Sambhal, Sambhalu, Nirgundi, Shimalu. Urdu: Sambhalu, Tukhmsambhalu. Bengali Nisinda, Sinduari, Beguna, Nishinda, Nishinde. In Kannada: Bile-nekki, Bilenekki, Karilakki, Lakkagida, Lakki, Lakkigida, Lakkili. In Malayalam: Bem-nosi, Indrani, Karunocci, Noch-chi, Nochi, Vella-noch-chi. In Marathi: Nirgunda, Nengar, Nirgur, Lingur, Nirguda, Nirgundi, Limgud, Negumd. In Oriya: Thingkhawilupa, Niligundi. In Tamil: Nallanocci, Nirkkundi, Nirkundi, Nochi, Sinduvaram, Tiriburamerittan. In Telugu: Nalla-vavili,



Nallavavili, Sindhuvaruma, Sinduvaramu, Tellavavili.[12] The subkingdom is Tracheobionta–Vascular plants, the Super division is Spermatophyte–Seed plants, the Division is Magnoliophyta–Flowering plants, the Class is Magnoliopsida – Dicotyledons, the Subclass is Asteridae, the Order is Lamiales, the Family is Verbenaceae – Verbena. The Genus is *Vitex* Linn and the Species Is *Panjghust* (*vitexnegundo*) Linn.[13] The Botanical description of *Vitex negundo* is a deciduous shrub that grows to a small tree and is scented and woody. Monk's pepper or the five-leafed chaste tree are other names for *Vitex negundo*. Its most remarkable characteristic is a group of five palm-like, pointy leaves. The tree is tall, 2–5 m, slender, and has branchlets that are quadrangular in shape. Five leaflets, lanceolate, sharp, glabrous, 4–10 cm long, hairy underneath, and pointy at both ends, are palmately arranged in the leaves. The petioles of the lateral leaflets are small, while those of the terminal leaflet are long. The up to 30-cm-long axillary or terminal panicle has bluish-purple flowers. When ripe, the fruit is a succulent, globose black fruit with four spherical, 4 mm-diameter seeds.[14] The effect of *vitex negundo* inn. In different pathogen and pests is as follows they act as antibacterial activity and their action against bacteria: *Escherichia coli*, *Proteus vulgarism*, *Klebsiella aero genes*, and *Pseudomonas aero genes*. They act as anti-feedant activity and their action against *Achoeajanata* (Castor semi-looper), and *Spodopteralitura* (Asian army-worm). They act as anti-filarial activity and they act against *Brugiamalayi*, a parasitic micro filarial. They most commonly used as anti-fungal activity and they act against *Curvular alunata* and *Alteernaria alternate candida albicans*, *Aspergillus Niger*, *Cryptococcus neoformans*, and *Trichophyton entagrophytes*. They act as Insecticidal activity and their action is pulse beetle, *Callosobruchus macularatus*. The potato-tuber

moth, *Phthorimaea operculella* *Sitotrogacerealella* (Grain moth of Angoumois) *Aphis gossypii* (the cotton melons aphid), *Aphis citricola* (the spirite aphid) and *Myzus persicae* (the green peach aphid). Then they act as Larvicidal activity and they act against *Anopheles subpictus*, *Culex quinquefasciatus*, *Culex tritaeniorhynchus* and *Anopheles stephensi* are the mosquito species. The diamond-back moth, *Plutella xylostella*. *Plasmodium falciparum*, *Cnaphalocrocis medinalis* (rice leaf folder), then they show the activity of Mosquito repellent and they act against *Culex tritaeniorhynchus*, *Aedes aegypti* (Mosquito)[15]

Photo of *vitex negundo* leaves.



Figure 1 . vitex negundo leaves.

