# Boswellia - *Frankincense Plant, Boswellia serrata, Boswellia sacra, Boswellia carterii, Frankincense, Salai Guggul*

## Common Indications

- Inflammation, including Rheumatoid Arthritis
- Chronic Colitis
- Asthma
- Immunomodulator - Tumor and cancer treatment
- Dyslipidemia

**General Comments:**

In Sanskrit, gajabhakshya suggests that *Boswellia spp.* has been ingested by elephants in Ayurvedic medicine since antiquity. Interest in this plant was aroused due to elephants being capable of carrying their weight over a long period of time, yet still outliving humans.[1] Traditionally, internally, it served in the treatment of the abdomen, as a purgative, as a stimulus to take food, liver and bladder ailments, for coughs, poisons, worms, and skin diseases, pain in the arms, and sores. It was known as a skin irritant, which caused better flow of blood, hence its use to stimulate menstruation. Externally, it served in the treatment of stiffness, vessels, joints, wounds of different kinds, inflammatory conditions, pain in the legs, demons, pus, stomach problems, pressure in the ear, and to stimulate birth. The oil was used as an ingredient in embalming liquids for mummification. Burning frankincense was said to enhance spirituality, mental perception, prayer, and consciousness. Burning it is said to produce a psychoactive substance-trans-hydrocannabinol. Chinese Herbalists used frankincense for moving qi/blood, rheumatism, menstrual pain, and as an external wash for sores and bruises.[2,3,4,5,6,7,8]

Uses in Ayurvedic medicine include asthma, rheumatism, chronic ulcers, diseased bones, dysentery, skin ailments, blood purification, bronchial conditions, would treatment, nervous diseases, cervical tuberculosis, lymphadenitis, urinary tract disorders, amenorrhea, dysmenorrhea, sore nipples, ringworm, jaundice, diarrhea, dyspepsia, and hemorrhoids. It was also used to perfume clothes, hair, rooms, and at traditional festivities or religious celebrations.[9,10]

**Benefits & Mechanism of Action:**

Boswellic acids (BAs) effect the production of antibodies and cell mediated immunity.[11] *B. serrata* is rich in BAs.[12] Keto-boswellic acids (AKBA, acetyl-11-keto-ß-boswellic acid, and KBA, 11-keto-ß-boswellic acid) are orally active, direct, and nonredox and non-competitive blockers of 5-lipoxygenase, which is the key enzyme of leukotriene biosynthesis.[11,13] These BAs decrease the pro-inflammatory 5-lipoxygenase products including 5-hydroxyeicosatetraenoic acid (5-HETE) and leokotriene B4 (LTB-4) levels. This increases permeability, therefore a lesser amount of WBCs are needed at the site of inflammation and trauma. As a result, the inflammatory response is dampened, thus allowing for quicker healing.[12] Further, non-steroidal anti-inflammatory drugs (NSAIDS) can cause disturbance of glycosaminoglycan synthesis and this may speed up articular damage in arthritic conditions. It is claimed that *B. serrata* extract may decrease the glycosaminoglycan degradation.[12] The BAs of the gum resin of *B. serrata* have a chemical structure that is similar to other pentacyclic triterpenes, hence their resemblance to anti-inflammatory drugs.

A randomized, blind study done by Fan and colleagues included testing the effects of *B. carterii* Birdw. gum resin on persistent hyperalgesia and edema in rats with peripheral inflammatory pain. They found that *B. carterii* manifested significant hyperalgesia and anti-inflammatory effects. They also assert that the antihyperalgesia could manifest by suppressed inflammation induced Fos protein in the spinal horn neurons of these rats.[14]

A randomized, double-blind placebo controlled crossover study was performed to test *B. serrat's* anti-inflammatory potential.[12] The study included 30 individuals, male and female; 45-72 years of age, with a mean age of 59. These individuals had clinicoradiological osteoarthritis of the knee and were taking NSAIDS and receiving physiotherapy. There were two groups of 15 individuals that got *B. serrata* extract (BSE) of Salki Guggul (Cap WokvelTM, which is manufactured by Pharmanza India) that had 333 mg of BSE(65% organic acids or minimum 40% BAs) in each capsule, or a placebo that had starch powder. Kimmatkar and colleagues did two interventions (four weeks each) where those receiving BSE for the first intervention were crossed over to receive the placebo for the second intervention, and vice-versa. A washout period of 21 days was given before the two groups crossed over.[12] The researchers reported statistically and clinically significant improvement in the BSE group compared to the placebo group as it relates to flexion, knee pain, being more capable of climbing stairs, kneeling, bending, squatting and sitting crossed legged. In general, the knee range of motion was better, there was a decrease in swelling in the knee joint though radiologically there was no change.[12] Kimmatkar and colleagues assert that BSE may help in the treatment of RA, JRA, degenerative diseases of the spine, spondylosis and other arthritis of the joints.

