

Herbal Innovations in Candidiasis Management: A Comprehensive Review of Aloe Vera and Betel Leaf Extract Based Antifungal Gel

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Abstract

Candidiasis is the most prevalent fungal infection in people, and it is caused by *C. albicans*, both primary and secondary. Herbal medications are still the backbone of around 75-80% of the world's population, primarily in poor countries, for basic health care due to superior cultural acceptance, compatibility with the human body, and less adverse effects. Herbal medicines are made from plants or plant parts and are used to cure injuries, diseases, and illnesses, as well as to promote health and healing. Plant-based medicinal products have a vital part in the healthcare of the remaining 20% of the population, who primarily live in developed nations. Aloe vera (Sanskrit Ghritakumari, Kumara; Hindi-Guarpatha, Ghikanvar) is a herb often known as the "medicinal plant" due to its numerous therapeutic characteristics. Aloe vera, botanically known as *Aloe barbadensis* Miller, is a member of the lily family. Aloe products are quite popular on the market and are extensively utilized in the skin care, cosmetics, medical, healthcare, and food industries. We are now employing piper betel leaf, commonly known as betel leaf (khaupan). Ayurvedic medicine from ancient India cites various medicinal advantages, including its antifungal properties. Candidiasis is the most prevalent fungal infection in people, and it is caused by *C. albicans*, both primary and secondary. "Abstract" is a necessary section in a research paper. It may be constructed by gathering main points (summary) from each section of the research paper.

Keywords: Aloe vera, Betel leaves, *Candida albicans*, antifungal activity, antibacterial, medicinal plants.

Introduction

The word "gel" as a categorization developed in the late 1800s, when scientists sought to describe semisolid substances based on their phenomenological features rather than their chemical makeup. At the time, analytical tools for determining chemical structures were insufficient. Compared to other drug administration techniques, the topical/transdermal (TT) route has various benefits, including increased patient compliance, consistent drug delivery, fewer side effects, and avoidance of the hepatic first pass effect.[1] Drugs for topical application are intended to be applied outside. Sunscreen, keratolytic agents, local anaesthetics, antiseptics, and anti-inflammatory drugs are examples of products with a localized action on one or more layers of the skin. Although some of the medicine in these topical formulations

may reach the circulation unintentionally, it is often at subtherapeutic dosages and has no notable negative effects, with the possible exception of pregnant or nursing patients.[2]

Transdermal drug delivery system (TDDS) denotes TDDS. It is sometimes referred to as patches. The first transdermal patches were authorized by the FDA in 1981. This approach is becoming more common and convenient for administering drugs to patients, as well as increasing therapeutic advantages to patients. External application of gel at skin gives some evident advantages such as fast release of medicine straight to the site of action, irrespective of the drug's water solubility, as opposed to lotions and ointments.[3] Gels, also known as jellies, are semisolid substances that comprise either big organic molecules interpenetrated by a liquid or suspensions made of minute inorganic particles, according to USP. There is reversibility between the gel and sol states in many polymer gels. On the other hand, because certain polymer gels' chains are covalently connected, their production cannot be reversed.[4]

The kingdoms of fungi, plants, animals, protests, and bacteria are distinct from one another. The primary distinction that sets fungi apart from other kingdoms is the presence of chitin in their cell walls, which is absent from those of other species. In the environment, fungi are present everywhere. Some of them are helpful; for instance, they are found in foods like baker's yeast and mushrooms, and they play significant roles in medicine. Most occurrences of localized fungal infections end with the issue going away once the bacteria start multiplying again.[5] Usually affecting the skin, nails, vagina, mouth, or sinuses, localized fungal infections A significant intestinal urgency, the use of catheters, neonatal intensive care, or liver transplantation are among the risk factors for the fourth most frequent inpatient acquired bloodstream infection, which is candidiasis infection. Although more than a dozen species of *Candida* can cause illness, *Candida albicans* is the most common in practically all patient populations and disease presentations. This study will concentrate on *Candida albicans*, which initially develops as a benign organism but has the potential to turn pathogenic, penetrating the mucosa and causing serious injury.[6]