Extraction process of *vitex negundo* leaves is the leaves were divided, thoroughly cleaned to get rid of any unnecessary material, dried in the shade, and then blended into a powder. Each leaf material weighed around 25 g, and it was extracted using methanol in a Soxhlet device. The ethanol extracts were dried in a desiccator, concentrated in a vacuum at low pressure, and filtered through Whatman No.1.[16] The phytochemical found in *vitex negundo* is alkaloids, flavonoids, terpenoids, tannins, saponins, glycosides, and sterols—the extracts of *Vnn* and *Vnp* were screened phytochemically.[17] and the chemical constituent was found to be Hexamethyl-3,6,7,3',4'-pentamethoxy flavone from leaves [18] Two types

of mussaenosidic acid, 6'-p-hydroxy benzoyl and 2'-p-hydroxy benzoyl. [19–20]

β -caryophyllene, sabinene, 4-terpineol, gamma-terpinene, caryophyllene oxide, 5, 3'-dihydroxy-7,8,4'-trimethoxyflavanone; 5,3'-dihydroxy-6,7,4'-trimethoxy flavanone.[21] viridiflorol; 1-octen-3-ol; globulol.[22] ursolic acid [2 β -hydroxyurs-12-en-28-oic acid]; betulinic acid [3 β -hydroxy lup-20-(29)-en-28-oic acid] n-hentriacontanol; β -sitosterol; p-hydroxybenzoic acid.[23] protocatechuic acid; oleanolic acid; flavonoids.[24] angusid; casticin; vitamin-C; nishindine; gluco-nonitol; p-hydroxy benzoic acid; sitosterol.[25]

The active chemical constituent present in *Vitex negundo*, commonly known as five-leaved chaste tree, contains several active compounds that exhibit antifungal properties. One of the key constituents is “caryophyllene”, as sesquiterpene known for its antifungal activity. Additionally, other compounds like flavonoids and essential oils in *Vitex negundo* may also contribute to its antifungal effects. These compounds work together to provide a range of medicinal properties, including antifungal activity.[26]

Acacia Nilotica (Babul)

Plants have great significance due to their nutritive value and are also a major source of medicines. Plants have served mankind through-out the history of human civilization.[27] *Acacia nilotica* also known as gum Arabic, Egyptian thorn in Egypt, scented tree in English, thorn in mimosa in Australia and commonly known as “Bagaruwa” among the Hausas, is a species of *Vachellia* and a genus of *Acacia*. It is a thorny *Acacia* found in different parts of the world (West Asia, Africa, Eastwards India, Australia).[28] *Acacia nilotica* L. (gum arabic, babul, Egyptian thorn, thorn mimosa or scented thorn in South Africa) is a species of *Acacia* native to Africa and the Indian subcontinent. The ethanolic extract of *Acacia*

nilotica (L.) stem exhibit remarkable hypoglycemic activity. Screening of the different organs of *Acacia nilotica* (L.) revealed the presence of tannins, saponins, coumarins, carbohydrates and/or glycosides, unsatd. Sterol, triterpenes, alkaloids and nitrogenous bases, flavonoids and cyanogenic compounds.[29] The herb *Acacia Nilotica* is commonly utilized in traditional medicine. Nearly every part of them, including the root, bark, leaves, flowers, gums, and pods, is utilized in medicine.[30] This herb possesses antibacterial, anti-plasmodial, anticancer, antimutagenic, and antioxidant properties. It is used to treat piles, hepatitis C virus, burns, scalds, and cough, sore throat, diarrhea, dysentery, and tuberculosis.[31]

Theyonyms is *Acacia arabica* (Lam.) Willd. *Mimosa arabica* Lam. *Mimosa nilotica* Linn. English Name is Babul, Black Babul, Indian, Gum arabic tree. Ayurvedic name is Babbuula, Babbuuri, Baavari, Aabhaa, Shuulikaa, Shitaka, Kinkiraata, Yugmakantaka, Sukshmapatra, Pitapushpaka. The unani is Aqaaqia, Babuul, Kikar, Mughilaan, Samur. The siddha / tamil is Karu-velamaram, Karuvelei. Velampisin (gum). [32] The taxonomical classification is as follows the subkingdom is tracheoionta, the super division is spermatophyta, the division is magnoliophyta, the classis magnoliopsida, the sub class is rosidae, the order is fabales, the family is fabaceae, the genus is *acacia* and the species is *nilotica*. [33]

The phytochemical present in the leaves through phytochemical screening of ethanolic extracts, tannins, alkaloids, and sterols were found in *Acacia nilotica* leaves; glycosides, saponins, resins, and flavonoids were not found. Additionally, alkaloids, saponins, cardiac glycosides, tannins, and flavonoids were shown by Mrityunjay Das et al.[34] Tannins: These poly phenolic substances are well known for having antibacterial and antioxidant qualities.[35]





Figure 2. Acacia nilotica leaves.

