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NARRATIVE REVIEWS

Saussurea costus: An Effective Treatment Against Candida

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Abstract

Saussurea costus, traditionally used in Ayurvedic medicine, is emerging as a powerful anti-Candida agent. With the growing challenge of Candida infections and increasing resistance to conventional antifungal drugs, there is an urgent need for new therapeutic options. This literature review emphasizes the significant anti-Candida activity of S. costus, which is attributed to its bioactive compounds, especially sesquiterpene lactones such as costunolide and dehydrocostus lactone. These compounds show inhibitory effects against various Candida species through mechanisms including membrane disruption and enzyme inhibition. Notably, S. costus has demonstrated comparable or even superior effectiveness to drugs like fluconazole, with potential benefits in safety and reduced toxicity. The review highlights the herb's potential as a treatment for Candida infections and its possible use as a natural food preservative. However, further research is necessary to fully realize its therapeutic potential and develop it into a viable treatment option.

Introduction

Saussurea costus, commonly referred to as costus or kushth, is a perennial herb native to the Himalayan region, particularly Nepal, India, and China. It has traditionally been used in folk medicine, especially in Ayurveda, for its medicinal properties. Recent scientific research has underscored its potential as an anti-Candida agent, making it a topic of interest in microbiology and pharmacology. This literature review aims to investigate the anti-Candida activity of *S. costus*, focusing on its chemical constituents, mechanisms of action, and potential applications in the treatment of Candida infections. The plant's roots contain diverse bioactive compounds, including costunolide, dehydrocostus lactone, and chloropicrin, all of which have been recognized as promising candidates for drug development. These compounds have demonstrated potent antifungal activity against *Candida species*, the causative agents of candidiasis, a common and often persistent fungal infection [1,2,3]. In addition to its medicinal uses, *S. costus* is also valued for its essential oil, which has been studied for its ability to repel food pests [4]. The plant is critically endangered, and the Indian government prohibits its export in either crude or processed form to ensure its conservation [5,6]. *S. costus* is native to the sub-alpine regions of India, thriving at elevations between 3,200 and 3,800 meters. It has long been used in traditional Ayurvedic medicine to treat various conditions, including asthma, cough, cholera, chronic skin diseases, and rheumatism [7,8]. The plant's anti-candidal properties have garnered increasing scientific interest, with researchers investigating the mechanisms through which its biochemical constituents exert their antifungal effects.

1.1. Pharmacological activities of *S. costus* constituents

S. costus contains various bioactive compounds, such as sesquiterpene-lactones (costunolide, dehydrocostus-lactone, and cynaropicrin), and other secondary metabolites [7]. These compounds are responsible for the herb's pharmacological activities, including its anti-*Candida* properties [1,2,7]. Sesquiterpene lactones are organic substances that are mostly found in asteraceae

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plants, structurally composed of a highly reactive lactone ring and a 15-carbon skeleton made up of three isoprene units. In particular, they have been identified as the primary constituents responsible for the antifungal activity of *S. costus* [8,9]. A study on two types of *Candida*, *albicans* and *parapsilosis*, showed that cells treated with the n-hexane extract of *S. costus* exhibited significant morphological alterations, including an enlarged surface and rough appearance. Sesquiterpene lactones modify cell shape through interactions with structural proteins, inducing oxidative stress, and activating stress-related signaling pathways. These effects result in increased cell surface area, membrane blebbing, and a textured appearance [9]. Costunolide has been shown to inhibit biofilm formation, a crucial factor in the pathogenicity of the *Candida species*. Another critical compound, dehydrocostus lactone, has also been found to possess potent antifungal properties, particularly against drug-resistant strains of *Candida*. This compound disrupts mitochondrial function and induces endoplasmic reticulum stress, leading to fungal cell death [7,9,10]. Recent studies have emphasized the potential of *S. costus* extracts in fighting fungal infections. For example, the n-hexane extract of *S. costus* roots exhibited the highest biocidal activity against *Candida species*, with considerable zones of inhibition observed in agar well diffusion assays [9]. Furthermore, the extract has induced complete morphological distortions and membrane lysis in *Candida parapsilosis*, further validating its effectiveness [11,12]. The structures of the bioactive forms of *S. costus* are illustrated in Figure 1 [12].

