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**Boswellic Acids: Potent Active Ingredients from a Traditional Remedy**

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**Abstract**

For thousands of years gum resin from the Boswellia serrata tree has been valued in diverse parts of the world. In eastern countries, it is known as "salai guggal" and in western countries it is known as "frankincense". Traditional ayurvedic medicine called for the gum to be used in the treatment of various inflammatory conditions of the skin, eye and gums, as well as respiratory disorders such as asthma, bronchitis, and laryngitis. And still today, medical practitioners in India use boswellia to treat arthritis, pain and respiratory ailments.

Modern analytical techniques have combined to unlock the chemical mysteries of the ancient remedy. And a continually-expanding knowledge of cellular biology has provided an explanation as to why the remedy has remained popular for centuries.

Recent research in Germany and India has shown that the pentacyclic triterpenoids present in Boswellia inhibit human leukocyte elastase and also block production of pro-inflammatory leukotrienes by inhibiting 5-lipoxygenase. Two of the compounds in the series, acetyl-11-keto-boswellic acid and 11-keto-boswellic acid, have been shown to be the most potent of the triterpenoids.

Personal Care formulators who want to take advantage of the anti-inflammatory and anti-aging potential of Boswellia serrata gum resin will find it is not appropriate for use because it has a strong odour and contains potentially sensitizing components. Depending on the purification methods used, extracts of Boswellia can contain mixtures of numerous compounds. However, an ultra-refined extract is now available that delivers very high concentrations (95%) of the two most potent compounds, in a convenient low-odour powder, with substantiation that supports anti-inflammatory and anti-elastase activity.

**Biological Activity of Boswellic Acids**

Inflammation is caused by a number of inflammatory mediators including histamine, cytokines, prostaglandins and leukotrienes. The leukotrienes are produced from arachidonic acid via 5-lipoxygenase. Inhibitors of 5-lipoxygenase effectively reduce inflammatory conditions such as topical irritation, arthritic conditions and respiratory ailments. Typical 5-lipoxygenase inhibitors are non-specific anti-oxidant based compounds such as nordihydroguaiaretic acid (NDGA) and caffeic acid esters.

Boswellic acids are a series of pentacyclic triterpenes from the gum resin of Boswellia serrata tree. These compounds have a history of anti-inflammatory activity and have been shown to be potent inhibitors of leukotriene biosynthesis, namely leukotriene B₄. As noted earlier, leukotrienes are produced from arachidonic acid via 5-lipoxygenase (5-LO); therefore it is understood that the boswellic acids inhibit the 5-lipoxygenase enzyme. Safayhi was able to demonstrate that the boswellic acids inhibit 5-lipoxygenase by an enzyme-directed, non-competitive, non-redox mechanism by binding to a pentacyclic triterpene selective effector site. Safayhi and Sailer reported that acetyl-11-keto-boswellic acid and 11-keto-boswellic acid were the most potent 5-lipoxygenase inhibitors of the series, with IC₅₀ values of 1.5 µM (0.7 ppm) and 3.0 µM (1.4 ppm), respectively. (The IC₅₀, called the half maximal inhibitory concentration, represents the concentration of a substance that is needed to inhibit fifty percent of an enzyme activity.)

Because of their potent anti-inflammatory activity the boswellic acids were evaluated for their effect on the Complement System, which is involved in inflammatory disorders ranging from rheumatoid arthritis to anaphylaxis. The boswellic acids were able to inhibit hemolysis and chemotaxis of leukocytes and were shown to work by inhibiting a key enzyme of the Classical Complementary pathway, namely C3-convertase, a serine protease. Kapil showed that acetyl-11-keto-
boswellic acid and 11-keto-boswellic acid, were as effective in this respect as aspirin at the same dose.

Neutrophil stimulation, resulting from inflammatory and hypersensitivity reactions, results in more than the formation of pro-inflammatory leukotrienes. It also causes the release of proteolytic enzymes such as human leukocyte elastase. Elastase and other proteolytic enzymes disrupt skin tissue and cause the redness, swelling and oedema that are characteristic of inflammation.

