

Review on Antifibrotic Action of Albizia lebbeck (Shireesha) with Pharmacological and Ayurvedic Perspective

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ABSTRACT

Oral Submucous Fibrosis (OSMF) is a chronic, progressive, and potentially malignant disorder of the oral cavity, strongly associated with tobacco and betel nut chewing [1]. Current management strategies, including corticosteroids, antioxidants, and physiotherapy, provide symptomatic relief but fail to reverse fibrosis [2]. Ayurveda identifies *Albizia lebbeck* (Shirisha) as Vishaghna (antitoxic) and Shothaghna (anti-inflammatory), with classical references to its use in visha lakshanas and mukharogas [3,4]. Modern pharmacological studies corroborate its antifibrotic, antioxidant, and wound-healing properties [5,6]. This article reviews the phytochemistry, pharmacology, and Ayurvedic rationale of *Albizia lebbeck*, highlighting its translational potential in antifibrotic therapy.

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INTRODUCTION

Tobacco chewing is prevalent in India, with 25.9% of adults using smokeless tobacco [1]. In tobacco chewers, OSMF manifests as mucosal blanching, trismus, burning sensation, and defective gustatory function, with malignant transformation rates reported between 7–13% [1]. Modern interventions such as Triamcinolone acetonide, antioxidants, and physiotherapy are limited by adverse drug reactions and poor long-term outcomes [2]. Ayurveda may correlate OSMF with Sarvasara Mukhapaka, a tridoshaja condition requiring both local and systemic management [7].

Phytochemical Constituents of *Albizia lebbeck*

The plant contains **alkaloids** such as anabasine compounds, which have modulatory effects on fibroblast activity and are implicated in reducing abnormal collagen synthesis [5]. These alkaloids also contribute to the plant's antitoxic properties described in Ayurvedic texts i.e. vishaghna.

Flavonoids like quercetin, kaempferol, rutin, and catechin act as potent antioxidants, reducing reactive oxygen species (ROS) and oxidative stress, which are major drivers of fibrosis [8]. Quercetin in particular has been shown to inhibit lipid peroxidation and stabilize cell membranes, thereby protecting oral mucosa from chronic irritant damage.

Saponins and glycosides provide immunomodulatory and anti-inflammatory effects [9]. They regulate immune cell activity, suppress pro-inflammatory cytokines, and enhance macrophage function, which helps in controlling chronic inflammation associated with OSMF.

Steroids and tannins contribute to collagen stabilization and wound healing [10]. Tannins act as astringents, reducing mucosal edema and promoting tissue repair, while plant steroids enhance epithelial regeneration and angiogenesis.

Volatile oils demonstrate anti-nociceptive and anti-inflammatory properties [6]. These oils reduce pain perception, burning

sensation, and hypersensitivity in oral mucosa, which are hallmark symptoms of OSMF.

Additionally, phytochemical screening has revealed the presence of **terpenoids, phenolic compounds, anthraquinones, and essential oils**, which contribute to antimicrobial, antioxidant, and anticancer activities [8,9]. Terpenoids are particularly important for mast cell stabilization, reducing histamine release and vascular permeability.

The **bark and seeds** of *Albizia lebbeck* have shown anti-histaminic properties, capable of stabilizing mast cells and reducing allergic reactions [14]. This mechanism is highly relevant in OSMF, where mast cell degranulation contributes to mucosal inflammation and fibrosis.

Experimental studies also highlight the **anticancer potential** of *Albizia lebbeck*, with extracts demonstrating pro-apoptotic effects on abnormal fibroblasts and precancerous cells, thereby reducing the risk of malignant transformation in OSMF [5,12].

Ayurvedic Perspective

Charaka Samhita classifies Shirisha under **Vishaghna Mahakashaya**, highlighting its role in neutralizing poisons and toxins, especially in cases of snake bite, insect bite, and toxic oral conditions [3]. This categorization emphasizes its systemic detoxifying capacity and its ability to counteract both internal and external visha manifestations.

