Boswellic Acid

Related terms:

Resin, Enzyme, Acid, Inflammation, Pain, Leukotriene, Boswellia, Boswellia serrata, Arachidonate 5 Lipoxygenase, Human

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Complementary and Alternative Medicine for Cancer

Narda G. Robinson, in Withrow and MacEwen's Small Animal Clinical Oncology (Fifth Edition), 2013

Boswellia

Boswellic acids exhibit potent antiinflammatory properties in vitro and in vivo. Triterpenes in boswellic acid reduce the synthesis of leukotrienes in intact neutrophils by inhibiting 5-LOX, the key enzyme involved in the biosynthesis of leukotrienes, which mediate inflammation.[85,86] *Boswellia* extracts exert immunomodulatory benefits by simultaneously inhibiting T-helper 1 (Th1) and promoting Th2 cytokine production.[87] They regulate vascular responses to inflammation[86] and stabilize mast cells.[89] In cases of intestinal inflammation, boswellic acids may modulate the adhesive interactions between leukocytes and endothelial cells by countering the activation of leukocytes and/or downregulating the expression of endothelial cell-adhesion molecules.[90,91]

Specific to their anticancer properties, boswellic acids induce antiproliferation, differentiation, and apoptosis in leukemia cell lines.[92-95] They exert cytotoxic effects on established human glioblastoma and leukemia cell lines, as well as on primary human meningioma cells.[96] Boswellic acids may help reduce cerebral edema in patients with brain tumors.[97]

Side effects of boswellic acids include abdominal discomfort, nausea, epigastric pain, hyperacidity,[98] and diarrhea.[99]

The presence of food in the stomach, as well as the type of food eaten, dramatically alters the bioavailability of boswellic acids, and bile acids significantly affect their absorption.[100] When human subjects ingested boswellic acids along with a high-fat meal, the areas under the plasma concentration-time curves and peak concentrations totaled several times higher than when the herbal preparations are taken in the fasting condition. A human study showed that the elimination half-life for *Boswellia* was approximately 6 hours, suggesting that oral administration would require dosing every 6 to 8 hours.[101]

Frankincense extracts, as well as boswellic acids themselves, display moderate-to-potent inhibition of human drug-metabolizing CYP450 enzymes,[102] but the clinical significance and comparative effects on nonhuman P450 enzyme systems remain largely unexplored.

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How to use the monographs

Principles and Practice of Phytotherapy (Second Edition), 2013

Pharmacokinetics

Boswellic acids have also been shown to cross the blood-brain barrier in rats.[75] Permeation studies of Boswellia extract in the in vitro Caco-2 model of intestinal absorption found poor permeability for AKBA and moderate absorption of KBA.[76] Most of these compounds were retained in the Caco-2 monolayer. In rat liver microsomes and hepatocytes, as well as in human liver microsomes, KBA but not AKBA, underwent extensive phase I metabolism.[77] This was verified in vivo, where it was found that KBA undergoes extensive first-pass metabolism, whereas AKBA does not. Hence, metabolism (e.g. deacetylation) is not mainly responsible for the relatively low bioavailability of AKBA.

The human bioavailability of boswellic acids has been established in several pharmacokinetic studies. These indicate that beta-boswellic acid exhibits relatively better bioavailability than KBA and AKBA. Twelve healthy adult men were given capsules containing 333 mg of Boswellia extract after a 7-day washout period.[78] Venous blood samples, drawn at various times after administration of the herb, were analysed for KBA. A mean peak plasma level of 2.72±0.18 μM was reached at 4.50±0.55 h, with an elimination half-life of 5.97±0.95 h. These results suggested that Boswellia is best

taken orally every 6 h and that this should achieve steady-state plasma levels after approximately 30 h.

