Boswellin

Keywords

Boswellia serrata
Anti-inflammatory
Boswellic acid
AKBBA

Summary

One of the most famous and powerful anti-inflammatory.

Boswellic acids - and esp. AKBBA - have been found to inhibit 5-lipoxygenase by one of two ways (direct interaction with 5-LO and Interacting with 5-LO activating proteins FLAP) as well as human leukocyte elastase (HLE).

Mechanism of anti-inflammatory

Inflammation is a complex process involving a series of actions and/or reactions and a broad range of biologically active substances (e.g. bradykinins, histamines, prostaglandins, thromboxanes, hydroxy-fatty acids, leukotrienes, lysosomal enzymes, and lymphokines) triggered by the body's immunological response to tissue damage. Leukotrienes, important mediators in inflammatory and allergic processes, are produced from arachidonic acid, an essential fatty acid synthesized in the body, via the key enzyme 5-lipoxygenase (5-LO). Earlier work identified the boswellic acids (BAs) as specific, non-redox inhibitors of 5-LO. Thus, they inhibit the production of inflammatory leukotrienes. Based on IC50 (effective inhibitory concentration of tested substance) values, **acetyl-11-keto-b-boswellic acid** alone provided the most potent inhibitory action due to its optimal structure.

Dual Inhibitory Action

Boswellia extract inhibit 5-LO by one of two ways:

- Directly interacting with 5-LO
- Interacting with the five-lipoxygenase-activating protein (FLAP).

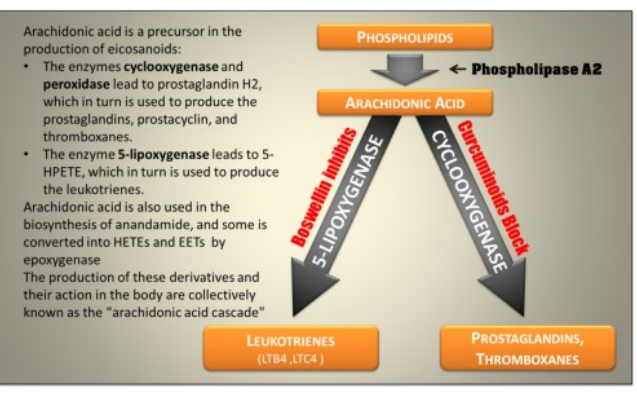
as well as, **human leukocyte elastase (HLE)**, the serine protease produced and released by polymorphonuclear leukocytes (PMNLs) which has been suggested to play a role in several diseases (pulmonary emphysema, cystic fibrosis, chronic bronchitis, acute respiratory distress syndrome, glomerulonephritis, and rheumatic arthritis) due to its aggressive and destructive properties.

This dual inhibitory action of two pathophysiologically important enzyme activities (HLE and 5-LO) is unique to the pentacyclic triterpenes from the boswellic acid series. Several leukotriene biosynthesis inhibitors furnished no HLE inhibitory activity : b-Boswellic acid, AKBA, ursolic acid, and amyrin significantly inhibited HLE. The HLE inhibition activity of AKBA and ursolic acid were comparable, however; ursolic acid's mode of inhibition is competitive.

Preclinical, in-vitro & Clinical studies

Anti-inflammatory Effects

Wildfeurer and coworkers studied Boswellia serrata as a leukotriene synthesis inhibitor of intact human PMNLs and as an herbal medicine for guinea pigs suffering from experimental autoimmune encephalomyelitis (EAE). Mixed acetyl boswellic acids significantly inhibited the ionophore-stimulated release of leukotrienes LTB.



Study of Rheumatoid Arthritis (Clinical Trials)

Conditions : Rheumatoid Arthritis, Ankylosing spondylitis, OsteoarthritisTotal 175 Subjects, 1 -6 years duration, 10-50 yearsGupta, V.N, Yadav, D.S., Jain, M.P., Atal, C.K
Results : 67% Good & Excellent, 30% Fair, 3% Poor

Inflammation and its Relationship to Glycosaminoglycans

- Glycosaminoglycans in the body form a ground substance found in connective tissue, mucous secretions and synovial fluids.
- In the process of chronic inflammation of connective tissue, as exemplified by autoimmunological disorders, e.g. lupus erythematosus or rheumatoid arthritis, one of the first casualties of the destructive process of inflammation is the wasting away of the ground substance that is an integral element of the connective tissue. Thus the wasting away of the glycosamino-glycans in the joints leads to continuously worsening joint disfigurement and limited mobility