Two studies did clinical trials to test *Boswellia's* anti-inflammatory properties, although they tested combination products that included *Withania somnifera, Zingiber officinale* and *Curcuma longa*.[15,16] For this reason, it is difficult to uncover further, the isolated effects of *Boswellia* on RA.

For the full anti-inflammatory effects it has been recommended that individuals take *Boswellia* with other enzymes such as papain, bromelain, trypsin, chymotrypsin,and losozyme.[17]

Chronic Colitis

Gupta and colleagues conducted a study on the effects of the gum resin of *B. serrata* in individuals with chronic colitis in 1997 and 2001. Each study was a non-randomized. In the recent study, individuals between the ages of 18-48 were treated for six weeks with either *B. serrat* , 900 mg daily in three divided doses or sulfasalazine, 3 g daily in three divided doses. It was found that 18 of the 20 *Boswellia* individuals entered remission while 6 of 10 in the sulfasalazine group did not. Histological improvement of biopsies was noted in 75% of *Boswellia* individuals vs. 40% of sulfasalazine individuals.[13,18] In the earlier study, Gupta and colleagues gave encapsulated powdered *B. serrata* gum resin, 350 mg three times a day or sulfasalzine; 1 g three times daily for six weeks to 42 individuals with ulcerative colitis. Interestingly enough, individuals were allowed to choose their therapy. Outcomes measured included improvement in symptoms of abdominal pain, diarrhea (90% of *Boswellia* subjects and the entire sulfasalzine group), sigmoidoscopic examination, rectal biopsy, histopathology (both groups 75%), stool characteristics, and serum values. It was reported that 82.4% of *Boswellia* individuals and 75% of sulfasalazine subjects went into remission.

Asthma

*Boswellia spp.* may be able to be used as a potential chronic therapy based on its known properties as an inhibitor of leukotriene biosynthesis. Gupta and colleagues performed another trial that was a 6 week, double-blind, placebo controlled study with 80 individuals. They were given either 300 mg powdered *B. serrata* or 300 mg of lactose as a placebo, orally, three times daily. Mean improvements were seen in both groups but improvements in the *Boswellia* group were greater. The median improvement in forced expiratory volume in 1 second (FEV1) was 25% in the *Boswellia* group vs. 5% in the placebo group. The mean forced vital capacity (FVC) improved by 21% in the *Boswellia* group vs. 9% in the placebo group. There was an obvious reduction of dyspnea, eosinophilia, and an absence of rhonchi after treatment in the *Boswellia* group. The number of asthma exacerbations reduced also.[13,18]

Immunomodulator - Tumor and cancer treatment

There are studies that assert boswellic acids as being anti-tumor and anti-carcinogenic.[19,20,21,22,23,24,25,26,27] A study to determine the chemistry and immunomodulatory activity of frankincense oil (*B. carterii*) showed contraction of the phrenic-nerve diaphragm muscle and inhibition of the twitch response to nerve stimulation. It also showed a spasmogenic effect on smooth muscle *in vitro*. These effects may be due to the action on the sarcoplasmic reticulum to increase intracellular calcium and post-junctional block of neuromuscular transmission.[28] During a lymphocyte proliferation (mitogenesis) assay, the oil of *B. carterii* in dimethyl sulfoxide (DMSO) induced a mitogenic response (90% lymphocyte proliferation) that Mikhaeil and colleagues are comparing to *Echinacea purpurea* aqueous extract (85%) and levamisole(85%).[28] Animal studies done in India and the United States suggest that ingesting defatted alcoholic extract of *B. serrata* decreases polymorphonuclear leukocyte infiltration and migration, decreases primary antibody synthesis and causes almost total inhibition of the classical complement and alternate pathway system.[12,29] AKBA and ABA have been shown to have apoptotic effects on malignant glioma cells, cancer cells, human melanoma, neurodermal tumors, and leukemia cells (Altmann, et al., 2000. Xiq, et al., 2005, Syrovets, et al., 2000 and Huang, et al., 2000).[20,22,23]