CANDIDIASIS

Candidiasis is brought on by fungus. The genus *Candida* has about 200 different species, although very few of them are dangerous and can cause more serious infections that can be either internal (if they penetrate the body) or external (if they are outside the body). The highly significant infections, known as *Candida albicans*, are ubiquitous and mostly coexist with an abundance of bacteria in the mouth, gastrointestinal system, and vagina. The microorganisms already present in the body and the immune system keep a close eye on candida; any disruption to either can lead to an infection from candida. These infections are mostly limited to the mouth, genital region, and skin, although they can affect anyone suffering from any major illness, such as HIV or cancer.[5]

HISTORY

In 1849, Wilkinson was the first to describe candidiasis. Haussmann subsequently demonstrated in 1875 that both oral and vaginal candidiasis are essentially caused by the same bacterium. Antibiotic development led to a progressive rise in the prevalence of candidiasis. In 1923, Christine Marie Burkhout provided the explanation of the *Albicans* species in her thesis at the University of Utrecht. As numerous new species were found throughout time, the genus *Candida* began to be classified. There are currently more than 200 species, with *albicans* being the most significant source of infections in humans. Among the other pathogenic species are *Krusei*, *Parapsilosis*, *Dubliniensis*, and *Lusitaniae*. The Latin words *albicare*, meaning "to whiten," and *candida* are the sources of the English term *albican*. is derived

from Latin word 'Toga.[4]

MODIFIED NAME OF CANDIDA SPECIES CAUSES CANDIDIASIS

Oral Candidiasis

Acute mucocutaneous candidiasis includes oral candidiasis. There are several types of oral candidal disorders, including hyperplastic candidiasis, erythematous, pseudomembranous, and HIV-associated candidiasis. Esophageal candidiasis develops from oral candidiasis in HIV individuals.

Pseudomembranous candidiasis

It usually affects those with weakened immune systems, the elderly, diabetics, HIV/AIDS patients, and those who have used antibiotics and steroids for an extended period of time. Most people refer to it as a "thrush." Thrush is asymptomatic and manifests as white, wipeable plaques that resemble coagulated milk. The tongue, buccal mucosa, and oral mucosa all have plaques. Newborns are most likely to be affected. About 35 percent of cases of candidiasis fit this description.[1]

Erythematous candidiasis

Oral mucosal erythema is a localized sign of erythematous candidiasis, which may or may not exhibit symptoms. When it manifests itself with symptoms like burning in the mouth due to a loss of filiform papillae on the tongue's dorsum. Similar symptoms are observed in the palate and dorsal tongue, with less of an effect on the buccal mucosa. The term "antibiotic sore mouth" refers to the kind of erythematous candidiasis caused by extended use of broad-spectrum antibiotics.⁽⁶⁾ Acute erythematous and chronic erythematous are the two types. Antibiotic-induced sore mouth syndrome is typically associated with acute erythematous candidiasis. In those who wear dentures, chronic erythematous candidiasis can develop.[1]

Hyperplastic candidiasis

Another name for it is "candidal leukoplakia." It has a white plaque-like appearance and affects the anterior buccal mucosa.

Denture stomatitis

The term "chronic atrophic candidiasis" is another name for it. If there are no symptoms, such as a burning feeling or slight pain, it is asymptomatic. The fitting surface of the dental replacement is where the erythema is located. The cause of this candidiasis is improperly fitted dental implants and inadequate oral and dental implant hygiene maintenance.

Epidemiological aspects

If a patient has diabetes, cancer, cirrhosis, malnourishment, AIDS, or has been on steroids, antibiotics, or other immunosuppressive drugs for an extended period of time, they may also have oral candidiasis, which is included under superficial candidiasis. The species that is responsible for esophageal candidiasis is *C. albicans*. Newborns' immature defense systems against infections and the deterioration of defense mechanisms in old patients are the main reasons why pediatric patients are harmed, according to a recent study. 1.4 million people in the US suffer with candidiasis each year.[4]

Types Of Candidiasis

Candidiasis is mostly of following different types.