Sushruta Samhita includes Shirisha in **Salsaradi Gana**, a group of drugs indicated for **kushta (skin disorders), inflammatory swellings, and wound healing** [7]. This reflects its broader therapeutic utility beyond oral diseases, showing its relevance in chronic inflammatory and fibrotic conditions.

Ashtanga Hridaya refers to Shirisha as **foremost among Vishaghna dravyas** [4], underscoring its clinical utility in combating toxic states. Vagbhata specifically mentions its use in **respiratory disorders (kasa, shwasa), inflammatory swellings (shotha), and toxic wounds (vishakta vrana)**, which may

parallels its antifibrotic and anti-inflammatory and thereby antibiotics potential in oral mucosal fibrosis.

Pratisarana Chikitsa involves the **local application of Panchashireesh Agad Churna**, prepared from equal parts of Shirisha root, bark, leaves, flowers, and fruit [3]. This poly-part usage reflects the Ayurvedic principle of maximizing therapeutic potency by combining various plant parts. When applied directly to the oral mucosa, the churna acts on fibrotic bands, reduces burning sensation, and promotes wound healing. This aligns with usage of agad in sthir and kathin lushta as stated in Charak Samhita, kushta chikitsa.

Additionally, **Bhavaprakasha Nighantu** elaborates Shirisha's synonyms such as *Bhandira*, *Kapitana*, *Shukapushpa*, and describes its **Shothaghna (anti-inflammatory)**, **Vishaghna (antitoxic)**, and **Vrana-ropaka (wound healing)** properties [10]. These descriptions align with modern pharmacological findings of anti-oxidant, mast cell stabilizing, and collagen-modulating effects, which eventually leads into anti-fibrotic action.

Kaiyadeva Nighantu further highlights Shirisha's qualities as *Madhura rasa*, *Laghu guna*, *Anushna virya*, and indicates its use in **visarpa (erysipelas)**, **kasa (cough)**, **shotha (edema)**, and **vishakta vrana (infected wounds)** [14]. This shows its systemic relevance in inflammatory and fibrotic pathologies.

Thus, classical Ayurvedic categorization consistently places Shirisha in groups associated with **detoxification, inflammation reduction, wound healing, and respiratory/oral disorders**, providing a strong traditional rationale for its antifibrotic application in OSMF.

Pharmacological Evidence

Preclinical Studies Hepatic fibrosis models showed reduced collagen deposition and improved liver enzymes [5]. Pulmonary fibrosis models demonstrated attenuation of bleomycin-induced fibrosis [6]. Oral mucosal models revealed softening of fibrotic bands and improved epithelial healing [8].

Clinical Studies Shirisha Beeja Churna with honey showed efficacy in tobacco-induced gingivitis [11]. Panchashireesh Agad Churna Pratisaran demonstrated symptomatic improvement in OSMF Grade II [12]. Comparative herbal studies highlight Shirisha's unique antifibrotic potential compared to Triphala, Turmeric, and Aloe vera [13].

Mechanism of Antifibrotic Action

The antifibrotic activity of *Albizia lebbeck* is mediated through antioxidant, anti-inflammatory, immunomodulatory, and wound-healing mechanisms [5]. Flavonoids and polyphenols neutralize reactive oxygen species, reducing oxidative stress and preventing fibroblast activation [8]. Anti-inflammatory constituents suppress TNF- α , IL-1 β , and IL-6, while upregulating IL-10, thereby reducing mucosal inflammation [9]. Mast cell stabilization prevents histamine release and reduces vascular permeability, alleviating burning sensations and mucosal edema [6]. Alkaloids and saponins inhibit fibroblast proliferation and collagen cross-linking, while enhancing matrix metalloproteinase activity to degrade excess extracellular matrix [5]. Bark and seed extracts exhibit anti-histaminic and immunomodulatory properties, reducing hypersensitivity reactions and chronic irritation [14]. Ayurvedic Pratisarana Chikitsa ensures direct mucosal contact, enhancing absorption and softening fibrotic tissue [3]. Experimental studies suggest pro-apoptotic effects on aberrant fibroblasts and anticancer potential, reducing malignant transformation risk in OSMF [12].