Also important to note is *B. serrata* being shown to inhibit TNF in human microvascular endothelial cells.[31] It was shown that mice that were given 12-O-tetradecanoylphorbol-13-acetate (TPA) to induce an increase in inflammation, epidermal proliferation, epidermal cell layers, and tumors had an inhibitory effect after being administered boswellin (methanol extract of the gum resin of *B. serrata).* After 7, 12-dimethylbenz[a]anthracene (DMBA) was used to induce tumors in these mice and it was found that the skin tumors decreased by 59-92% (with 1.2-3.6 mg of the extract being applied topically, twice weekly for 16 weeks). The researchers are saying boswellic acid and its derivatives may be cancer chemopreventive and anti-hyperlipidemic agents.[20]

When conventional chemotherapy is given for acute myelocytic leukemia (AML) with cytarabine or daunorubicin administered as single agents, remission is usually provoked. When both substances are used, total remission is seen in 50% of individuals, while 30-40% of individuals go into remission on a single substance. Long term survival that is disease free is only seen in 25-50% of individuals that reach total remission. Most individuals with AML die, hence the researchers desire to study the mechanism of the cytotoxic effect of boswellic acid acetate (BC-4).[23] The boswellic acid and their acetates of *Boswellia serrata* and *Boswellia carterii* Birdw. were separated from their gummy exudates (a 1:1 mixture of α- and ß-boswellic acid acetate). This study was done on six myeloid leukemia cell lines. DNA and morphological fragmentation assays showed that the cytotoxic effect of BC-4 was moderated by the induction of apoptosis. Over 50% of the cells went through apoptosis after treatment with 20 µg/ml of

boswellic acid for 24 hours. The data suggests that BC-4 causes myeloid leukemia cell apoptosis by increasing levels of death receptors, thereby activating capsase-8.[23] Another study done also purified BC-4 from *Boswellia carterii* Birdw. The researchers compared the growth inhibition and differentiation induction of BC-4 in myelocytic leukemia and erythroleukemic cell lines. The study shows BC-4 induced monocyte differentiation of myeloid leukemic cells at a does under 12.5 µg/ml.[21] Jing and colleagues show that BC-4 was a strong inducer, with 90% of the cells showing morphological changes and 80-90% of the cells showing nitroblue tetrazolium (NBT) reduction. BC-4 also increased non-specific and specific esterase (an enzyme that accelerates the hydrolysis or synthesis of esters). BC-4 inhibited growth of all cell lines tested and the growth inhibition effect was dose and time dependent. In HL-60 cells, 20 µg/ml of BC-4 lowered viable cell numbers by 60% at 24 hours. At 3 days there were no biable cells.[21] Again, DNA and morphological fragmentation proved that BC-4 induced cell apoptosis. BC-4 specifically induced myelocytic leukemia cell differentiation at low concentration, and inhibited the growth of all leukemia cell lines tested at high concentration.[21] Jin, Xia, and their colleagues agree that BC-4 is a potent ally in the fight against leukemia.

As stated, boswellic acids have been shown to inhibit leukotriene synthesis via 5-lopoxygenase.[20,32] Hostanska and colleagues tested the ethanolic extract of *B. serrata* gum resin containing boswellic acids (3.68% AKBA, 3.29% KBA, and 5.39 % acetyl BA), for their cytotoxic, cytostatic, and apoptotic activity on five leukemia and two brain tumor cell lines by WST-1 assay and flow cytometry. It was found that the *B. serrata* extract induced dose-dependent anti-proliferative effects on all of the human malignant cells tested. Morphological changes after 24-27 hours, as well as the detection of apoptotic cells confirmed that apoptotic cell death.[32]

Topoisomerases are key enzymes that modify and control the arrangement and topological state of DNA.[22] These key enzymes act by sequential breakage and reunion of either one DNA strand (topoisomerase I) or both DNA strands (topoisomerases II). Replication, recombinant repair, and transcription is allowed to take place by topoisomerase mediated strand passing, which lead to the lowering of DNA twists and supercoiling relief. Rapidly proliferatiging and transformed cells have a greater level of topoisomerases, hence pharmacological inhibition of these enzymes have gotten special appeal after the realization that they are the aim of different anti-tumor and antimicrobial drugs.[22] The researchers' goal in this study was to investigate the mechanism of action of acetyl- BA and show that these compounds are very strong inhibitors of human topoisomerases.[22] It was found that the inhibitory effect of acetyl-BA on topoisomerase I and II αcan be compared to camptothecin and amsacrine or etoposide. Further, their research found that acetyl-BA neither stimulates the organization of DNA- strand breaks in the presence of topoisomerases nor insert into DNA. Their findings show that acetyl-BA impairs the activity of

topoisomerases I and II α through specific interaction with these enzymes and very much suggest that these compounds compete with DNA for binding to topoisomerase. Therefore, Syrovets and colleagues identified acetyl-BA as a unique dual catalytic inhibitor of human topoisomerases.