Indetail discription of leaves are bipinnate, pinnate 3-10 pairs, 1.3- 3.8 cm long, leaflets 10-20 pairs, and 2-5mm long [36] Chemical constituent present in leaf it has 12.4% crude protein, rutin, 6-8-bis-Dglucoside, and 8% digesting protein.[37] A nilotica could be a potential source of antimicrobial agents since lot of chemical compounds and extracts have been assessed for antimicrobial activity and noteworthy results have been found.[38] Bioactive cassane diterpene, niloticane showed inhibitory activity against both gram- positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*, MIC values of 4 $\mu\text{g/mL}$ and 8 $\mu\text{g/mL}$ respectively) as well as gram-negative bacteria (*Klebsiella pneumoniae* and *Escherichia coli*, MIC values obtained were 16 $\mu\text{g/mL}$ and 33 $\mu\text{g/mL}$, respectively), isolated from ethyl acetate stem bark extract of *A. nilotica* subsp. *Kraussiana*. [39]

Medicinal use of all part of acacia nilotica plant is the root are used against cancers and/or tumors (of ear, eye, or testicles), tuberculosis and indurations of liver and spleen.[40] The leaf is chemopreventive, antimutagenic, anti bacterial, anticancer, astringent, anti microbial activity Tender leaves are used to treat diarrhea, Aphrodisiac, dressing of ulcers, anti-inflammatory and Alzheimer's diseases.[41] The gum are astringent, emollient, liver tonic, antipyretic and antiasthmatic.[42] The stem bark are anti bacterial, antioxidant, antimutagenic, cytotoxic bark is used as astringent, acid cooling, styptic, emollient, and the linctus,

aphrodisiac, diuretic, expectorant, emetic, nutritive, in hemorrhage, wound ulcers, leprosy, leucoderma, small pox, skin diseases, biliousness, burning sensation, toothache, leucoderma, dysentery and seminal weakness. The trunk bark is used for cold, bronchitis, diarrhoea, dysentery, biliousness, bleeding piles and leucoderma.[43] The seed is Spasmogenic activity and antiparasitic activity.[44] and the pods are act as anti hypertensive and antispasmodic, anti-diarrhoeal, astringent, anti-fertility and against HIV-1 PR, Inhibited HIV-1 induced cytopathogenicity, antiplatelet aggregatory activity and antioxidant.[45] Antifungal and antiviral activity of *Acacia nilotica* species can be regarded as promising resources for antibacterial drugs due to its highly active nature. Have showed antifungal activity of methanolic extracts and aqueous extract of *Acacia nilotica* with percentage inhibition ranging from 34.27 ± 1.45 to 93.35 ± 1.99 (14,15). Dried fruits of *Acacia nilotica* are active against *C. albicans* and used to treat oral candidiasis. Methanolic extract of the plant is active against two animal viruses: New castle Disease and Fowl pox Viruses.[46] Active chemical constituent act against fungal infection is Tannins these polyphenolic compounds can inhibit fungal growth and disrupt cell walls.[48] Flavonoid these compounds such as quercetin and kaempferol have demonstrated antifungal properties against various fungi.[49] Saponins these can disrupt fungal cell membranes, leading

to cell lysis. Alkaloids they some alkaloids found in the plant may exhibit antifungal effects.[50] The essential oils is compounds like eugenol may also contribute to antifungal activity.[51] Pharmacological use of acacia nilotica are high antibacterial activity against *Staphylococcus aureus*, *Escherichiacoli*, *Proteusvulgaris*, *Proteusmirabilis*, *SalmonellaparatyphiB*, *Klebsiellapneumoniad* etected by D eshpande SN.[47]