In a randomised, open, single-dose, two-way crossover study, 12 healthy male volunteers received 786 mg of Boswellia extract either with or without a standard high-fat meal.[79] Plasma concentrations of boswellic acids were measured up to 60 h after oral dosing. Administration in conjunction with a high-fat meal led to a substantial improvement in the bioavailability of the boswellic acids. For example, the maximum concentration for AKBA and KBA respectively was 6.0 and 83.8 ng/mL for the fasted conditions versus 28.8 and 227 ng/mL with food. However, as might be expected, the time at which this and other maxima were reached was delayed by the meal. In contrast, a pilot study involving six healthy volunteers found an average concentration of KBA of 43 ng/mL 2 h after the administration of 500 mg of a Boswellia extract.[80] No relationship to meals was specified.

Steady-state concentrations of boswellic acids in the plasma of Crohn's disease patients receiving 2400 mg/day of a Boswellia extract were 6.35±1.0 μM for beta--boswellic acid, 0.33±0.1 μM for KBA and 0.04±0.01 μM for AKBA.[11]

As part of a method validation process, 10 different boswellic acids were found in the plasma of a brain tumour patient (glioblastoma multiforme) who took 3144 mg/day of Boswellia extract for 10 days.[81] The highest concentration was found for beta--boswellic acid at 10.1 μM.

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Medicinal Plants as Remedies for Gastrointestinal Ailments and Diseases

R. Arora, ... M.S. Baliga, in Bioactive Food as Dietary Interventions for Liver and Gastrointestinal Disease, 2013

2.3 Boswellia serrata

B. serrata is an important Indian medicinal plant, and studies have shown that boswellic acid was effective in various gastrointestinal ailments. Scientific studies have shown it to be effective in ameliorating 2,4,5-trinitrobenzene sulfonic acid (TNBS)-induced colitis in rats (Latella et al., 2008) and in patients with ulcerative colitis (Gupta et al., 1997, 2001). Additionally, studies have shown that the semi-synthetic form of acetyl-11-keto-□-boswellic acid, an active principle of *B. serrata*, also prevented dextran sodium sulfate (DSS)-induced experimental murine colitis as assessed by gross and histological observations (Anthoni et al., 2006). The gum

resin extract is also reported to reduce the electrically, acetylcholine-, and barium chloride-induced contractions in the isolated guinea pig ileum and to inhibit the upper gastrointestinal transit in croton oil-treated mice as well as castor oil-induced diarrhea (Borrelli et al., 2006). Boswellic acids, the active compounds, are also reported to possess antiulcer effects in the pyloric ligation, ethanol/HCl, (acute and chronic) acetylsalicylic acid, indomethacin, and cold restraint stress models of study (Singh et al., 2008).

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Veterinary Herbal Medicine: A Systems-Based Approach

Susan G. Wynn, Barbara J. Fougère, in Veterinary Herbal Medicine, 2007

BOSWELLIA *(BOSWELLIA SERRATA)*:

Extracts of the gum resin possess anti-inflammatory properties. In particular, the boswellic acids inhibit the enzyme 5-lipoxygenase, which is responsible for the production of leukotrienes. Inflammatory bowel disease (IBD) is associated with enhanced leukotriene function, and the benefits of Boswellia in the treatment of patients with chronic colitis (ulcerative colitis) or Crohn's disease have been investigated. A total of 20 patients with chronic colitis received Boswellia gum resin (900 mg/d for 6 wk), and another 10 patients were given sulfasalazine (3 g/d for 6 wk). Of 20 patients treated with Boswellia, 14 went into remission (70%, compared with 40% for sulfasalazine) (Bone, 1999). The safety and efficacy of a Boswellia extract were compared against mesalazine for the treatment of 102 patients with active Crohn's disease in an 8-week, randomized, double-blind study. The authors concluded that the Boswellia extract was as effective as mesalazine (Bone, 2004).