Acetyl-11-keto-boswellic acid and 11-keto-boswellic acid have been reported to inhibit elastase in a dose dependent manner with IC$_{50}$ values in the µM range. These two boswellic acids are reported to be more effective than typical elastase inhibitors such as ursolic acid, which lacks the ability to inhibit 5-lipoxygenase$^7$.

In addition to inhibiting human leukocyte elastase, the boswellic acids have been reported to prevent the breakdown of glycosaminoglycans (GAGs) by inhibiting glycohydrolases such as beta-glucoronidase and beta-acetylglucosamidase$^{11}$. Inhibition of GAGases prevents damage to the extracellular matrix of the skin. Reddy$^{11}$ also showed that the boswellic acids inhibit cathepsin D, a chymotryptic enzyme present in the stratum corneum that is reported to be involved in human epidermal desquamation$^{12}$.

Although the proven anti-inflammatory benefits associated with Boswellia serrata are appealing to Personal Care formulators, the gum resin produced by the tree is not acceptable because of high odour and potentially sensitizing components.

Considerable refinement is needed to make this ingredient viable for use in anti-aging cosmetic products.

**Boswellic Acids in ViaPure™ Boswellia**

Boswellia gum resin and crude extracts currently on the market contain more than fifteen compounds including mono-, di-, and triterpenes. Many of the monoterpenes present in crude extracts (such as thujone) are known sensitzers. Over eleven pentacyclic triterpenes have been identified but, as noted before, the most potent anti-inflammatories are reported to be acetyl-11-keto-boswellic acid and 11-keto-boswellic acid.

One commercially available product, ViaPure™ Boswellia, is highly refined. A unique extraction and refinement process purifies only these two important constituents, resulting in a product containing a minimum of 95% acetyl-11-keto-boswellic acid and 11-keto-boswellic acid (Figure 1).

A series of experiments has been conducted to confirm the anti-inflammatory and anti-elastase activity of the refined product, ViaPure™ Boswellia. These are described below.

**Inhibition of Leukotriene B$_4$ Release from Neutrophils**

The ability of ViaPure™ Boswellia to inhibit release of Leukotriene B$_4$ from human neutrophils has been studied. Neutrophils were isolated from the blood of healthy donors and stimulated with calcium ionophore. Leukotriene B$_4$ (LTB$_4$) released by stimulated neutrophils was measured with a specific enzyme immunoassay (EIA) kit. ViaPure™ Boswellia was added to the isolated cells and evaluated for ability to

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![11-keto-boswellic acid](image1)

![Acetyl-11-keto-boswellic acid](image2)

Figure 1
inhibit LTB₄ release. The results show that a concentration of only 10 ppm, Via Pure™ Boswellia inhibits 95% of LTB₄ release, indicating that this is extremely potent inhibitor of a pro-inflammatory compound (Table 1).

### Inhibition of LTB₄ Release from Activated Neutrophils (Average of 3 trials)

<table>
<thead>
<tr>
<th>Leukotriene B₄ picogram/ml</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12000</td>
</tr>
<tr>
<td>ViaPure™ Boswellia 10 μg/ml</td>
<td>619</td>
</tr>
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Table 1

**Inhibition of Elastase Activity**

In a study similar to the one described above, the ability of ViaPure™ Boswellia to inhibit elastase released from human neutrophils was examined. Again, neutrophils were isolated from the blood of healthy donors and stimulated with calcium ionophore in the presence and absence of ViaPure™ Boswellia. Elastase activity was measured by the release of p-nitroaniline from a MeO-Suc-Ala-Ala-Pro-Val-p-nitroaniline substrate. The result shows that 10 ppm ViaPure™ Boswellia strongly inhibits the activity of elastase released from stimulated human neutrophils. (Table 2). ViaPure™ Boswellia was further evaluated for its ability to inhibit human leukocyte elastase activity over the range of 0 to 10 ppm. The reaction rate (Vmax) was determined for enzyme inhibition and ViaPure™ Boswellia was shown to be a potent inhibitor with an IC₅₀ of 1.8 ppm. This result is ten times more potent than the industry standard, ursolic acid (Figure 2).