Hibiscus Rosa-Sinesis

Hibiscus rosa-sinensis is a flowering plant that belongs to the Malvaceae family, also known as the "mallows," which is valued for its medicinal properties and herbal tea. It is a showy, evergreen, woody shrub that reaches a height of approximately 5 to 8 feet and is smooth in texture. It is widely grown as an ornamental plant in tropical settings, both at home and in public spaces. For medicinal trust, the red-flowered type is more favored.[52-53] Many nations, including Egypt, China, Ethiopia, Syria, Southern Iraq, and central and western Sudan, farm the plant extensively. They flourish in pleasantly warm conditions that witness the herbal plant's broad proliferation in the southern Mediterranean and the tropics, including the horn of Africa. Additional research has demonstrated the several health advantages of *Hibiscus rosa-sinensis*. For instance, drinking hibiscus tea reduces high blood pressure, speeds up blood circulation (which lowers blood pressure in a group of individuals who are pre-hypertensive and mildly hypertensive), and fortifies the heart.[54] One of the most exquisite shrub stop lantin tropical and sub tropical gardens is the hibiscus. It is refer red to by the colloquial names Rudrapushpa, Sthalpaddo, Bettada Taware, and Dasala. It is also known as the Queen of Tropics. Commonly known as Chinese hibiscus, Rose of China, Hawaiian hibiscus, Blacking plant, or Shoe flower, it is a flowering plant that grows in hot, temperate climates. The world's leading hub

for hibiscus cultivation is Florida. Through successful breeding efforts, the American Hibiscus Society contributes to the evolution of valuable innovations.[55] Simple oblong or ovate-lanceolate leaves with coarse teeth at the tip are present. Flowers are composed of five red petals and have pedicels. The young leaves are said to have medicinal properties and are frequently eaten as a vegetable in the Nigerian state of AkwaIbom. Because *Hibiscus rosa-sinensis* has special chemical components that are biologically active, it has had a significant impact on human health [56]. More than half of all clinical drugs used today have natural product origins. Hibiscus has long been used as an analgesic, anti-inflammatory, anti-tumor, anti-asthmatic, anti- pyretic, and anti-convulsant.[57] The Synonyms of *hibiscus rosa-sinesis* is *Hibiscus arnottii* Griff. ex Mast.; *Hibiscus boryanus* DC.; *Hibiscus cooperiauct.*; *Hibiscus festalis*Salisb., *Hibiscus liliiflorus* Griff. exMast., *Hibiscus rosiflorus* Stokes and *Hibiscus storcki* iSeem.[58] The subkingdom is Tracheobionta, the Super divisionis Spermatophyta, the Division is Magnoliophyta, the Class is Magnoliopsida, the Subclass is Dilleniidae, the Order is Malvales, the Family is Malvaceae the Genus is *Hibiscus* and the Species is *Hibiscus rosa-sinensis*. [59] The botanical description is *Hibiscus rosa-sinensis* is an evergreen, woody, glabrous, showy shrub that grows to a height of 5-8 feet, according to S. Verma. The leaves are lanceolate or ovate, short petiolated, bright green, and about acuminate. They are also subulate, glabrous, and have a few tiny stellate hair son the nerves behind the stipules. The leaves are also irregularly and coarse lyser rated towards the top, entire toward the base, and glabrous on both sides. Pedicels are united above the middle, axillary, solitary, and longer than the leaves. Large, solitary, axillary, bisexual flowers with five petals form a bell shape. The pistil is red, and orange stamens protrude from the center of the



flower. In the original types, the blossoms are usually crimson but usually smell nothing. In addition, a wide selection of colors— including white, yellow, orange, red, pink, purple, and soon—are offered in single, double, or multiple tones.[60] Phytochemical constituent of hibiscusrosa-sinesesis as follows Research on Hibiscus rosa sinensis is extensive. According to the report, it includes total phenols, total proanthocyanidin, total flavonoids, tannins, steroids, alkaloids, and saponins. Additionally, it has been observed to include primarily quercetin3,7- diglucoside, quercetin-3- diglucoside, anthocyanins and flavonoids, and cynidin-3- sophoroside-5-glucoside. In addition,

additional substances such as quercetin, hentriacontane, cyaniding chloride, cyclopeptide alkaloid, and vitamins (thiamine and ascorbic acid) are found. Sterols, sugars, glycosides, tannins, triterpenoids, saponins, mucilage, and flavonoids are all present in the root so fH.sinensis. Cyaniding diglucoside, flavonoids, vitamins, thiamine, riboflavin, niacin, and scorbic acid are all present in hibiscus flowers. H.rosasinensis extract is a source of numerous potentially beneficial antioxidant sand anticancer elements such as quercetin, glycosides, riboflavin, niacin, carotene, malvalic acid gentisic acid, margaric acid and lauric acid[61]