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Nutraceuticals in Arthritis

Ramesh C. Gupta, in Nutraceuticals, 2016

Boswellia serrata Extract

The Boswellia serrata plant is native to India, and its extract has been used as a traditional medicine for centuries. The *B. serrata* extract has boswellic acids, which

provide beneficial health effects. These organic acids consist of a pentacyclic triterpene, a carboxyl group, and at least one other functional group. Alpha-boswellic acid and beta-boswellic acid both have an additional hydroxyl group; they differ only in their triterpene structure. The chemical structure of alpha-boswellic acid is shown in Figure 13.5. One of the six boswellic acids, acetyl-keto-beta-boswellic acid (AKBA), is present at 2–3% of the total extract and is the most important for positive health effects. The extract and/or boswellic acids have been found to be effective in ulcerative colitis, chemically induced hepatic damage, bronchial asthma, and other diseases (Gupta et al., 1998; Kiela et al., 2005; Jyothi et al., 2006; Anthoni et al., 2006). Acetyl-boswellic acids exhibit anti-inflammatory properties by inhibiting leukotriene synthesis (Ammon et al., 1993).

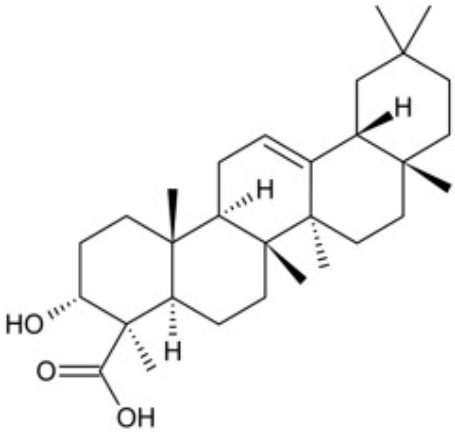

Figure 13.5. Chemical structure of alpha-boswellic acid.

5-Loxin (a patent-pending product of PLT Health Solutions, Inc.), with 30% AKBA as its active ingredient, provides improvement in joint mobility and comfort within 1 week. 5-Loxin provided significant benefits in WOMAC, Huskisson's visual analog scale (VAS), and Lequesne's functional index (LFI) standardized testing methodologies for joint health. It inhibits MMP-3, an enzyme that breaks down cartilage, collagen, and connective tissue. 5-Loxin positively impacts biomarkers of inflammation and arthritis (such as TNF□, CRP, and IL-6). In a recent study, Wang et al. (2014) reported the pharmacokinetics of boswellic acids in arthritic rats and compared these with Huo Luo Xiang Ling Dan (HLXLD), which has 11 ingredients including boswellic acids. The results revealed that there were significant differences in pharmacokinetic parameters between normal and arthritic groups, and the absorptions of two boswellic acids (11-keto-□-boswellic acid and 3-*O*-acetyl-11-keto-□-boswellic acid) were significantly higher in HLXLD than *B. serrata* extract alone. It has been suggested that 5-loxin is safe and well-tolerated in OA.

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Asthma

John D. Mark MD, in Integrative Medicine (Fourth Edition), 2018

Boswellia (*Boswellia serrata*)

Boswellia (also known as salai guggal or Indian frankincense) is a botanical used frequently in Ayurvedic medicine and traditionally used for inflammatory disorders, such as asthma and arthritis. Boswellic acid, the major constituent of *Boswellia,* is thought to inhibit 5-lipoxygenase and leukotriene synthesis, and this may be the mechanism for its antiinflammatory properties. *Boswellia* may enhance the effectiveness of conventional leukotriene modifier medications (see later). A small placebo-controlled study in adults reported that subjects taking *Boswellia* had fewer asthma exacerbations and improved lung function.[26]

Dosage

A common dosage recommendation is 300 mg three times/day.

Precautions

Few precautions have been reported other than occasional gastrointestinal effects, such as epigastric pain, heartburn, nausea, and diarrhea.