Apoptosis Induction by AKBA

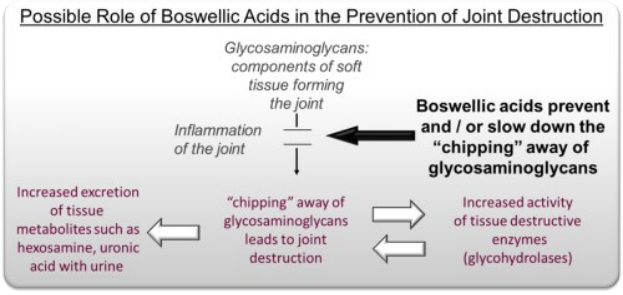
Apoptosis or programmed cell death (PCD) is an essential process in normal animal development and in the renewal of cell populations in the human body.12,13 The effects of AKBA were studied in two human cancer cell lines, HL-60 and CCRF-CEM. AKBA reduced the viability and proliferation of the leukemic cells from both lines in a dose-dependent manner.

Antitumor Activity

Shao and coworkers examined the antitumor activity of the four major pentacyclic triterpene acids of Boswellia serrata. All the compounds exhibited inhibitory activity in a dose-dependent manner. Based on cell morphology and NBT (nitroblue tetrazolium) reduction, BC-4 induced monocytic differentiation in myeloid leukemia cells in all three cell lines. Clinical studies on Malignant Glioma, Ulcerative Colitis and Bronchial Asthma were also performed.

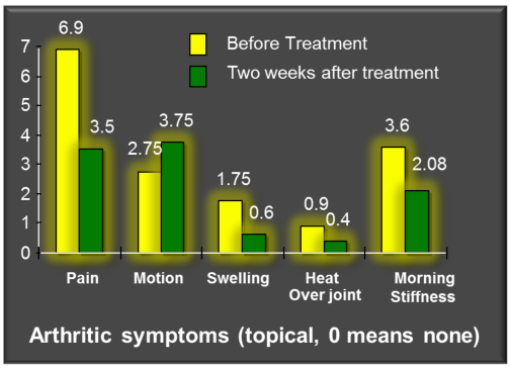
Topical Use

Mean scores of arthritic symptoms as evaluated in an open field study of boswellic acids-containing topical analgesic Chilisin® (TM of Sabinsa Corp). In addition, a four week study as well as a three month toxicity study showed that administration of boswellic acids at 5 to 10 times the ED50 value did not cause side effects.



Inhibition of Leukotriene Synthesis

The presence of a specific AKBA-binding site on 5-LO that is distinct from the arachidonate substrate-binding site was determined using photo affinity labeling. Among the several compounds classified as leukotriene synthesis inhibitors, nonredox inhibitors, such as boswellic acids, are preferred. Unlike redox type inhibitors they do not interact with other biological redox systems, lessening the likelihood of side-effects like methaemoglobin formation. AKBA has been identified as the only leukotriene synthesis inhibitor so far that inhibits 5-LO activity by noncompetitive, nonredox mechanisms.



Recommended dosage

Oral : 75 to 200mg of extract - 2-3 times a day

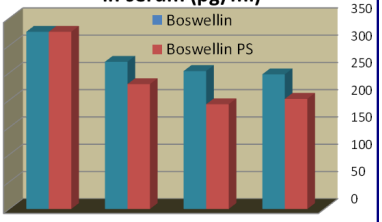
Topical : 3% to 5%

As it acts as a strong anti-inflammatory agent, BS extract may be used in stand alone or in combination with COX-2 inhibitors or nutrient enhancer (Bioperine®).

Boswellin® PS

Boswellin PS from Sabinsa represents an improvement over the existing conventional *Boswellia serrata* extracts, providing manufacturers with a more water soluble version with enhanced joint health support potential. Boswellin® PS offers a unique release profile for the active ingredients. In addition to boswellic acids, the PS version contains Polysal™, a natural polysaccharides fraction from the gum resin of *B. serrata*. The Polysal fraction is water soluble, and enhances the healthful role in the extract.

Extracellular in vivo TNF-α est. in serum (pg/ml)



Boswellin PS is more significant (p>0.001) than Boswellin in decreasing TNF-α