The antifungal activity of *S. costus* is not confined to its crude extracts; even treated cotton fabrics infused with its extracts have demonstrated notable activity against *Candida albicans*, indicating potential applications in medical textiles [1,4,13,14]. SEM images of treated and untreated Candida albicans and Candida parapsilosis before and after exposure to n-hexane extract of *S. costus* is shown in Figure 2 [14].

1.2. Medical and Therapeutic Uses of *S. costus*

S. costus has been studied for its broader pharmacological potential. The herb exhibits anti-inflammatory, antioxidant, and anticancer activities primarily because of its rich phytochemical composition [14–16]. For instance, costunolide and dehydrocostus lactone have been shown to inhibit tumor necrosis factor-alpha (TNF-α) production and suppress inflammatory pathways, making them promising candidates for treating inflammatory diseases [17,18]. Furthermore, *S. costus* extracts have demonstrated hepatoprotective effects, particularly in reducing liver injury caused by toxins, which highlights their therapeutic versatility [19–21]. Its immunomodulatory and anti-inflammatory properties suggest possible applications in COVID-19 treatment. In addition, the plant's flavonoids and antioxidants may support thyroid function, although evidence remains inconclusive [22–25]. Despite these promising findings, further research is needed to fully elucidate the mechanisms of action of *S. costus* compounds and confirm their effectiveness in clinical settings. Standardized extraction methods and thorough clinical trials are vital for utilizing the full potential of this critically endangered medicinal plant [26,27].

1.3. Candidiasis

Candidiasis is a fungal infection primarily caused by *Candida albicans*, though other species such as *C. glabrata, C. tropicalis, C. parapsilosis, C. krusei, and C. auris* can also be responsible [28]. The infection is particularly problematic for immunocompromised individuals, such as HIV/AIDS patients, or those undergoing chemotherapy [29]. Diagnosis methods include direct examination, culture, and biopsy. Treatment typically involves antifungal drugs, with fluconazole being the first-line option [28]. Ongoing research aims to uncover immune mechanisms and develop new anti-fungal strategies to combat candidiasis more effectively.

2. Anti-Candida Activity of *S. Costus*

2.1. In Vitro Studies

Numerous in vitro studies have demonstrated that extracts of *S. costus* and their isolated compounds possess significant antifungal properties against *Candida species* [2]. A study assessed the antifungal efficacy of *S. costus* extract against *C. albicans*, demonstrating its effectiveness in

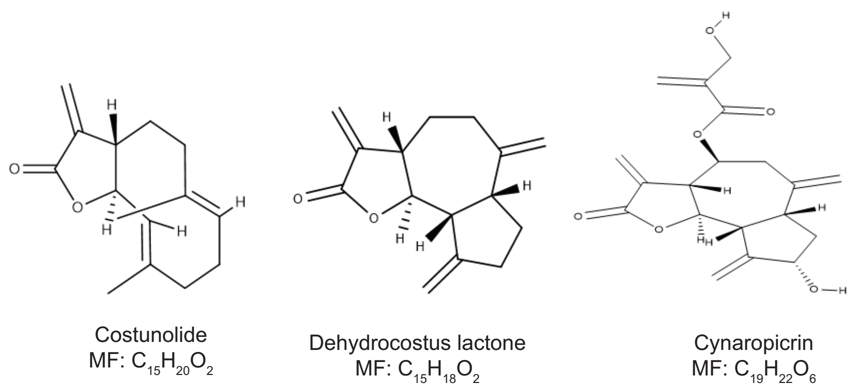


Figure (1): Structure of *Saussurea costus* bioactive molecules such as costunolide, dehydrocostus lactone, and cynaropicrin.

