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Review Article

AN UPDATE ON PHARMACOLOGICAL PROFILE OF *BOSWELLIA SERRATA*

NAMEETA PILKHWAL[1], SUNEELA DHANESHWAR[2]*

[1]Department of Pharmacology, Amity Institute of Pharmacy, Amity University Uttar Pradesh Lucknow Campus, Lucknow, Uttar Pradesh, India. [2]Department of Pharmaceutical Chemistry, Amity Institute of Pharmacy, Amity University Uttar Pradesh Lucknow Campus, Lucknow, Uttar Pradesh, India. Email: sdhaneshwar1@lko.amity.edu

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ABSTRACT

Boswellia serrata (Burseraceae) is one of the oldest and most explored herbs in Ayurveda. In Unani system of medicine, oleo-gum resin of *B. serrata* named Kundur has been a key component of modern quality perfumes. The gum is used as a remedy for the treatment of illness especially skin diseases and rheumatism in Indian system of medicine (Siddha, Ayurvedic, and Unani) for the preceding centuries. Salai guggul is one of the accepted drugs for various complaints such as dyspepsia, dysentery, lung diseases, urinary disorder, hemorrhoids, and corneal ulcer in Unani system of medicine for the past few decades**.** The present article is aimed to provide an overview on various pharmacological activities of *B. serrata*. The resin fraction of Salai guggal is rich in boswellic acids and its essential oils that are composed of a mixture of mono-, di-, and sesqui-terpenes while gum fraction chiefly contains pentose and hexose sugars. The oleo-gum resin is highly sought after by the practitioners of traditional system because it has shown broad range of efficacy in asthma, cancer, microbial/fungal infections, hyperlipidemia, inflammation, arthritis, diarrhea, and management of pain. An exhaustive review of literature was conducted using various databases on ScienceDirect, Scopus, PubMed, Google Scholar, and Free Patents online. This review is a sincere attempt to discuss and present the current status of pharmacological profile of *B. serrata*.

Keywords: *Boswellia serrata*, Inflammation, Boswellic acids, Leukotriene synthesis, Pharmacology.

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INTRODUCTION

Boswellia serrata (Fig. 1) (Kundur) is commonly known as "Salai guggal" owned by the family Burseraceae. The tree is commonly found in Southern Arabia, West Asia, Oman, South Africa, and Yemen. In India, it is widely distributed in Western Himalayas, Madhya Pradesh, Gujarat, Orissa, Rajasthan, Bihar, and Maharashtra. It is a moderate to large deciduous tree with a circumference of 2.4 m and medium height of 4–5 m. The papery bark changes its color from greenish-gray, yellow, or reddish to ash color which can be easily peeled off. On peeling or incision, the barks secrete an exudate in the form of translucent lumps, tears, or droplets of white to yellow-colored gummy oleo-gum resin. The aromatic gum has balsamic odor and bitter taste. In Ayurveda, an Indian traditional system of medicine, the gum is used for the treatment of number of inflammatory diseases affecting skin, eye, gums, and gastrointestinal tract in addition to the respiratory disorders such as asthma, bronchitis, and laryngitis [1].

Salai guggal or oleo-gum resin is a mixture of gum, resin, and essential oil. Hexose and pentose sugars with certain digestive and oxidizing enzymes make up the gum. Combination of some phenolics, mono-, di-, and sesqui-terpenes and a diterpene alcohol is found in the essential oil fraction. The resin part of almost all species of *Boswellia* is mainly made up of boswellic acid (BA), a pentacyclic triterpene acid [2,3].

A number of reviews and research papers focusing on pharmacological studies have highlighted the usefulness of BAs in the management of several chronic inflammatory diseases including chronic ulcerative colitis, rheumatoid arthritis, Crohn's disease, and bronchial asthma; in addition to its antidepressive, antianxiety, and beneficial effects in brain tumor patient [4].

The two most efficient anti-inflammatory BAs of *Boswellia* are 11-keto-beta-BA (KBA) and acetyl-KBA (AKBA) [5]. BAs selectively inhibit leukotriene formation by inhibiting 5-lipoxygenase (5-LOX) in a non-competitive, non-redox, and enzyme-directed manner. They also exhibit various effects such as antioxidant, cancer drug sensitizing, antinociceptive, antibacterial, insulin resistance lowering, and cardioprotective.