Thrush

Thrush is the name given to a condition when white patches appear on the inside of the mouth, above the tongue, and around the lips. The surface is often red and inflamed beneath the white patch. It's possible for the lip's edge to burst, revealing a red, wet spot that might hurt a little.

Cutaneous Candidiasis

Cutaneous candidiasis is an infection of the skin that occurs in places of the skin with very little ventilation and very little moisture. These most frequently include the diaper region, hands that are frequently covered in rubber gloves, the area around the crotch, the cleavage of large breasts, and the base of fingernails. The skin becomes red in areas that are wet.[4,5]

Vaginal Candidiasis

In essence, this virus cannot be spread through sexual activity. Females are more susceptible to vaginal candidiasis and will most likely experience at least one episode in their lives. A history of pregnancy or diabetes increases their susceptibility to vaginal infections. It can itch and hurt the vagina, look like a thick cheese discharge, burn the area around the vagina, and irritate the vagina during sexual activity. Profound Candidiasis Deep Candidiasis is the term for when fungi infiltrate the body, get into the bloodstream, and spread throughout the entire body. It usually affects those with very compromised immune systems, such as cancer patients or HIV patients, and can result in extremely dangerous infections. The symptoms might range from a high temperature to acute organ failure.[4]

Morphology

Pseudohyphae, hyphae, and yeast are the three morphologies of *Candida albicans*, a human fungal infection. When colonies flip, new morphological forms emerge. For instance, cells in the opaque phase become oblong rather than oval like those in the yeast phase. Due to the fact that both pseudohyphae and hyphae are elongated forms of the fungus, attempts have occasionally been made to discern between the two. Although there is currently no scientific evidence, the capacity to switch between the hyphae, yeast, and pseudohyphal morphologies is frequently considered to be crucial for virulence. Agar substratum is invaded by hyphae and pseudohyphae, both of which are invasive when they develop in a lab. One can undergo a morphological transition from yeast to filamentous forms under a variety of environmental situations. Even though regulatory gene expression may be involved, the switching is spontaneous and reversible.[6]

CANDIDA ALBICANS:

Taxonomy: In 1839, Langenbeck made the discovery of *Candida albicans*.

Table 1 : Taxonomy of *Candida albicans*

Superkingdom	Eukaryote
Species	albicans
genus	Candida
Family	Debaryomycetaceae
Order	Saccharomycetales
Subclass	Saccharomycetidae
Kingdom	Fungi
Phylum	Ascomycota
Subphylum	Saccharomycotina
Class	Saccharomycetes

Yeast physiology

Yeast is a common organism found in the human body's digestive environment and seldom causes issues. These colonies might have wrinkles or be smooth. The same species of candida can transition between the stages as a means of adaptability. An additional strain of candida that exhibits shape-shifting may form seven distinct kinds of colonies. This reversible conversion capacity is passed down from one generation to the next. Because its nucleus contains two copies of the chromosomes to create two distinct cells, Candida hyphae reproduce sexually.[6]



Figure 1 : C. Albicans

Signs and symptoms

1. White areas on the mouth, cheeks, and throat.
2. Redness in mouth .
3. Loss of taste sensation .
4. Dryness of mouth.

Epidemiological aspects

here are 1.5 instances of candidemia-affected patients in the United States annually. The United States recorded a 49% fatality rate from candidemia between 1997 and 2001 . Over 2,50,000 people are affected with invasive candidiasis, and 50,000 people die from it annually. Although *C. glabrata* was a more common bacterium in Northern Europe, *Candida albicans* is the most common microorganism that causes invasive candidiasis. In parts of Southern Europe, Asia, and South America, *C. parapsilosis* was predominant. Because *Candida* has varying degrees of virulence, the fatality rates were higher.[1]

Symptoms

1. Fever
2. Chillness
3. Should the infection extend to the brain, eyes, joints, bones, heart, and brain.⁽⁴⁾

Risk factors

1. Long-term ICU staying
2. Prolonged utilization of glucocorticoids
3. Abdominal medical procedure
4. Central venous catheter
5. Immunosuppressive disease
6. Solid-organ tumors
7. Hemodialysis
8. Neonates

Treatment

There are two objectives to treat candidiasis.