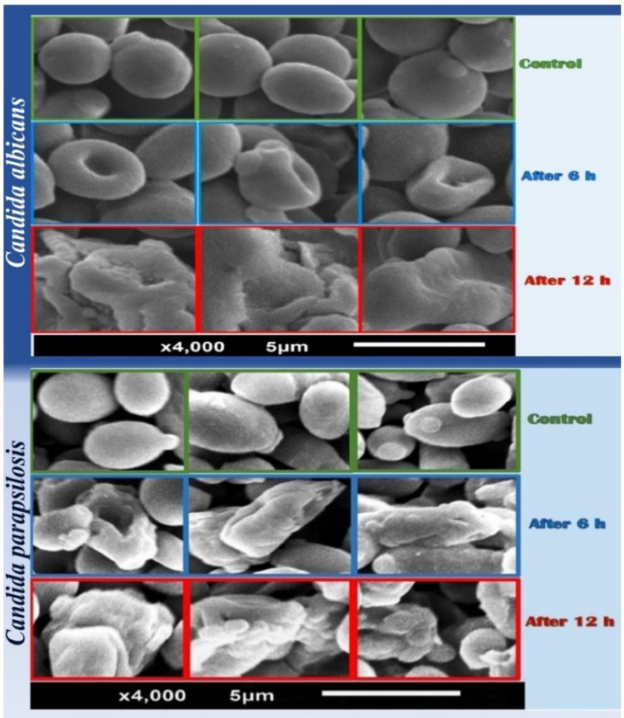


Figure (2): Scanning electron microscopy images of both treated and untreated for two types of candida albicans, parapsilosis before and after treating with n-hexane extract of *Saussurea costus* [14].

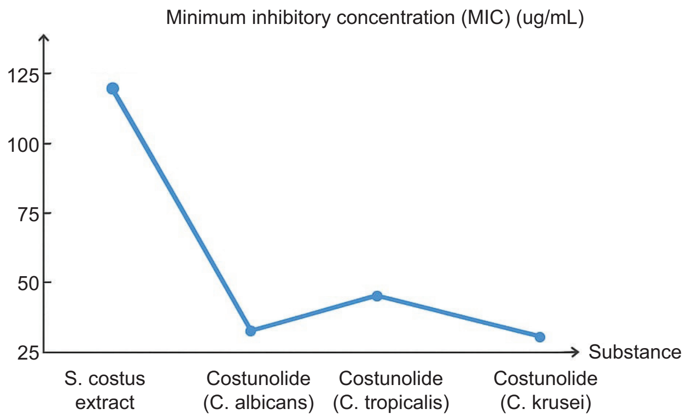


Figure (3): Antifungal efficacy of *Saussurea costus* extracts.[14]

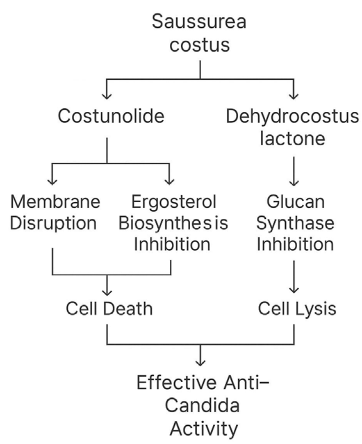
inhibiting fungal growth [17,30,31]. Moreover, experimental studies in rats have shown that treatment with the root extract of *S. costus* following exposure to the plant growth regulator Ethephon results in improved liver recovery compared to Ethephon treatment alone. This suggests that *S. costus* may offer hepatoprotective effects and help reduce Ethephon-induced liver toxicity [31]. The extract's minimum inhibitory concentration (MIC) was 125 μg/mL, comparable to that of established antifungal agents, such as *fluconazole*. Another study examined the antifungal capabilities of costunolide against various *Candida species* [2]. The findings indicated that costunolide displayed intense inhibitory activity against *C. albicans, C. tropicalis, and C. krusei,* with MIC values ranging from 6.25 to 25 μg/mL, as shown in Figure 3 [14]. Furthermore, the study found that costunolide induced apoptosis in *C. albicans* cells, suggesting a potential mechanism of action [32,33].

2.2. Mechanisms of Action

The anti-Candida activity of *S. costus* is attributed to various mechanisms, including membrane disruption, inhibition of enzyme activity, and interference with cellular processes. Costunolide, for instance, has been shown to disrupt the fungal cell membrane, resulting in a loss of cellular integrity and, ultimately, cell death [2]. In addition, costunolide is reported to inhibit the activity of ergosterol biosynthesis enzymes, which are essential for synthesizing the fungal cell membrane [7]. Dehydrocostus lactone, another principal component of *S. costus*, has been found to inhibit the activity of glucan synthase, an enzyme involved in the synthesis of *β-glucan*, a crucial element of the fungal cell wall. Inhibiting glucan synthase disrupts the structural integrity of the cell wall, resulting in fungal cell lysis [26]. This is illustrated in Scheme 1.

