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Boswellia: NSAID Alternative © NIE

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Boswellia serrata (frankincense) is a large tree that grows in the dry and hilly parts of India. There are several other *Boswellia* species found in Eastern Africa and Southern Arabia. The gum resin, an exudate of the tree, usually obtained by incisions made in the tree's bark, has been used in the ancient medical systems of India (Ayurveda) and China for the treatment of inflammatory and chronic degenerative diseases. Since ancient times frankincense has also been used in cosmetic preparations and perfumes, and also as a fixative in soaps, creams, lotions and detergents.

The chief anti-inflammatory effect of boswellia gum resin has been investigated more recently and is believed to be related primarily to the inhibition of leukotriene synthesis, specifically involving the enzyme, 5-lipoxygenase. This biological property of boswellia gum resin was found due to its content of pentacyclic triterpinic acids (i.e. beta boswellic, acetyl beta boswellic, 11-keto beta boswellic, and acetyl 11-keto beta boswellic acids). These compounds have been listed here in order of their increasing inhibitory effects on 5-lipoxygenase and the synthesis of pro-inflammatory leukotrienes.

Boswellic Acids as NSAIDs

Boswellic acids have recently emerged as effective non-steroidal anti-inflammatory compounds

Boswellia Shown Effective in OA of Knee

A randomized, double-blind placebo-controlled study was conducted at Indira Gandhi Medical College, Nagpur, India, to assess the efficacy, safety and tolerability of *Boswellia serrata* extract from Geni Inc. in 30 patients with osteoarthritis (OA) of the knee. Two groups of 15 patients each were randomly allocated to receive either a 333 mg capsule of *Boswellia serrata* or a placebo three times a day, for eight weeks. After this intervention, a wash out period of 21 days was followed. Then the patients were crossed over to receive the opposite intervention.

Patients were asked to assess the severity of pain, loss of function and swelling at the start and completion of both the interventions—X-rays were also taken at the same time.

(NSAIDs) without NSAIDs' characteristic gastrointestinal side effects. Compared experimentally with the anti-inflammatory drug phenylbutazone, boswellic acids did not produce injury to the gastrointestinal mucosa.

The safety of boswellic acids should be emphasized since even the most popular NSAID, aspirin, although much better tolerated than its parent compound salicylates, still has serious side effects, such as gastrointestinal irritation and bleeding which limit its long-term use. In addition, aspirin is contraindicated in patients who have experienced asthma, urticaria (general allergic reactions), and should be administered with caution in children and teenagers due to the risk of Reyes syndrome.

There is an increasing body of evidence that standardized boswellic acids have been found effective in typical NSAID applications in alleviating rheumatoid arthritis and osteoarthritis. In one clinical study a standardized extract of boswellic acids (200 mg thrice daily [tid]) was evaluated in a four-week double-blind, crossover trial in 30 patients suffering from rheumatoid arthritis. The mean arthritic score (sum of symptoms) and the biochemical index of inflammation in the group receiving boswellic acids came down significantly after the treatment. However, when the placebo was substituted (crossover), the subjective and objective indices of arthritis rose again.

In another 20-patient, double-blind, crossover study a boswellia gum resin extract (200 mg tid) combined in an herbomineral formula was evaluated in the treatment of rheumatoid arthritis and separately in osteoarthritis. Active and placebo treatments were given for a period of three months. After a washout period of two weeks the regimens were crossed-over.

All the patients receiving *Boswellia serrata* extract treatment reported decrease in knee pain, increased knee flexion, and increased walking distance. The frequency of swelling in the knee joint was also decreased. When these findings were compared to the baseline data and effect obtained with placebo, the findings with *Boswellia serrata* extract were statistically significant (Wilcoxon signed rank test). Radiologically, there was no change in the findings.

A long-term study has been planned to evaluate its effect on progression of osteoarthritis of the knee.

From these preliminary findings, *Boswellia serrata* extract may be recommended for those with osteoarthritis knees as an anti-inflammatory, with possible therapeutic use in other forms of arthritis such as juvenile rheumatoid arthritis, rheumatoid arthritis, ankylosing spondylitis, degenerative diseases of the spine and osteoarthritis of other joints.