It is important to note that elastase inhibitors like ViaPure™ Boswellia, in addition to blocking inflammatory proteolytic activity, have another cosmetically-relevant benefit. They have been shown to increase skin firmness.

### Safety Evaluations

Singh13,14 has evaluated and reported on the safety and efficacy of the boswellic acids in acute, sub-acute and chronic models. His work provides a favourable framework for the cosmetic industry, as he cites the lack of adverse effects, lack of eye irritation, no adverse behavioural changes and an LD50 > 2g/kg.

### Chemical Analysis of ViaPure™ Boswellia

LC-MS analysis using negative ion mode electrospray ionization confirmed the presence of 11-keto-boswellic acid and acetyl-11-keto-boswellic acid, with molecular weights of 470 and 512 respectively, in ViaPure? Boswellia.

Comparison of ViaPure™ Boswellia and another commercial product, using reversed-phase C-18 HPLC, shows that the ViaPure™ product is much more highly refined, comprising more than 95% acetyl-11-keto-boswellic acid and 11-keto-boswellic acid (Figure 3) as shown on the next page.
Conclusion

Modern research and analytical techniques have combined to unlock the chemical mysteries of a traditional ayurvedic anti-inflammatory medicine. The ancient remedy contains pentacyclic triterpenoid components that have been shown to block production of pro-inflammatory leukotrienes and inhibit human leukocyte elastase. The two most potent components have been isolated, refined, and studied extensively.

Using this knowledge, ViaPure™ Boswellia was developed for use by the Personal Care Industry. It is a convenient low-odour high-purity powder whose claim substantiation supports anti-inflammatory and anti-elastase activity. It is recommended for use in topical products designed for soothing relief of sensitive skin, treatment of chronic or excessively damaged skin, protection of the skin’s extra cellular matrix and skin firming.

References

**Authors’ Biographies**

Jon Anderson, Ph.D.

Dr. Jon Anderson has dedicated his academic and industrial careers to the discovery and development of high purity bioactives from natural sources for human and animal health care. Jon spent 8 years at Purdue University School of Pharmacy, Department of Medicinal Chemistry and Pharmacognosy as a graduate student, Post-doctorate, and Research Scientist working on bioactive compounds from higher plants. In 1992 he joined Estee Lauder and as Senior Principal Scientist worked on developing novel high purity ingredients for skin treatment products. While his academic training focused on the search for anti-cancer compounds and agrochemicals, his industrial work has broadened that focus to include anti-inflammatories, anti-allergens, antioxidants, protease inhibitors, modulators of proliferation and differentiation, and other pathways pertinent to skin treatment. In 2000 Dr. Anderson joined Bill Williams to form Actives International LLC. With research efforts in laboratories in New Jersey, Jon heads up the development of prototype active ingredients and coordinates outside manufacturing with partner companies around the world. Recognized as an industry leader, Dr. Anderson is a frequent speaker at scientific meetings on Pharmacognosy, Microbiology, and Cosmetic Chemistry. His achievements include 7 patents, 25 peer-reviewed scientific publications and 20 scientific podium presentations. Jon continues his interest in understanding and using the chemistry of plants, marine products and fermentations.

Mary Davis earned a BS degree in chemistry, with honours, from the University of Delaware. She also holds an MBA from the University of North Carolina, and has taken extensive courses in Finance and Internet Business Systems. Mary’s career has focused on the Personal Care Industry. She has formulated skin and cleansing products for several retail manufacturers, including Avon Products and has extensive experience in the supply side of the industry. She worked at ICI Americas (now Uniqema) as a Senior Development Chemist, at Van Dyk as Technical Business Manager, and at International Specialty Products as Global Director of Skincare Marketing. Most recently, Mary served as Director of Consumer Products at Genencor (now part of Danisco). Mary joined Actives International in 2006 as Director of Marketing and Technical Services. She is a frequent speaker at industry meetings and is active in the Society of Cosmetic Chemists.

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