1. Put an end to Candida's bodily proliferation
2. Diminish the elements that promote the growth of the Candida species, such as an ideal habitat

A dosage will be selected based on the patient's age and immunological state. Certain invasive infections of the heart, brain, joints, or bones require ongoing care.

Antifungal medications are used such as,

1. Amphotericin-B
2. Fluconazole
3. Caspofungin
4. Voriconazole
5. Mainly, "Amphotericin-B is used for "non-neurogenic patients".[1]

Genital Candidiasis

VVC is the most common kind of vaginal yeast infection. Roughly 75% of women will at some point in their lives be able to cause VVC, 40–50% of women will cause further bouts of infection, 20–50% of women will remain asymptomatic, and 5% will recur. Moreover, it was producing a fluctuating degree of irritation along with a white, copious, and flocculent discharge. Although it does not pose a threat to life, it is uncomfortable, dangerous, and frequently occurs in pregnant women, especially in the final trimester. At that moment, there is a change in progesterone, estradiol, and glycogen, which has been linked to an increase in vaginal PH and is conducive to the onset of these infections. In addition to the unusual consideration shown in this case due to the anticipated occurrence of the baby becoming contaminated in the uterus, it has also been shown that vaginal candidiasis is more prevalent in individuals with diabetes. Patients underwent a wide range of antibiotic therapies, including the use of oral contraceptives, to treat bacterial infections. Additionally, there are significant variables linked to increased VVC incidence rates. The main risk factors for this type of infection include diabetes, antibiotic use, and a sexual partner's vaginal secretions.[1]

Objectives

The study's objectives were to stop vulvovaginal irritation in its tracks and to provide immediate, total relief from its symptoms.

Treatment options

Topical medications, such as azoles

(all used for a duration of one to seven days based on risk classification):

1. OTC miconazole.
2. OTC butoconazole
3. OTC clotrimazole

Mechanism of Action of Anti-candida natural Products:

Plant-based natural compounds have been shown to have anti-Candida modes of action that can affect germination, biofilm development and inhibition, cell metabolism, cell wall integrity, and membrane flexibility.[15]

DRUG PROFILE:

For millennia, aloe vera has been utilized medicinally in a number of countries, including Greece, Egypt, India, Mexico, Japan, and China. Nefertiti and Cleopatra, the queens of Egypt, included it into their daily

beauty regimens. It was used to cure soldiers' wounds by Christopher Columbus and Alexander the Great. John Goodyew translated Dioscorides' medical work *De Materia Medica* in A.D. 1655, which is when aloe vera was first mentioned in English. Aloe vera was being used as a laxative in the United States by the early 1800s, but its effective application to the treatment of severe and chronic radiation dermatitis in the mid-1930s marked a paradigm shift in the field.[5]

Plant description:

The plant features fruits that are filled with many seeds, yellow tubular blooms, and triangular, fleshy leaves with serrated edges. Every leaf has three layers to it.

1. An interior transparent gel composed of glucomannans, amino acids, lipids, sterols, and vitamins, with the remaining 99% being water.
2. The sour yellow sap, or middle layer of latex, which includes glycosides and anthraquinones.
3. The rind, a thick outer layer made up of 15–20 cells, is protective and is used to synthesise proteins and carbohydrates. Vascular bundles found inside the rind are in charge of moving materials like starch (phloem) and water (xylem).[5]

Medicinal species :

More than 300 different varieties of aloe may be found; the majority are indigenous to Madagascar, Arabia, and South Africa. The amounts of the active components vary slightly throughout the species. *A. vulgaris*, *A. arborescens*, *A. ferox* (Cape aloe), *A. perryi* (Socotrine or Zanzibar aloe), and Aloe vera are a few examples of distinct species. Aloe barbadensis miller is the name of the plant in botany. It is a perennial, shrubby or arborescent, xerophytic, succulent, pea-green plant that is a member of the Asphodelaceae (Liliaceae) family.