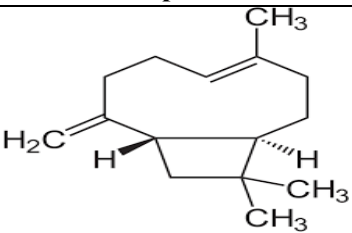
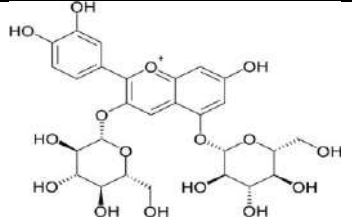
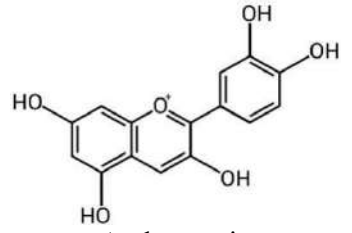
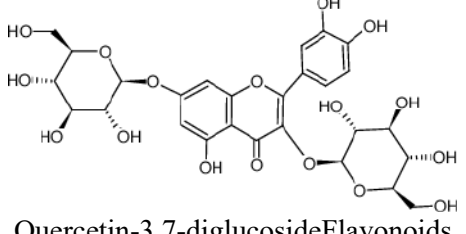
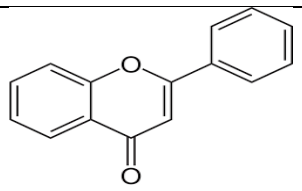
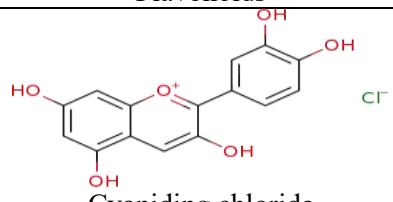


figure 3. hibiscus rosa-sinensis leaves

Extraction process of hibiscus rosa-sinensis is anthocyanin extraction process involved the use of various extraction techniques and solvents. Citric acid, ethanol, and water were among the solvents employed. Conventional extraction, microwave-assisted extraction, and ultra sound-assisted extraction are the three extraction techniques. There are three replications for each of the nine therapiesthat make up the treatment. The study employed a completely randomized statistical design for its execution. The data obtained were

evaluated statistically.[62] Antifungal activity of leaves is flavonoids by rupturing fungal cell membranes and preventing fungal growth, substances such as quercetin and kaempferol show antifungal effects. Tannins are those substances have the ability to impede the development of fungi by attaching to proteins and disrupting their metabolic processes and the phenol acids conten research has shown that certain phenolic compounds have antifungal properties against arrange of infections.[63]

TABLE 1: Plants and their chemical components with corresponding mechanism of action:

Plant	Chemical components principle bioactive compound	Mehanism of action	Reference
Vitex negundo	 Caryophyllene	Inhibition of cell wall formation	[24]
Hibiscus rosa- sinesis	 Cyanidin 3,5-diglucoside Anthocyanin	Cell Membrane Disruption	[61]
Hibiscus rosa- sinesis	 Anthocyanin	Inhibition of Enzyme Activity	[61]
Hibiscus rosa- sinesis	 Quercetin-3,7-diglucoside Flavonoids	Inhibition of DNA/RNA or protein synthesis	[61]
Hibiscus rosa- sinesis	 Flavonoids	Plasma membrn disputation	[61]
Hibiscus rosa- sinesis	 Cyaniding chloride	Mytocondriyal dysfunction	[61]

CONCLUSION:

Bioactive substances with strong antifungal effects are abundant in medicinal plants. They are excellent candidates because of their many modes

of action. fighting off a variety of fungal diseases. Using the potential of these natural cures gives new hope in the search for sustainable and efficient antifungal therapies, as the prevalence of



antifungal resistance keeps increasing. New antifungal drugs made from medicinal plants may be developed as a result of combining traditional herbal knowledge with contemporary scientific study.

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