The three-month active therapy resulted in a significant decrease in severity of pain, morning stiffness, improved joint mobility score, grip strength score and the overall disability score compared to the placebo group. The biochemical index of inflammation was also significantly improved due to the treatment.

Ulcerative colitis is an example of a chronic inflammatory process in the intestinal tract, which may be caused and/or aggravated by excessive leukotriene production. Effects of *Boswellia serrata* gum resin (350 mg tid for 6 weeks) vs. the NSAID sulfasalazine was studied in patients with ulcerative colitis. The tested parameters, including stool properties, histopathology of rectal biopsies, and blood biochemistry improved after treatment with the gum resin. As a result of the treatment, 82 percent of patients went into remission, as compared to a 75 percent remission rate obtained with sulfasalazine.

Boswellic acids were also tested in the management of asthma, since a new generation of anti-asthmatic drugs are based on the premise of being leukotriene inhibitors. In a double blind, placebo-controlled study 40 patients with several years' history of bronchial asthma were treated with 300 mg tid of boswellia gum resin for six weeks. Seventy percent of the patients responded to the treatment as evidenced by a reduction in respiratory symptoms of asthma such as number of attacks and improvement in lung tests and blood biochemistry. Only 27 percent of the patients receiving placebo showed clinical improvement.

The anti-inflammatory properties of boswellic acids can also yield interesting applications for topical and cosmetic use. Boswellia cream for the management of inflammatory conditions has been available for several years in the U.S. market. Its therapeutic composition includes approximately 5 percent boswellic acids, 0.025 percent capsaicin, an extract of *Capsicum annum* fruits (fam. Solanaceae), a botanical recognized by the U.S. FDA for its analgesic properties, and 10 percent methyl salicylate.

New Research Directions

Due to known overlaps in anti-inflammatory and anti-cancer mechanisms, the potential chemopreventive and therapeutic effects of boswellic acids have been explored. In one clinical study the therapeutic effect of boswellic acids (1200 mg per day for seven days) in the management of certain types of brain tumors (i.e. malignant glioma), has been described and anti-proliferative and apoptosis (programmed cell death) promoting effects in human leukemic cells in vitro have been demonstrated.

Sabinsa Corporation has recently undertaken a cooperative effort with one of Europe's leading universities in evaluating purified boswellic acids as potential anti-cancer compounds in hepatocellular (liver cancer) cancer and adenocarcinoma of the colon. The specific focus of these studies is to investigate the role of boswellic acids in inducing apoptosis of cancerous cells.

One of the prominent mechanisms of regulating apoptosis is through a group of cell enzymes called caspases. The role of these enzymes is to inactivate mechanisms in the cell that prevent apoptosis. In these studies, boswellic acids, especially acetyl 11-keto beta boswellic acid, have shown strong apoptotic effects in human liver and colon carcinoma cells in vitro, by activating specific caspase enzymes.

In another study, feeding mice with a diet supplemented with standardized boswellic acids (0.2 percent in the diet) prevented formation of aberrant crypts in the colon, which are changes in the colon epithelium that may lead to cancer formation. Further studies may prove that pure boswellic acids have potential as safe and broad-acting cancer chemopreventive, as well as therapeutic agents.

Standardization of Boswellic Acids

The safety, efficacy and predictability of boswellic acids in nutraceutical use as discussed above depends on a standardized composition of the preparations. In a quest to evaluate boswellic acids scientifically, Sabinsa has developed HPLC methods to analyze, standardize and validate the activity of boswellia extracts for the four main beta boswellic acids, as well as total boswellic/organic acids.

Prior to the industrial use of the HPLC, the predominant method of analysis to determine boswellic acids in nutraceuticals was a titrimetric evaluation giving a total organic acids content, not specific boswellic acids. The titrimetric method, including all organic acids, typically gives higher readings of "boswellic" acids as compared to an actual value of boswellic acids obtained by the HPLC method. For example, a reading for a given batch of boswellic acid analyzed by Sabinsa showed a total boswellic acids content of 25.8 percent by HPLC, and a corresponding total organic acids content of 70.33 percent by the titrimetric method.

A precise method of analyzing such a composition is essential to its standardization. This is of particular importance in view of the emerging applications boswellic acids show evidence of in health conditions ranging from minor to chronic inflammation, to chemoprevention, where prolonged administration of a safe and predictable product is required. **NIE**

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