Pharmacognostical characteristics of Indian *Boswellia*

Macroscopically, the oleo-gum resin occurs as transparent, brownish-yellow, 2 cm thick, stalactic tears that constitute agglomerates of different sizes and shape, fracture, fragrant, brittle; ruptured waxy surface and translucent; and burn voluntarily and emanate an appealing characteristic, balsamic resinous odor and taste is pungent, bitterish, and slightly aromatic but agreeable. Microscopically, debris of fibers, rectangular cork, yellowish oil globules, and innumerable large or small, oval to round or rhomboidal crystalline fragments are present [6]. In general, exudate, bark, trunk, and oleo-gum resin of *B. serrata* are used medically [7].

In India, it is one of the most common trees found in some parts of Khandesh, Loonawara, and other neighboring territories [8]. It is a native of the mountainous parts of Coromandel, attaining a large size [9]. It is also spotted in dry hilly forest regions of Madhya Pradesh, Rajasthan, Bihar, Orissa, Assam, as well as peninsular central regions of Andhra Pradesh [10]. Table 1 gives the botanical description of the plant [11,12].

Phytochemistry

Various important phytochemicals are found in oleo-gum resin mixture. These include mucus, pure resin, and essential oil. The content and composition of oleo-gum resin may vary from species to species depending on resin's quality, age, and geographical conditions. The resins of *Boswellia* species chiefly contain higher terpenoids, i.e., pentacyclic triterpenes and tetracyclic triterpenes and are responsible for its pharmacological effects [13,14].

The six major BAs are α- and β-BAs (10–21%), KBA (2.5–7.5%), acetylated α- and β-BAs (0.05–6%), and 3-o-AKBA (0.1–3%). The content of BAs in commercially available standardized extract varies from 37.5 to 65% [13].

The dry extract of *B. serrata* contains approximately 50–60% of various α- and β-BAs, of which 1–3% is the most bioactive AKBA fraction [15,16]. Among all the BAs of *Boswellia*, the two most active, potent, and anti-inflammatory agents are AKBA and KBA. The lipophilic part of AKBA with a β-configuration has been described to have

Fig. 1: ***Boswellia serrata***

Table 1: Botanical genesis and native names of *Boswellia serrata*

Botanical origin	Native names
Species: Serrata	English – Indian frankincense
Genus – Boswellia	Hindi – Salai, Kundur
Family – Burseraceae	Gujarati – Gugali, Dhup
Class – Anacardiales	Malayalam – Saambraani, Parangi
Over-class – Rutanae	Telugu – Saambraani, Phirangi
Subtribe – Rosidae S. lat.	Sanskrit – Kunduru, Ashvamurti, Shallaki
Tribe – Rosopsida	Tamil – Saambraani, Parangi
Sub- division- Angiospermae	Kannada- Guguladhuph, Chitta
Division- Spermatophyte	Bengali- Salai, Kundur

superior anti-inflammatory properties over α-configuration [17]. Some other BAs isolated from *Boswellia* are 9, 11-dehydro-α-BAs and its isomer and their acetylated group form. The other phytoconstituents found in *Boswellia* are incensole acetate, acetyl-lupeolic acid, lupeolic acid, incensole oxide, and isoincensole oxide [18-24].

Modification in chemistry of BAs alters their biological effect. When 11-keto group of BA is modified to methylene group, 5-LO activity has been observed to decrease. However, reduced form is more efficient toward induction of apoptosis and inhibition of topoisomerases. Removal of acetyl group or reduction of 11-keto group to alcohol in AKBA produces slight decrease in activity of 5-LO inhibition suggesting that the 11-keto functionality and pentacyclic triterpene ring are critical for receptor attachment to produce anti-inflammatory activity [25].

The essential oil of Salai guggul mainly contains monoterpenes such as α-pinene (major monoterpene), *trans*-pinocarveol, myrcene *cis*-verbenol, borneol, limonene, phellandrene, cadinene, verbenone, thuja 2, 4(10)-diene, *p*-cymene, and small amount of diterpenes [26].

Chemistry of various BAs

Structures of various pentacyclic triterpenic acids (BAs) are illustrated in Fig. 2.

Pharmacokinetics properties of BA

AKBA and KBA are lipotropic fractions of BA responsible for their poor intestinal penetration and high retention [28,29]. Literature reports that the bioavailable plasma levels of various BAs were enhanced many folds by simultaneous administration of a fat-rich food [16].

Various studies to improve bioavailability of BA have been reported in literature. Recently, Bairwa and Jachak (2016) developed a polydilactide coglycoside-based nanotechnique for KBA to enhance its oral bioavailability and *in vivo* anti-inflammatory activity [30]. Hüsch *et al.* (2013) formulated *B. serrata* gum resin extract into Casperome, a soy lecithin formulation which showed significantly high level of KBA and β-BA fraction [31].