Comparative Evaluation

Symptom relief with modern drugs such as corticosteroids, antioxidants, and physiotherapy is often **moderate**, providing temporary reduction in burning sensation and improvement in mouth opening, but relapse is common once therapy is discontinued [2,12]. In contrast, *Albizia lebbeck* demonstrates

strong symptomatic relief, particularly in reducing burning sensation, softening fibrotic bands, and improving oral flexibility.

Fibrosis reversal with corticosteroids is generally **poor**, as these agents primarily suppress inflammation without addressing collagen deposition or fibroblast proliferation [2]. Preclinical studies of Shirisha, however, show **promising antifibrotic activity**, with evidence of collagen modulation, inhibition of fibroblast proliferation, and activation of matrix metalloproteinases that degrade excess extracellular matrix [5,8].

DISCUSSION

The antifibrotic activity of *Albizia lebbeck* is supported by both **Ayurvedic rationale and modern pharmacology**, making it a unique candidate for integrative management of Oral Submucous Fibrosis (OSMF) [3,5]. Its dual action — Vishaghna (detoxifying) and Shothaghna (anti-inflammatory) — directly aligns with the pathophysiology of OSMF, which involves chronic irritation, inflammation, and progressive fibrosis [4].

Preclinical evidence demonstrates **collagen modulation, fibroblast inhibition, and antioxidant effects**, which are crucial in halting the progression of fibrosis [8]. These findings are consistent with Ayurvedic descriptions of Shirisha as Vishaghna and Vrana-ropaka, highlighting its ability to detoxify and promote wound healing.

Clinical observations suggest **symptomatic improvement**, including reduction in burning sensation, softening of fibrotic bands, and improved mouth opening, when Panchashireesh Agad Churna is applied locally as Pratisarana therapy [12]. This supports the Ayurvedic principle of direct mucosal contact for enhanced absorption and targeted action.

However, challenges remain in **dosage standardization**, as variability in phytochemical content across plant parts and geographical regions can affect therapeutic outcomes [13]. **Bioavailability of active phytochemicals** such as flavonoids and saponins is another limitation, as oral mucosal absorption may be inconsistent without advanced delivery systems [9]. Furthermore, the absence of **large-scale randomized controlled trials** restricts the generalizability of current findings and prevents global acceptance of Shirisha as a validated antifibrotic agent [13].

Future directions include integrating Panchashireesh Agad Churna into **novel drug delivery systems** such as mucoadhesive gels, nanoparticles, and bio-enhanced formulations, which can improve local retention, controlled release, and deeper tissue penetration [12]. Additionally, combining Shirisha with other Ayurvedic herbs like Triphala or Turmeric may provide **synergistic antifibrotic effects**, as suggested by comparative herbal studies [13].

Another important area is **long-term safety evaluation**, since most clinical studies have been short-term. Establishing pharmacokinetic profiles, dose-response relationships, and toxicity thresholds will be essential for regulatory approval. Finally, **translational research bridging Ayurveda and modern pharmacology** can help position *Albizia lebbeck* as a cost-effective, accessible, and culturally integrated antifibrotic therapy, especially in regions with high prevalence of OSMF.

CONCLUSION

Albizia lebbeck (Shirisha) represents a promising antioxidant, anti-inflammatory with vishaghna (antitoxic), shothaghna, vrananashak may attributing in antifibrotic agent, bridging Ayurvedic wisdom and modern pharmacology [3,5]. Its phytochemical richness, safety profile, and classical references support its role in OSMF management [7]. Rigorous clinical trials and advanced drug delivery approaches are warranted to establish its therapeutic potential in fibrosis-associated disorders [12].

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