2.3. Comparison with Conventional Antifungal Agents

The anti-Candida activity of *S. costus* has been compared to that of conventional antifungal drugs like fluconazole and amphotericin. *S. costus* extract exhibited comparable or even superior antifungal activity against *C. albicans* compared to fluconazole. Moreover, the extract demonstrated a broader spectrum of activity, inhibiting not only *C. albicans* but also other *Candida species*, such as *C. tropicalis* and *C. krusei* [14,34]. Plant-derived compounds like costunolide and dehydrocostus lactone are more effective than synthetic antifungal agents because they are less toxic and have fewer side effects. In addition, the increasing resistance of *Candida species* to conventional antifungal drugs highlights the need for alternative treatments, making *S. costus* a promising candidate [2]. Table 1 presents a comparative overview of MIC values, toxicity profiles, and antifungal spectra between *S. costus* extracts and conventional antifungal agents [14,35–38].



Scheme (1): Anti-Candida mechanisms *Saussurea costus*.

Table (1): Comparison of antifungal efficacy and safety between the *Saussurea costus* extract and conventional antifungal agents.

Agent	MIC against *Candida albicans* (µg/mL)	Toxicity Profile	Spectrum of Activity
Saussurea costus extract[35]	12.5–50[36]	Low cytotoxicity	Broad (*C. albicans*, *C. krusei*, etc.)
Fluconazole[37]	0.25–32[36]	Possible hepatotoxicity	Narrower (resistance in *C. krusei*)
Amphotericin B[38]	0.03–1[36]	Nephrotoxicity	Broad but toxic

2.4. Toxicity and Safety

Several studies have investigated the safety and toxicity of *S. costus* extracts and their bioactive compounds, such as costunolide. Reference [1] reported low acute toxicity in rodent models for ethanolic and aqueous extracts, with LD_{50} values exceeding 2,000 mg/kg. However, variability was noted based on extraction methods and plant parts. In vitro studies by Reference [39] further demonstrated costunolide's low cytotoxicity in human hepatocytes (HepG2 cells), showing an IC_{50} >100 µM, which was attributed to its antioxidant properties. However, Reference [40] emphasized the need for deeper toxicological evaluation, including chronic exposure effects, genotoxicity, and pharmacokinetic interactions, as existing research predominantly focuses on acute toxicity and lacks standardization in extraction protocols. These gaps highlight the necessity for comprehensive studies to ensure safe therapeutic applications of *S. costus* and its constituents.

2.5. Potential Applications

The anti-Candida activity of *S. costus* indicates its potential use in treating *Candida* infections, especially in situations where conventional anti-fungal medications are ineffective because of resistance [41]. This herb could be developed as a natural alternative or complement to existing antifungal therapies. Furthermore, the antifungal properties of *S. costus* position it as a promising candidate for food preservation, where it could serve as a natural preservative to prevent fungal contamination [42].

3. Conclusion

S. costus shows promising anti-Candida potential, largely attributed to its active constituents, especially costunolide and dehydrocostus lactone. These compounds have demonstrated strong antifungal activity through mechanisms such as disrupting fungal cell membranes and inhibiting biofilm formation in various *Candida species.* The mechanisms of action include disrupting membranes, inhibiting enzyme activity, and interfering with cellular processes. Compared to conventional antifungal medications, *S. costus* offers a safer and potentially more practical alternative, especially in light of increasing drug resistance. Identification of active compounds in *S. costus* and evaluation of their activity against *Candida species* remain essential future directions.

Disclosure

The authors declare no conflicts of interest or external funding.

Author Contributions

RW, RFA, MHJ: Conceptualization; RFA, KZ, OM: Data curation; RW, KZ, MHJ: Formal analysis; RW, RFA, KZ: Funding acquisition; RFA, RW, MHJ: Investigation; RW, RFA, KZ: Methodology; KZ, RFA, RW: Project administration; KZ, RFA, RW: Resources; MHJ, RFA, RW: Software; KZ, RW, RFA: Supervision; KZ, OM, RFA: Validation; OM, KZ, RFA: Visualization; KZ, , RFA: Writing–original draft; OM, MHJ, RFA: Writing – review & editing.

Conflict of Interest

The authors declare no conflicts of interest with respect to research, authorship, and/or publication of this article.

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