Sengupta *et al.* (2011) characterized a novel formulation called Aflapin, which consists of *B. serrata* extract (BSE) rich in AKBA and non-volatile oil part of *B. serrata* resin. In Aflapin-supplemented animals, the level of AKBA is increased by 51.78% in systemic circulation in comparison with 30% standardized AKBA extract. Aflapin showed better anti-inflammatory efficacy in Freund's complete adjuvant-induced inflammation model in Sprague-Dawley rats [32].

Fartyal *et al.* (2011) studied floating microspheres using BA for prolongation of gastric retention time [33]. Sharma *et al.* (2010) studied the complexation of BA with phosphatidylcholine (PC) to enhance its bioavailability [34]. The compound showed better hypolipidemic activity and anti-inflammatory activity as compared to BA. The obtained result revealed that increased bioavailability of BA-PC complex may be due to amphiphilic nature of the complex, which, in turn, enhanced the lipid and water solubility of BAs.

Goel *et al.* (2010) developed AKBA-loaded polymeric nanomicelles which showed magnified antiarthritic, anti-inflammatory, and skin permeability activities [35].

Mechanism of action

The most promising targets for BAs are 5-LO, angiogenesis, topoisomerases, and cytochrome p450 enzyme (Fig. 3) [17,36-38].

5-LO inhibition

In neutrophils, 5-LO predominantly converts endogenous arachidonic acid to leukotrienes and 5-hydroxyeicosatetraenoic acid. They cause vasoconstriction, bronchospasm increased permeability and chemotaxis. BA is a unique, specific, non-redox inhibitor of 5-LO as it neither impairs the cyclooxygenase and 12-lipoxygenase enzyme properties nor inhibits the peroxidation of arachidonic acid [17,31,34,36-46].

Topoisomerase inhibition

BAs have a real catalytic inhibitory action on human topoisomerase. BAs not only inhibit DNA formation in human leukemic promyelocytic cells in a dose-dependent manner but also inhibit topoisomerase through binding with the enzyme [17,41-44].

Leukocyte elastase inhibition

The human elastase decreases the elasticity of lungs, constricts the lungs passages, damages the secretion of mucus in lungs, and decreases the removal of the mucus. In addition to this, it disrupts skin cells and causes swelling, redness, and edema that are symptoms of inflammation. BAs reduce the activity of elastase enzyme which is responsible of emphysema. AKBA and KBA have been expressed to retard elastase in a dose-dependent way [44].

Inhibition of C2 and C3 convertase

BAs inhibit the C2 convertase enzyme which has the most significant role in the classical complement pathway for specific immunity [45]. BAs have been observed to inhibit hemolysis and chemotaxis of leukocytes and inhibit a crucial enzyme C-3 convertase of the classical complementary pathway [45,47,48]. Safayhi and Sailer reported that AKBA and KBA were the strong 5-LO inhibitors with half maximal inhibitory concentration values of 1.5 μM and 3.0 μM, respectively [37,49].

Effect of BA on various organs

BAs are characterized by their ability to act on multiple targets which are compiled in Table 2.

