



# HerbClip™

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**File: ■ Frankincense (*Boswellia* spp.)**  
**■ Medicinal Uses**  
**■ Boswellic Acids**

**HC 011064-407**

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**RE: *Boswellia* Resin Activity Involves More than just Boswellic Acids**

Moussaieff A, Mechoulam R. *Boswellia* resin: from religious ceremonies to medical uses; a review of in-vitro, in-vivo and clinical trials. *J Pharm Pharmacol*. Oct. 2009;61(10):1281-1293.

Frankincense (*Boswellia* spp.) resin has been used as incense in religious ceremonies for thousands of years. The medicinal uses of frankincense resin include the treatment of inflammatory conditions,<sup>1</sup> wounds, and skin conditions. Over 200 compounds have been isolated from frankincense resin.

The anti-inflammatory effects of frankincense resin have been attributed to the boswellic acids and their derivatives: acetyl- $\beta$ -boswellic acid (ABA), 11-keto- $\beta$ -boswellic acid, and acetyl-11-keto- $\beta$ -boswellic acid (AKBA). Some studies have found the anti-inflammatory effects of whole frankincense resin are greater than those of purified boswellic acids. After bioassay-guided fractionation of *Boswellia carteri* resin, the authors of this review discovered that the fraction containing boswellic acids did not affect inhibitory  $\kappa$ B $\alpha$  (I $\kappa$ B $\alpha$ ) protein degradation, which is involved in the activation of nuclear factor  $\kappa$ B (NF- $\kappa$ B). NF- $\kappa$ B is an inducible transcription factor involved in immune response, carcinogenesis, and inflammation. They found that the frankincense compounds incensole acetate and incensole indirectly inhibit I $\kappa$ B $\alpha$  degradation and cytokine- and lipopolysaccharides (LPS)-mediated NF- $\kappa$ B activation. One study has found that frankincense extract affects 113 of 522 genes known to be induced by tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), an inflammatory cytokine. The study also showed that frankincense extract blocked the expression of matrix metalloproteinases and mediators of apoptosis induced by TNF- $\alpha$ .

The authors write that the anti-inflammatory effect of frankincense resin "probably involves boswellic acids to some extent," but incensole acetate and its derivatives may be "the major anti-inflammatory constituents of *Boswellia carterii* [sic] resin." Incensole acetate has also been shown in vitro to inhibit cytokines downstream of NF- $\kappa$ B activation, including interleukin-1 $\beta$  (IL-1 $\beta$ ), IL-6, TNF- $\alpha$ , and prostaglandin E2. An ethanolic extract of *B. serrata* and one of its constituents, AKBA, inhibits the activity of 5-lipoxygenase, an enzyme which oxidizes arachidonic acid (AA), and  $\beta$ -boswellic acid antagonizes this effect. Studies have suggested "that the immunomodulatory effects of boswellic acids are not all inhibitory." Boswellic acids, notably AKBA, have been shown to inhibit cyclooxygenase-1 (COX-1) and less efficiently COX-2 activity, and incensole acetate has been shown to inhibit COX-2 activity in pre-clinical studies. Boswellic acids, including AKBA, also activate p42 and p38 mitogen activated

protein kinases (MAPKs). Calcium ions are involved in the MAPK activation and in the inhibition of 5-lipoxygenase by AKBA.

Extracts of *Boswellia* spp. and boswellic acids have been shown in vitro to potently and non-selectively inhibit cytochrome P450 (CYP) metabolic enzymes 2C8/2C9 and 3A4 and inhibit P-glycoprotein (Pgp) efflux transporter protein, which could cause interactions with their drug substrates. Boswellic acid derivatives have been shown to induce apoptosis (programmed cell death) in multiple cancer cell lines. AKBA has a selective pro-apoptotic effect on cancer cells, and does not induce apoptosis in normal human lung fibroblasts. The mechanism of action for the pro-apoptotic effects of boswellic acids may involve the inhibition of topoisomerase or inhibition of NF- $\kappa$ B. AKBA inhibits angiogenesis in vivo. Incensole acetate has been shown to potently activate the transient receptor potential cation channel, subfamily V, member 3 (TRPV3).

In vivo studies have confirmed the acute and chronic anti-inflammatory effects of frankincense resin extract. In vivo studies have also demonstrated anti-arthritis effects, including reduction of arthritis in rabbits and a reduction in the degradation of glycosaminoglycans by boswellic acids. A commercial *Boswellia serrata* extract (H15) and AKBA have been shown to reduce indomethacin-induced ileitis in rats, and AKBA has been shown to improve colitis effects in mice. AKBA has also been shown to prevent experimental diarrhea and normalize intestinal motility in mice. AKBA has been shown to reduce the size of atherosclerotic lesions in mice, possibly through NF- $\kappa$ B inhibition. In vivo studies have also demonstrated prolonged survival times and reduced tumor volumes in rats inoculated with C6 glioma cells and treated with boswellic acids.

Topical application of AKBA- $\gamma$ -cyclodextrin has shown anticancer effects, including the concentration-dependent inhibition of proliferation and tumor growth and the induction of apoptosis. Studies have indicated that frankincense resin also possesses antimicrobial effects on biofilms in vitro. *B. carteri* resin possesses neuroprotective effects shown by the authors in mice that "can be attributed, at least partially, to incensole acetate and its derivatives." Animal studies indicate that an extract of *B. serrata* has sedative and analgesic effects. The authors of this review have demonstrated that incensole acetate possesses anxiolytic, anti-depressive, and sedative effects in vivo. The compound does not bind to any of the known pharmacological targets, but it activates the TRPV3 channel in vitro. The sedative effect, but not the anti-depressive and anxiolytic effects, was observed in TRPV3-null mice.

"Although *Boswellia* resin seems to exert anti-inflammatory and anti-cancer effects in several clinical trials, these remain to be further corroborated and underlying mechanisms are to be characterized." Small clinical trials demonstrate that *B. serrata* resin may be beneficial in the treatment of inflammatory conditions such as bronchial asthma and chronic colitis.<sup>2</sup> The 5-Loxin® *B. serrata* extract with 30% AKBA (distributed by PL Thomas & Co. Inc.; Morristown, New Jersey; manufactured by Laila Nutra; Vijayawada, India) has been shown to reduce pain and improve physical functioning in patients with osteoarthritis. A small study has found that the H15 *B. serrata* extract reduces edema, but not tumor size, in 2 of 7 patients with glioblastoma brain tumors and progressive edemas; this resulted in clinical improvement and was well-tolerated. There has been a single case report of contact dermatitis associated with topical *B. serrata* resin. Other studies have found that *B. serrata* resin is well-tolerated in human subjects with the exception of mild adverse gastrointestinal effects. They note that boswellic acids are not well absorbed, but failed to mention that absorption is much greater when taken with a high-fat meal as compared to fasting.<sup>3</sup>

Research indicates that frankincense gum resin possesses immunomodulatory and anti-inflammatory effects. Additional clinical trials are needed to confirm the biological effects of frankincense gum resin. Research on the wound-healing properties of frankincense gum resin is also warranted.

—Marissa Oppel-Sutter, MS

#### References

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