Name : Aloe vera



Figure. 1 Aloe Vera

Aloe vera is also called Barbados aloe, *A. vulgaris*, *A. arborescens*, *A. ferox* (Cape aloe), and *A. perryi* (Socotrine or Zanzibar aloe). There are around 300 species of aloe, the bulk of which may be found in South Africa, Madagascar, and Arabia. The concentrations of active chemicals differ between species. Aloe vera is scientifically known as *Aloe barbadensis miller*. This plant belongs to the Asphodelaceae (Liliaceae) family and can be either shrubby or arborescent, perennial, xerophytic, succulent, or pea-green in color. The aloe plant has triangular, fleshy leaves that can grow up to 20 inches long and 5 inches wide, with spikes on the edge.[15]

Botanical name : Aloe barbadensis miller

Plant part used : leaves

Family- Asphodelaceae.

Chemical constituents : Aloe vera gel includes water, amino acids, vitamins, lipids, sterols, tannins, and enzymes, as well as phenol, saponin, and anthraquinone components with antiviral, antibacterial, and antifungal effects.

Uses : aloe vera is a medical plant that has antioxidants and antibacterial properties. Aloe vera advantages include lowering dental plaque, hastening wound healing, avoiding wrinkles, and controlling blood sugar. Aloe vera, also known as Aloe barbadensis, is a plant with thick, short stems that retain water in its leaves.

Name : Betel Leaf



Figure. 2 Betel leaf

Piper betle Linn., known locally as "Paan" The dioecious annual creeper Piperaceae climbs to a height of around one meter through a multitude of little, adventitious, rootless climbers. It is often found in warmer, more humid regions of the nation [3, 4]. It is widely distributed in wet woodlands and is spread over India and other Southeast Asian nations, including China and Vietnam. It may be found in Bengal, Orissa, Tamilnadu, Andhra Pradesh, Uttar Pradesh, Bihar, and Karnataka in India. Three types of piper betle leaves—Sirugamani, Karpoori, and Velaikodi—are mostly available in Tamilnadu. The plant is used in several Ayurvedic preparations, including Lokantha Rasa, Puspadhava Rasa, Brhat Sarwajwarahara, Lanha, Laghu Sutaseknara Rasa, and Brhat Visamaj Warantaka Rasa. In addition to being used alone as medication, betel leaf juice is frequently used in Ayurveda as an adjuvant and coupled with various other medicines, perhaps for greater results.[8]

Botanical Name : Piper Betle L.

Plant part used : Leaves

Family – Piperaceae

Chemical Constituents: Piperol-A, Piperol-B, and methyl piper betlol have all been identified as being present in the Piper betle leaf and have also been separated [9]. The betle leaves include diastases, sugars, starch, and an terpinen-4-ol, safrole, allylpyrocatechol monoacetate, eugenol, eugenyl acetate, hydroxyl chavicol, eugenol, piper betol, and the betle oil contains, among other important ingredients, cadinene carvacrol, allyl catechol, chavicol, p-cymene, caryophyllene, chavibetol, cineole, estragol, etc

Use :

1. A paste made from Piper betle leaves mixed with salt and hot water can be used to treat filariasis.
2. One Piper betle leaf mixed with Piper may help cure obesity.