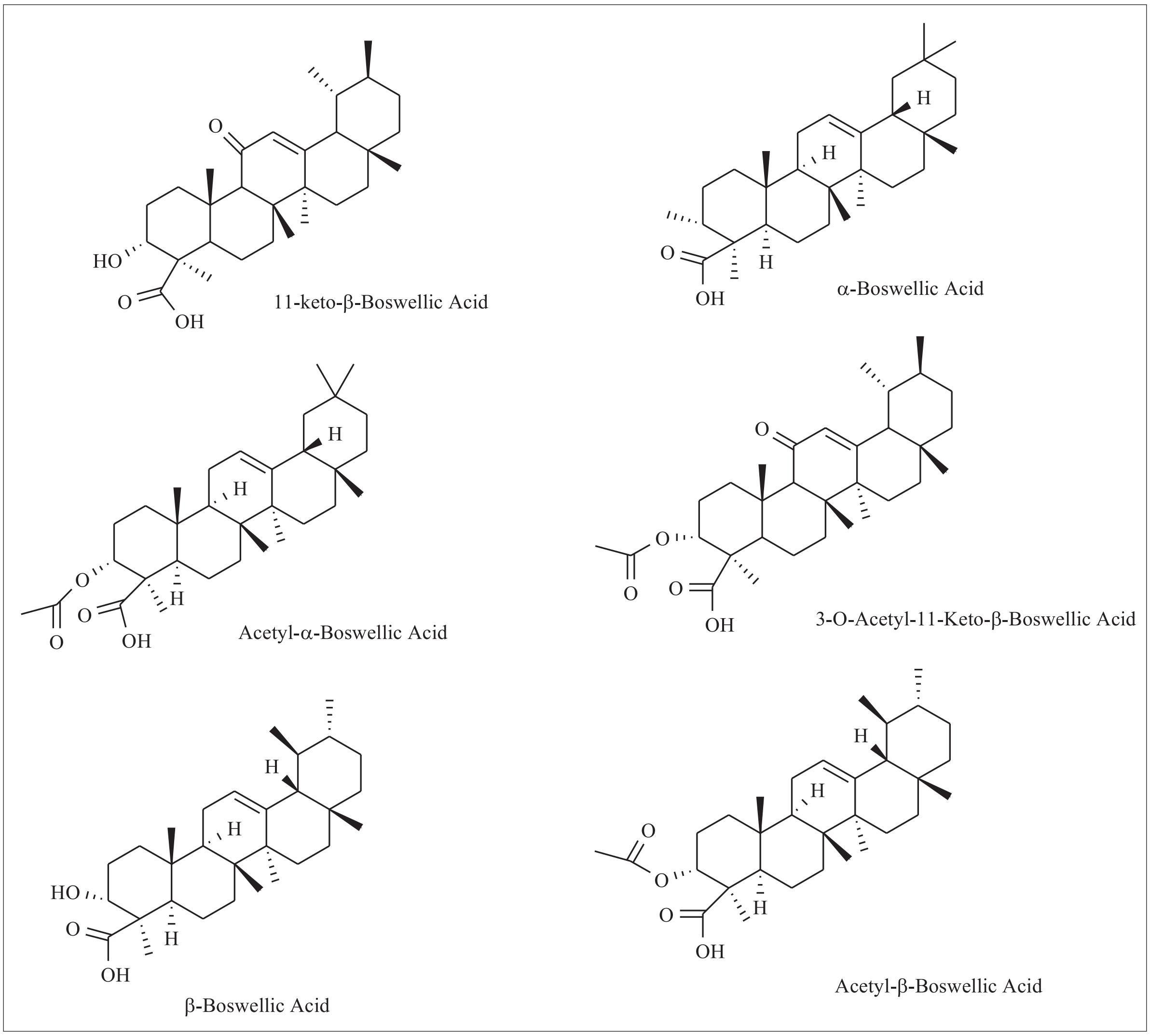

Fig. 2: Structures of various boswellic acids (pentacyclic acids) present in frankincense [27]

Table 2: Beneficial uses of Salai guggul in the standard Indian Ayurvedic system [1]

Organ and functional system	Effects
Cardiovascular system	Cardiotonic
Gastrointestinal tract	Carminative
	Regulating color of stool
	Anthelmintic
	Improving digestion
Nervous system	Mental tonic
	Analgesic
	Eye tonic
Fever	Antipyretic
Skin	Increases perspiration
	Wound healing
Urogenital system	Diuretic
	Improving menstruation
Whole organism	Anti-inflammatory
	Antiseptic
	Reducing fat

Pharmacological profile of BAs

Antiarthritic and anti-inflammatory activity

Carrageenan and dextran are widely utilized to induce paw edema for screening of anti-inflammatory action of drugs. Singh and Atal observed that oral administration of an alcoholic extract of the oleo-gum resin of BS caused inhibition of the carrageenan-induced edema in rats and mice and dextran-induced edema in rats. Numerous scientific studies clearly support the privilege that BS possesses potent anti-inflammatory activity [50].

The anti-inflammatory activity of BAs is due to inhibition of leukotriene synthesis through 5-LO; however, they have no effect on cyclooxygenase, 12-lipoxygenase arachidonic acid peroxidation by ascorbate, and iron. The data demonstrated that BAs from *B. serrata* are specific, non-redox inhibitors of leukotriene synthesis either by interacting immediately with 5-LO or restricting its translocation and thus act as a potent anti-inflammatory agent [17]. The inhibition of 5-LO by BAs that lead to decreased production of leukotrienes has received high attention by scientific society since a variety of chronic inflammatory diseases are connected with increased leukotrienes activity [51].

Extract of *B. serrata* leads to inhibition of carrageenan-induced paw edema by 39.75% and 65–73% with a dose of 50–200 mg/kg (p.o) and 50–100 mg/kg (i.p) appropriately compared to 47% inhibition seen with phenylbutazone (50 mg/kg p.o.). The anti-inflammatory activity was equally well noted in adrenalectomized rats. Inhibition of paw swelling (34% and 49%) has been seen with the mycobacterial adjuvant-induced polyarthritis in rats [50].