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Herbal approaches to system dysfunctions

In Principles and Practice of Phytotherapy (Second Edition), 2013

Topical anti-inflammatories

In addition to immediate, often physical, properties, a number of plants have demonstrated useful anti-inflammatory properties in skin conditions in clinical trials (see also Chapter 8). The known systemic effects of the boswellic acids were tested topically in a double blind placebo-controlled study on the effects of photo-aging on the faces of 15 women, each acting as her own control. The cream containing boswellic acids comparatively reduced measures of photo-ageing skin damage, such as transepidermal water loss and skin thinning over 30 days, sustained after 2 months of followup.[12] It was considered that this benefit involved improved keratinisation and repair in the damaged skin. In another study that claimed to be blinded, 86 patients diagnosed with alopecia areata were divided into treatment and control

groups. The treatment group performed a daily scalp massage with the essential oils Thymus vulgaris (thyme), Lavandula angustifolia (lavender), Rosmarinus officinalis (rosemary) and *Cedrus atlantica* (cedar) in a carrier oil blend of jojoba and grapeseed. They then wrapped a warm towel around the head to aid absorption of the oils. The control group performed the same procedure with only a moderately perfumed carrier oil combination. On a blind double-marking of standardised photographs, 44% of the treatment group showed significant improvement compared with 15% of the control group.[13]

Curcumin from turmeric also has pronounced anti-inflammatory action on the skin. An open label study found that phosphorylase kinase was highly elevated in 10 untreated psoriasis patients and was substantially and significantly reduced to near normal in 10 patients using a topical curcumin (as a 1% gel preparation).[14] A small uncontrolled trial in 12 patients with psoriasis given curcuminoids (4.5 g/day) for 12 weeks found that two of the eight patients who completed the trial had responded to treatment.[15] A larger placebo-controlled trial is necessary, as suggested by the authors. A US dermatologist described the successful outcomes of a number of cases treated with topical curcumin in the same gel preparation referred to above (see turmeric monograph for more details).[16]

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Selected herbal supplements and nutraceuticals

Manashi Bagchi, ... Debasis Bagchi, in Reproductive and Developmental Toxicology, 2011

Boswellia serrata

The novel anti-inflammatory properties of the gum resin derived from Boswellia serrata, also known as Salai guggal in Ayurvedic medicine, are well recognized and highly recommended for human consumption. The active constituents of the gum resin are boswellic acids. Among the boswellic acids, 3-acetyl-11-keto-beta-boswellic acid (AKBA) potently inhibits 5-lipoxygenase product formation with an IC_{50} of 1.5 μM. The genetic basis of the anti-inflammatory effects of Boswellia was explored in a system of TNF□-induced gene expression in human microvascular endothelial cells. Boswellia significantly prevented the TNF□-induced expression of matrix metalloproteinases and adhesion molecules (ICAM-1 and VCAM-1), and inducible expression of the mediators of apoptosis. With such interesting findings, we plan to determine the broad spectrum safety of Boswellia.

Acute oral, acute dermal, primary skin and eye irritation, and dose-dependent 90-day subchronic toxicity studies were conducted. In safety studies, acute oral LD_{50} of Boswellia was found to be greater than 5,000 mg/kg in both male and female Sprague-Dawley rats. No changes in body weight or adverse effects were observed following necropsy. Acute dermal LD_{50} of Boswellia was found to be >2,000 mg/kg. Primary skin irritation test was conducted with Boswellia on New Zealand albino rabbits and Boswellia was classified as non-irritating. A primary eye irritation test was conducted on rabbits and Boswellia was classified as mildly irritating to the eye. A dose-dependent 90-day subchronic toxicity study demonstrated no significant changes in selected organ weights individually and as percentages of body and brain weights. Boswellia supplementation did not cause changes in hepatic DNA fragmentation on 30, 60 or 90 days of treatment. Hematology, clinical chemistry and histopathological evaluations did not show any adverse effects in all organs tested. Taken together, these results demonstrate the broad spectrum safety of Boswellia (Lalithakumari *et al.*, 2006).