3. Two months are advised for nigrum.
4. Piper betle juice mixed with honey is useful for treating children's dyspepsia, dyspnea, and coughs.
5. Women who are nursing can apply oil-smearred Piper betle leaves to their breasts to encourage the production of milk.
6. For inflammatory swelling conditions including mastitis, arthritis, and orchitis, a local application is advised.
7. To treat cough and dyspnea in children and the elderly, leaves are combined with mustard oil, warmed, and applied to the chest.[8]

PHARMACOLOGICAL ACTIVITY

Antiulcer activity : The plant's lectin content may be the reason why *A. vera* extract prevents the release of acids. Since lectins have been demonstrated to prevent parietal cells from taking up aminopyrine, the extract's capacity to reduce stomach acid production may be the consequence of its direct interaction with these acid-producing cells. pylorus ligation, acute stress, and HCl-ethanol were used to induce experimental stomach ulcers in rats in order to test the antiulcer properties of the hydroalcoholic extract of Piper betel (HEPB) leaves. All of the models used for research showed a significant increase in stomach pH and a decrease in gastric fluid volume after pretreatment with Piper betel extract, combined with an ulcer-protective effect. Its antiulcer activities are probably attributed to the hydroalcoholic extract of Piper betel leaves.[9]

Antihypercholestermic : The study's findings suggested that the hypoglycemia impact of aloe vera gel extract may be caused by hypoglycemic trace elements including Cr, Zn, and Mn, which increase the action of insulin. Aloe vera gel extract's antioxidant activity may also have contributed to the glucose-lowering impact, since it reduced oxidative damage in the blood of rats given alloxan-induced diabetes.

Antioxidants

The mean IC₅₀ (g/ml) of the ascorbic acid radical DPPH in the betel leaf ethanol extract was determined to be 3.128. The ethanol extract's mean IC₅₀ (g/ml) value was discovered to be 9,362. The DPPH radical was hardly affected at all by the ethanolic extract of Piper betle L. leaves. It has been demonstrated in studies using rabbits as the experimental animals that the ethanol extract of betel leaf (Piper betle) at various concentrations (5%, 10%, and 15%) has an antioxidant effect. After being shaved, the bunnies' backs. One of the key indicators of any disease's pathophysiology is the production of reactive oxygen species, or ROS. As a barrier against reactive oxygen species (ROS), antioxidants help prevent chronic and degenerative illnesses¹³⁰ The primary health issues, such cancer.[9,13]

Anti bacterial/ anti fungal/ anti viral actions

Through its anti-inflammatory properties, aloe vera gel's antibacterial activity promotes the healing of wounds. Aloe gel inhibits two microorganisms, namely *Stomatococcus faecalis* and *Stomatococcus pyogenes*. Six Betel leaf preparations, essential oils, extracts, and isolated chemicals are effective against a variety of Gram-positive and Gram-negative microorganisms. The microorganisms that were studied included multidrug-resistant (MDR) bacteria, which cause serious infectious illnesses in people, as well as foodborne pathogens.[7] Minimum inhibitory concentration (MIC), minimum fungicidal concentration (MFC), and inhibition zones have been obtained from a variety of techniques used to evaluate the antifungal qualities of betel leaves, including solid dilution, broth dilution, micro-dilution, well diffusion, and solid diffusion assays. Recalculating MIC and MFC as well as measuring the MFC/MIC ratio to ascertain fungicidal and fungistatic effects were also carried out, in a manner similar

to that of antibacterial activity. A variety of techniques, such as solid dilution, broth dilution, micro-dilution, well diffusion, and solid diffusion assays, have been used to evaluate the antifungal qualities of betel leaves. The results have produced minimum inhibitory concentrations (MIC), just fungicidal concentrations (MFC), and inhibition zones. In a manner similar to that of antibacterial activity, fungicidal and fungistatic effects were also ascertained by recalculating MIC and MFC and measuring the MFC/MIC ratio.[7]