Ammon *et al.* (1991) implemented studies on leukocytes migration into the inflammatory exudates induced by carrageenan. Extract of *B. serrata*

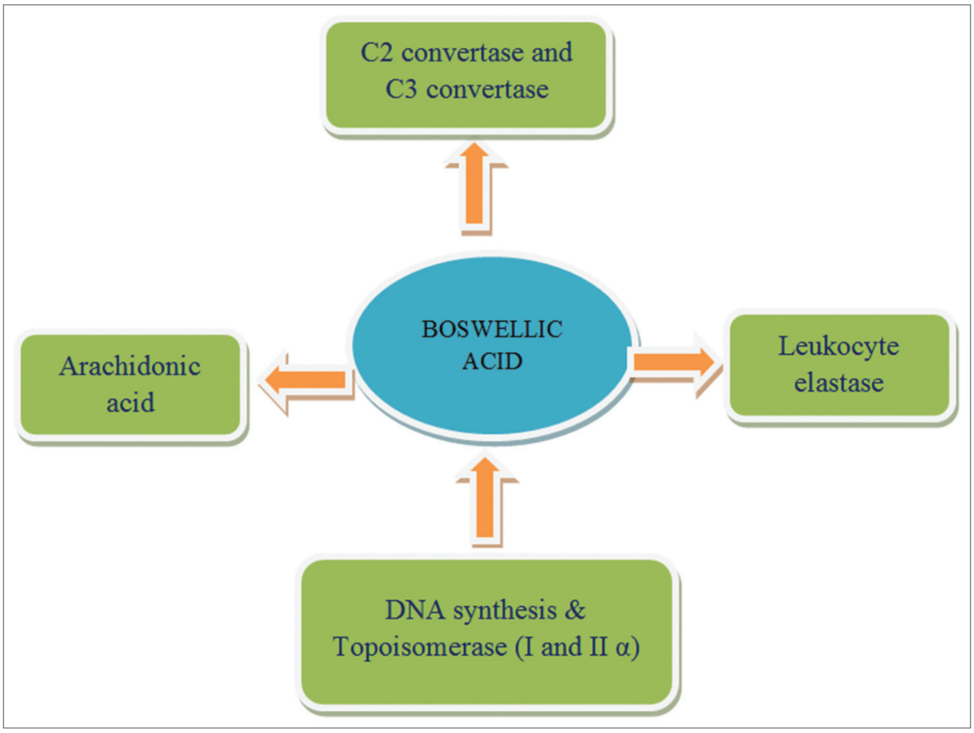

Fig. 3: Mechanism of action of boswellic acids

in dose of 100 mg/kg orally showed significant diminishing effect on both the leukocytes population and volume of pleural exudates [36]. Singh and Atal (1984) calculated the anti-inflammatory effect of mixture of BAs, and in formaldehyde arthritis model, it exhibited 45–67% antiarthritic activity. It has been shown to be effective in adjuvant arthritis (35–59%) as well as in established arthritis (54–84%), also relieved fever [50]. Kulkarni *et al.* and Chopra *et al*. have conducted clinical trials for establishing anti-inflammatory properties of *Boswellia,* in combination with *Curcuma longa, Zingiber officinale,* and *Withania somnifera.* Treatment with this combination produced significant decrease in disability score and severity of pain [52,53].

Sharma *et al.,* in 1989, studied the effectiveness of BA on bovine serum albumin (BSA)-induced arthritis model in rabbits. The oral administration of BA (25, 50, and 100 mg/kg/day) remarkably lessened the leukocytes in BSA-injected knee which changed the electrophoretic pattern of the synovial fluid protein [51]. Gupta *et al.* (1992) found BAs to be much more effective in the latex of papaya-induced model of inflammation than carrageenan-induced inflammation. In the carrageenan model, the effect of acetylsalicylic acid was compared with the action of prednisolone and BAs. This suggests that the anti-inflammatory activity of BAs is different from aspirin-like drugs and prednisolone. BAs did not inhibit prostaglandin synthesis but were more effective in inhibition of leukotriene synthesis [54].

It has been also reported that BAs produce the anti-inflammatory actions in mouse macrophages and human peripheral blood mononuclear cells through inhibition of mitogen-activated protein kinases (MAPK), NO, tumor necrosis factor-alpha (TNF-α), and interleukin-1β [55].

Khosravi *et al.,* in 2011, organized a double-blind randomized clinical trial to assess the effectiveness of *Boswellia* in moderate plaque-induced gingivitis. They reported that the *Boswellia* extract had the ability to lessen the inflammation of periodontium associated with plaque-induced gingivitis [56].