A document found on the USPTO Patent Full-Text and Image Database found that an ethanolic extract from the gum resin of *B. serrata* was efficient in reducing a peritumoral brain edema 22-48% in one individual. The treatment was given over seven days and thereafter; the treated tissue of the tumor did not show a tendency of proliferation after two weeks.[33] The researchers used a product by the name of H 15, which was a standardized extract of *B. serrata.*

Dyslipidemia

Based on rat studies, It has been shown to lower cholesterol and triglyceride levels *in vivo* and in *vitro*.[4,34]

**Dose:**[4,9,35]

- Gum resin: 2-3 g
- Dried powder: 2-3 g, 2-3 times a day; 250-400 mg, 2-3 times a day; 200-400 mg standardized to 37.5% BAs per dose
- Powdered extract: 4:1 concentrate Bark decoction: 56-112 ml
- Oil: 1-1.5 ml

In aromatherapy, the preferred type of *Boswellia* is the steam distilled oil that is also prepared to put in topical aids.[36,37]

*Boswellia spp.* is taken as a capsule/or tablet, decoction of the bark, or the oil is used. Most of the research had people taking oral capsules/or tablets. The recommended dosage is based on historical practice or available trials. Presently, it is not clear what the optimal dose is to balance safety and efficacy. The manufacturing of *Boswellia spp.* products varies from one produce to the next and this makes it even more difficult for standardization to happen. It is important to note that most of the trials I found used various products made by various manufacturers, so clinical effects may not be comparable.[4,9]

**Standardization:**

- Volatile oils: 4-8%
- Acid resin: 56-65%
- Gum: 20-36%

The volatile oils contain alpha thujene and p-cymene. The resin (guggals) contains a mixture of terpenoids made up of four pentacyclic triterpene acids: ß-boswellic acid (the

most abundant), 3-O-acetyl ß (ABA), 11-keto-ß-boswellic acid, and 3-O-acetyl-11- keto-ß-boswellic acid (AKBA). The triterpenoids are the active constituents and are collectively called boswellic acids. The gum resin of *B. serrata* usually contains 43% boswellic acids. Standardized extracts from commercial sources usually contain 37.5-65% boswellic acids.[5,10,36]

The gum contains arabinose, galactose, xylose, galacturonic acid and digitoxose. The main constituents extracted from the leaves are: D-fructose, D-lactose, D-glucose, L-sorbose, raffionse, raminose, and D-galactose.

**Cautions & Side Effects:**

Boswellia is an emmenagogue, which may induce abortion, it is not recommended to be used during pregnancy.[4,38]

Some experts believe that using it regularly may hide the symptoms of asthma in children and possibly slow down a diagnosis.[4]

Symptoms that may indicate acute toxicity include:

- Skin Reactions - *Boswellia spp.* used in adhesive plasters and perfumes has caused dermatitis in sensitive people. Applying *B. serrata* to the skin may cause contact dermatitis, allergic contact dermatitis, or phytodermatitis.[4,39]
- Gastrointestinal Reactions - *Boswellia* extract has been connected with mild GI upset including abdominal fullness, epigastric pain, gastroesophageal reflux symptoms, diarrhea, hyperacidity and nausea.[13,18,40]

Medication interactions

Medications that can increase the amount of *Boswellia* include:

Medications with increased effects while taking *Boswellia* include:

- Lipid-lowering medications
- Anti-proliferative agents - increased adverse effects[4,21,41]
- Leukotriene inhibitors[42,43]

Medications that can decrease the amount of *Boswellia* include:

- NSAIDS - frequent use COX-2 inhibitors[44]

Medications with decreased effects while taking *Boswellia* include:

- Lipid-soluble medications

Patients with the following disease states or conditions should not use *Boswellia*:

- Pre-existing gastritis
- GERD

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