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Dosage and dosage forms in herbal medicine

In Principles and Practice of Phytotherapy (Second Edition), 2013

Analytical methodology

One weakness of some standardised extracts on the market is the poor or inappropriate choice of the analytical methodology employed to measure the marker compound(s). A number is only as consistent, reliable or relevant as the technique used to measure it. This is particularly evident for standardised extracts from Ayurvedic or Chinese herbs, but is by no means confined to these.

The following examples will serve to illustrate some aspects of this issue. *Boswellia serrata* extract is standardised to boswellic acids which, because of their anti-inflammatory activity, are important as marker compounds. However, for the majority of extracts on the market the level of boswellic acids is determined by simple acid-base titration. This method will measure the level of any acid in the extract, so an unscrupulous manufacturer could readily add a fruit acid that would result in a false and elevated reading for boswellic acids.

Sometimes gravimetric methods are used to standardise extracts. Here the attempt is to isolate the marker compound from the extract and weigh it. However, the

isolation techniques used are generally quite crude and the methodology is consequently prone to much interference. This problem is exemplified by an extract of Andrographis paniculata which was supposed to contain 10% andrographolide (determined by a gravimetric technique) but by a more accurate method was found to contain no andrographolide whatsoever. Another example is a *Tribulus terrestris* extract certified to contain 40% saponins (gravimetric), but which contained about 4% when a more accurate analytical technique was applied.

Even the popular St John's wort standardised extract is not free of this problem. The determination of 'total hypericin' is usually based on a method from the DAC (German Pharmaceutical Codex). But there are two methods found in different editions of the DAC. The earlier method will give a number for total hypericin that is about 25% higher than the later, preferred method. However, some manufacturers intentionally base the level of 'total hypericin' in their St John's wort extract on the earlier, outdated method in order to inflate the value. Both these methods give a higher level of total hypericin than that obtained by HPLC (high performance liquid chromatography).

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Herbal and Nutritional Supplements for Painful Conditions

Andrea H. Zengion ND, MSAOM, Eric Yarnell ND, in Pain Procedures in Clinical Practice (Third Edition), 2011

Boswellia serrata (Frankincense)

Boswellia acts as an antiinflammatory by its inhibition of 5-lipoxygenase, although it has no apparent effect on cyclooxygenase. Because it is a resin, it is relatively hydrophobic and must be tinctured by using a menstruum with high ethanol content. In Chinese herbal medicine, *Boswellia carterii*, a similar species, is an important herb for treatment of pain and healing of ulcers and is often paired with myrrh. Extracts may be standardized to 37.5% to 65% boswellic acids (considered to be the active constituents), although it may also be taken as crude herb in pill or capsule form, or, in Chinese herbal medicine, used topically or added in small amounts to decoctions of other herbs. Adverse effects may include gastrointestinal symptoms because tannins are sometimes difficult to digest.

Osteoarthritis: *B. serrata* increases joint flexion and reduces pain in knee osteoarthritis. Compared to valdecoxib, *Boswellia*'s therapeutic activity had a

slower onset but persisted longer (valdecoxib's effects did not persist after cessation of therapy, whereas the *Boswellia* group maintained improvement up to 1 month after cessation). *Boswellia* administration resulted in statistically significant improvement of pain, stiffness, and ability to perform daily activities.[49] A double-blind, placebo-controlled clinical trial for 5-loxin, a *Boswellia* extract enriched with 30% 3-*O*-acetyl-11-keto-beta-boswellic acid (AKBA) found that, administration of the drug resulted in statistically significant reduction of pain, improvement of functional ability, and reduction in levels of matrix metalloproteinase-3 in synovial fluid. Diarrhea, abdominal pain, nausea, mild fever, and weakness were reported as adverse effects.[50]
Collagenous colitis: A small study demonstrated greater clinical remission rate with administration of *Boswellia* extract than with placebo after 6 weeks of treatment.[51]
Dosage: 150 to 400 mg boswellic acid taken three times daily.
Caution/contraindications: Caution: may cause contact dermatitis or mild diarrhea or urticaria.[21]

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