Notarnicola *et al.* assessed the effectiveness of the combination of BA-methylsulfonylmethane (MSM) in comparison to glucosamine (GS) as an effective supplement in the management of knee arthritis through a clinical trial. It was found that the BS-MSM combination showed promising and satisfactory results with respect to GS [57].

Review articles published in the past for preclinical and clinical studies have clearly highlighted and supported the anti-inflammatory activities of *B. serrata.*

Analgesic effect

B. serrata is used to treat muscular and arthritic pain in various systems of medicine [58-60]. Menon and Kar exhibited that the non-phenolic fraction of *B. serrata* possesses remarkable analgesic and sedative effect. They also revealed significant reduction in the spontaneous locomotor activity after treatment with *Boswellia* [61]. Sharma *et al.* investigated the analgesic activity of various fractions of *B. serrata* distinctly by formalin test, acetic acid-induced writhing, hot plate methods, and tail immersion model of analgesic in rats [60]. Both peripherally and centrally mediated analgesic action were measured. Tail immersion methods and acetic acid-induced abdominal constriction elucidated central and peripheral activity, respectively, although the formalin test measured both. Peripheral effects were elucidated by hot plate method [62]. They not only assessed the analgesic activity but also elucidated the mode of action. The oleo-gum resin fraction showed maximal inhibition (60.54%) as compared to gum (54.88%) and oil (20.70%) fraction. In 2005, Bishnoi *et al.* examined the analgesic activity of AKBA at different dose levels by tail flick and acetic acid-induced writhing method in mice. In acetic acid-induced writhing method, a dose-dependent increase in antinociceptive activity of AKBA was shown while in tail flick method, 100 mg of AKBA showed similar response to 200 mg. AKBA was found to be significantly better than positive control, nimesulide [63]. Al-Harrasi *et al.* used formalin-induced pain and acetic acid-induced writhing to investigate the analgesic activity of *Boswellia sacra* in mice. Polar subfraction was observed with highest analgesic activity, almost double of positive control, aspirin. The study proposed that *Boswellia* seems to produce antinociceptive effect by both peripheral and central mechanism [64].

Antifungal activity

In a study using agar well diffusion method, Chaurasia and Gharia investigated the antifungal activity of *B. serrata* against plant pathogenic fungus (red rot disease-causing agent) *Colletotrichum falcatum*. They extracted the plant with water, ethanol, and chloroform and concluded that the ethanolic extract of plant was much more efficient than chloroform extract [65].

Garg (1974) studied antifungal activity of *B. serrata* and found that on hydrodistillation *B. serrata* produced 0.6% of essential oil. The oil has mild antifungal activity against human pathogens and highly effective against plant pathogens, seen by inhibition of the tested organisms, namely *Phytophthora parasitica* [66].

Antihyperlipidemic and antidiabetic activity

Olibanum gum resin has traditionally been used in the treatment of diabetes in patients and has been recognized with its beneficial effects in a large number of diseases. Several investigations in rat's model showed that BSE of olibanum gum resin significantly decreased total cholesterol and has potential hypolipidemic and hepatoprotective activities [67,68]. A study has also been carried out for comparison between olibanum resin and placebo for the curing of type 2 diabetes in double-blinded clinical trial on 71 patients. They suggested that olibanum gum resin improves glycemic control and lowers the blood levels of glucose, HbA1c, insulin, total cholesterol, and triglycerides [69].

An herbal formulation of *B. serrata* gum resin has been documented to induce powerful hypoglycemic effect by affecting hepatic gluconeogenesis and phosphoenolpyruvate carboxykinase [70]. At different dose levels (25–50 mg/kg. p.o.), the alcoholic extract exhibited antihyperlipidemic activity with hypercholesterolemic animals and lowered cholesterol (30–50%) and triglycerides (20–60%) levels [71]. The past studies and research clearly revealed that *Boswellia* is an effective antihyperlipidemic agent. Hydrophilic portion of BSE enhanced high-density lipoprotein and diminished the concentration of total cholesterol (38–48%) in experimental animals. Zutshi *et al.* observed that Salai guggal retains optimum levels of serum cholesterol and triglycerides in animals, which were fed high cholesterol and saturated fat-rich diet [72]. AKBA has been exhibited to inhibit the activity of nuclear factor kappa B (NF-kB) in atherosclerosis. Liu *et al.* found that AKBA is known to have anti-adipocyte property by virtue of which it induces lipolysis in mature human adipocytes [73].