Anti inflammatory action

An injury triggers inflammation, the body's natural reaction that causes swelling, discomfort, redness, and heat and slows down the healing process. Aloe vera gel's inflammatory properties speed up healing in addition to providing pain and discomfort relief. The effects of acetylated mannan in Aloe gel are similar to those of mannose-6-phosphate's anti-inflammatory agent.[6] A phytochemical analysis was carried out after the hydroalcoholic extract of betel leaf (HEPBL) was extracted using the Soxhlet apparatus. The experimental animals used in this study were Swiss albino mice of both sexes, weighing 22–25g, and Wistar rats, weighing 150–220g (aged 8–12 weeks). The analgesic action was evaluated using the tail-flick and acetic acid induction techniques, while the anti-inflammatory activity was examined using cotton pellet granuloma and carrageenan-induced paw edoema models. Significant analgesic effectiveness was shown by HEPBL at doses of 100 and 200 mg/kg.[9]

Anti-diabetic activity

Piper betel is an effective treatment for diabetes. Certain plants, such bitter melon (which increases sperm mitochondrial activity), have antidiabetic properties that were seen after treating semen with different dosages of Piper betel. This shown that Piper betel can act as a contraceptive and reduce mitochondrial activity in human sperm. The mitochondrial activity of the semen samples was measured after varying incubation durations. It is commonly known that aloe vera gel lowers blood sugar. However, depending on how differently the mucilaginous layer and anthraquinones separate, the outcomes might change. In addition to lowering blood sugar, it also decreases plasma and problem cholesterol, triglycerides, free fat acids, and phospholipids.[9]

Anticancer

Chemotherapy, radiation therapy, and surgery are often used cancer therapies for cancer patients. Cancer patients often have adverse effects from treatments linked to medication toxicity and drug resistance. Therefore, it is very desirable to have alternative medicine therapies with lower levels of toxicity. Every year, more and more studies are conducted on the use of plants and herbal remedies as chemotherapeutic agents.[12]

RECENT PROGRESS IN THE DEVELOPMENT OF VACCINES AGAINST CANDIDIASIS

the past ten years, several defensive and highly immunogenic vaccination regimens against candidiasis have been developed. Immunizations may be seen of as organic planning that increases vulnerability to a certain disease. Immunizations involve a vaccine that resembles a pathogen and is incorporated using either a dead or, on the other hand, weakened form of the pathogen, one of its surface proteins, or its toxins. This activates the immune system's defense mechanism, causing the immune system to recognize the vaccine as an antigen and destroy it. demonstrated that heat-killed *Saccharomyces* (HKY) is a protective vaccine against coccidioidomycosis and aspergillosis. They focused on the effect of HKY against fundamental candidiasis in order to test the hypothesis that the survival of HKY-induced security may be due to the cross-responsive antigens in the cell walls of the diverse species. Different regimens

of HKY were administered subcutaneously to male CD-1 mice prior to an intravenous test with *Candida albicans*. They observed that HKY protects mice against *C. albicans*-related illness in a dose- and routine-related manner.[1,7,11]

CONCLUSION

According to this review, the aloe vera and piper betel leaves are a source of many phytoconstituents that can be used for a variety of medicinal applications and show antifungal properties. In order to improve the applications of leaf extract for the creation of various medicines, more critical investigations on the material should be required. Candidiasis is the fungal infection caused by *Candida albicans*. It causes different type of candidiasis infections in the blood, heart, eyes, brain, bones also other parts of our body. It can be cured by using natural compounds or synthetic compounds or semisynthetic compounds. *Aloe vera* is a medicinal plant that has been used since ages for its diverse therapeutic properties. The chemical composition of *Aloe vera* is particularly interesting as several of its components have therapeutic and pharmacological properties. Gels are semisolid formulas that are generally accepted in society. Since the skin is the body's most accessible organ, accidents can occur easily to it. Topical preparations, such gels, are the best choice for treating cuts, burns, and wounds.

ACKNOWLEDGMENT

We are very thankful to respected Director Dr. R. Mujuriya and Management of Institute of Pharmaceutical Science and Research (IPSR), Balaghat (MP), 481331, India for their support.

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