Antimicrobial and antioxidant effects

Ismail *et al.* reported that the resin extract of Salai guggal powder demonstrated microbicidal activity in different concentration ranges (25, 50, 75, and 100 mg/ml) against of Gram-negative (*Proteus vulgaris, Klebsiella pneumonia, Pseudomonas aeruginosa,* Escherichia *Coli,* and *Enterobacter aerogenes*) and Gram-positive (*Staphylococcus aureus, Bacillus subtilis,* and *Streptococcus pneumonia*) microbes. They observed the inhibition zone and compared with antibiotic ciprofloxacin (5 µg/ml) as positive control and dimethyl sulfoxide as a negative control [74].

Patel and Patel evaluated the antibacterial activity of extracts of *B. serrata* in acetone, water, methanol, and petroleum ether on Gram-negative urinary tract infection pathogens (*K. pneumonia*, *E. coli*, *P. vulgaris*, and *P. aeruginosa*) by disk diffusion method. The acetone extract was found to have significant antibacterial activity against *K. pneumonia* and *E. coli* with minimum inhibitory concentration value of 12.5 µg/µl [75]. Baratta *et al.,* 1998, studied antimicrobial and antioxidant activity and determined the essential oil of *B. serrata* by gas chromatography (GC) and GC–mass spectrometry. The volatile oil portion possessed significant antimicrobial activity against all the test organisms and comparable antioxidant activity to butylated hydroxytoluene and α-tocopherol [76].

Raja *et al*. tested the antibacterial activity of BAs against a variety of pathogenic Gram-negative and Gram-positive bacteria and concluded that AKBA was the most potent constituent with antibacterial potential among all BAs but only against Gram-positive bacteria [77].

Antiasthmatic activity

The resins of *B. serrata* have been described to inhibit leukotriene biosynthesis and have a beneficial effect on respiratory disorders. It is used in massages, bath and treatment of cough, excessive discharge or buildup of mucus in the nose or throat, asthma, and bronchitis.

It was confirmed by Gupta *et al.* (1998) that alcoholic extract of *B. serrata* has remarkable effect in asthma. In a double-blind placebo control clinical study, they studied promising antiasthmatic effect of alcoholic extract of Salai guggal with 70% of the patients showing recovery in physical symptoms and signs of bronchitis and dyspnea. Mobilization of intracellular Ca^{2+} and induction of MAPK were also observed [78,79].

Liu *et al.* investigated the antiasthmatic potential and studied the action of BA in murine model of asthma. They found that the animals treated with the BA could suppress the allergic inflammation, hyperresponsiveness, Th2 cytokines secretion, and ovalbumin-specific IgE [80]. BA was reported to reduce the infiltration of cells, lessen the demolition of lung structure, and attenuate fibrotic lungs by 5-LO inhibition action in an experimental model of pulmonary fibrosis using bleomycin [81].

Antidiarrheal activity

BAs from *B. serrata* were effective in controlling diarrhea without causing constipation in patients with inflammatory bowel syndrome. They also inhibited contraction of intestinal smooth muscles, thereby controlling acetylcholine and barium chloride-induced diarrhea [82].

Anticancer activity

BSE has been shown to halt the brain tumor and breast cancer metastases. BSE comprised 60% BAs have apparently repressed inflammation and tumor in mice. Antineoplastic effect has been investigated in mice with Ehrlich ascites carcinoma and S-180 tumor by interfering with the biosynthesis of DNA, RNA, and protein which caused inhibition in cell proliferation. The potency of BSE against the peritumoral edema can be magnified by enhancing the bioavailability of AKBA [2].

B. serrata showed antitumor effect in diverse types of tumor cells including prostate, colon, leukocytes, brain, and liver. AKBA was found with an inhibitory effect on NF-kB and also potentiated apoptosis and inhibition of angiogenesis in neoplastic cells by signaling transducer pathway and activation of transcription 3-related pathways [43,83-88].

In addition to this, Sinha *et al.* showed *in vivo* Matrigel plug assay that BAs inhibit basic fibroblast growth factor-induced angiogenesis [89].

Ahmed *et al.* studied the potency of *B. serrata* methylene chloride extract against colon cancer induced in animals and also evaluated the serum epidermal growth factor, matrix metalloproteinase (MMP)-9, MMP-7, plasma transforming growth factor-β (TGF-β), and TNF-α levels using ELISA. Cyclin D1 and colon cyclooxygenase-2 (COX-2) expressions were estimated by immunohistochemical technique. Colon cancer group was found with sufficient elevation in cyclin D1 and COX-2 expressions in colon cells, whereas all treatment groups showed marked decrease in cyclin D1 and COX-2 expression. This study reflected the therapeutic role of *B. serrata* against colon carcinoma developed in rats [90].

Pang *et al.* prepared BA nanoparticle formulation for the treatment of prostate cancer. BA nanoparticles caused DNA fragmentation, which is a hallmark of apoptosis [85].

McCarty reported BAs as cancer chemopreventive agents and was found to lessen tumor cell invasiveness and tumor cell motility, to moderate tumor development, and to reduce tumor angiogenesis [91].

Anticomplementary activity

In a study of antibody-coated sheep erythrocytes by pooled guinea pig serum, BAs have been found to inhibit immunohemolysis. Retardation of the C3-convertase enzyme with a threshold concentration of 100 µg of the classical complement pathway caused decreased in immunohemolysis. BA has also showed hindering effect on guinea pig serum by *in vivo* technique [92].

BAs were also found to inhibit hemolysis and chemotaxis of leukocytes and were shown to work by inhibiting the key enzyme of the classical complementary pathway, namely C3-convertase, a serine protease [45,47,48] and were found to possess anticomplementary activity.

Clastogenic activity

The consumption of *Boswellia serrata* is believed to improve memory, learning, performance, and cognitive behavior. It is also recommended for pregnant women to raise the intelligence and memory of their offsprings [93]. Aqueous extract of *B. serrata*, *W. somnifera,* and *Spirulina alga* produced clastogenic effect and was found to be effective in stress relief and memory boost. All these results were recognized to be dose dependent and may be due to the binding of BAs with neurotransmitter signaling pathways or protein kinase pathways in brain [94].

Antidepressant activity

B. serrata has been reported to be efficient in acute model of depression. Prabhakar *et al.* showed that at a dose of 100 mg/kg, *B. serrata* has notable antidepressant activity in acute models of depression and that they lessen the immobility period in forced swim experimental model [95].

Branded formulations containing *B. serrata* [1]

Apart from its use in spiritual ceremonies, *Boswellia* has been practiced as an important adhesive in lotions, creams, perfumes, and detergents, with an oriental note in its scent, in prominent products of the perfume and cosmetic industry. Many preparations with *B. serrata* are assessable in the markets which are elaborated below:

- *Boswellin*®, a certified trademark by Sabinsa Corporation was popularized in the US and European markets in 1991. It is available in tablet or capsule forms and also in a calming pain diminishing cream consisting capsaicin. Product comprises BAs ranging from 150 to 250 mg/capsule or tablet, to be taken orally twice to thrice a day.
- *Niltan*® is a cream formulation for external use, produced by Dr. Reddy's Laboratories Limited, Hyderabad. It is a unification of active herbal extracts (arbutin, boswellin, coriander seed oil, and liquorice extract in a semisolid base). It imparts its action by reducing the enzyme tyrosinase in the skin, also diminishing the level of melanin, which is responsible for darkness of skin.
- *Shallaki*®, each capsule consists of 125 mg *B. serrata*. It has certified anti-inflammatory and analgesic effects advantageous in relieving joint pains, produced by Himalayan Company, Makali, Bengaluru.
- *Rheumatic-X*® consists of 20 mg "Shallaki" along with a number of ingredients, produced by Sunrise Herbals, Banaras (U.P., India), and prescribed for osteoarthritis, gout, rheumatoid, and pain.

CONCLUSION

The present review focuses on the scientific recognition of the remedial usefulness and action of *B. serrata* once used in cultural and religious ceremonies but now valued for its numerous beneficial medicinal effects. BAs are the bioactive phytoconstituents which have demonstrated promising results in numerous experiments and clinical studies. Their medicinal properties are also widely recognized for the treatment of ailments ranging from inflammatory conditions, microbial infections to cancer. In addition to this, its products have been recommended for topical use in the treatment of chronic and excessively damaged skin. Future challenges are toward understanding the drug-drug interactions, molecular mechanism, and development of strategies to improve their pharmacokinetic profile.

AUTHORS' CONTRIBUTIONS

Nameeta Pilkhwal; Department of Pharmacology, Amity Institute of Pharmacy, Amity University, Lucknow Campus, has searched the databases, collected, compiled, analyzed the data, and drafted the review article.

Prof. (Dr.) Suneela S. Dhaneshwar; Director, Amity Institute of Pharmacy, Deputy Dean of Research (S & T), Amity University, Lucknow Campus, has guided Ms. Nameeta for writing this review article and also critically reviewed, redrafted, and revised the same.

CONFLICTS OF INTEREST

Authors have no conflicts of interest to declare.

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