PROTOCOL FOR LIFE BALANCE®

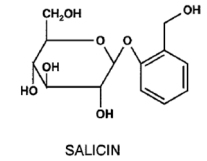
Dietary Supplement Information
for Physicians with Naturokinetics®
PRODUCT CODE: P3122
CATEGORY: JOINT SUPPORT*

Ache Action™

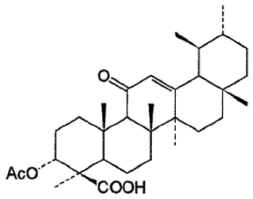
TECHNICAL SUMMARY

Ache Action™ is a blend of complementary herbs that may help to support a healthy response to normal physiological stress.* Maintenance of a normal balance of key immune mediators has been shown to play a key role in healthy cardiovascular function, as well as in joint health.* By helping to support a balanced response to these signals, the herbal components of Ache Action™ may assist in the maintenance of healthy joints and may help to relieve occasional minor pain resulting from overexertion or stress.*

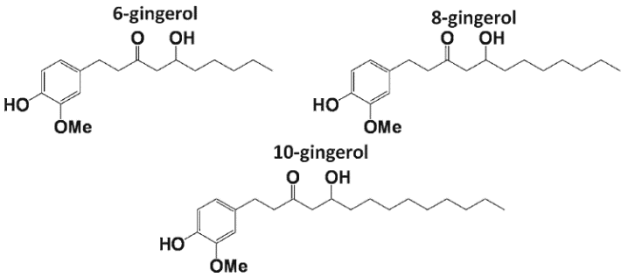
Structure Formula:



SALICIN



Chemical structure of the pentacyclic triterpene AKBA



Chemical structures of 6-, 8-, and 10-gingerols

Chemical Name: This product consists of three standardized botanical extracts: willow bark extract standardized to 14% salicin; ginger root extract standardized to a minimum of 5% gingerols; and an extract of the gum resin of *Boswellia serrata* standardized to 10 mg 3-O-Acetyl-11-Keto-ß-Boswellic Acid (AKBA).

Allergen and Additive Disclosure: Not manufactured with yeast, wheat, gluten, soy, milk, egg, fish, shellfish, or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Vegetable capsule.

ROLE AS NUTRIENT/FUNCTION

Willow bark: Salicin is the main active constituent of willow bark. Other naturally occurring active components such as polyphenols and flavonoids play a role in the analgesic activity of willow, as well as its ability to modulate the immune system's response to environmental stressors.* The mechanisms of action of willow bark extract have been explored *in vitro* and in various animal models, and it has been found to regulate the activity of many enzymes and the release of certain compounds involved in acute immune responses to biological stress.*

Supplement Facts

Serving Size 2 Veg Capsules Servings Per Container 60

Amount Per Serving	
Willow Bark Extract (*Salix spp.*) (min. 14% Salicin)	400 mg**
Ginger Root Extract (*Zingiber officinale*) (min. 5% Gingerols)	250 mg**
AprèsFlex® - *Boswellia serrata* Extract (Indian Frankincense) (Gum Resin) [Standardized to 10 mg 3-O-Acetyl-11-Keto-ß-Boswellic Acid (AKBA)]	53 mg**

** Daily Value not established.

Other ingredients: Microcrystalline Cellulose, Hypromellose (cellulose capsule), Stearic Acid (vegetable source) and Silicon Dioxide.

- **For Occasional Minor Aches & Pains of Overexertion***
- **Advanced Formula with AprèsFlex®**

SUGGESTED USAGE: Take 2 capsules twice daily, preferably with food, or as directed by your healthcare practitioner.

Ginger root: Ginger root is teeming with bioactive compounds. Gingerols are among the best known, as they are responsible for the pungency of the fresh ginger. Ginger is known to have many biological functions including regulating the release of compounds involved in acute immune responses to biological stress.*

Boswellia gum resin: Biologically active compounds pentacyclic triterpenic acids known as boswellic acids, including AKBA, are known to be potent regulators of the activity of specific enzymes involved in the immune responses to biological stress.*

NATUROKINETICS®

Liberation: Ache Action™ vegetable capsules dissolve in a USP test of dissolution in water within 60 minutes.

Absorption: Salicin: After ingestion of willow bark extract, no salicin can be detected in serum, indicating that salicin is extensively metabolized before being reaching the bloodstream. From model animals, it appears that salicin is partially hydrolyzed to saligenin by intestinal bacteria and converted to salicylic acid after absorption of saligenin. Laboratory data suggest that both salicin and saligenin are able to pass the ileum wall unchanged, with saligenin crossing faster. Its metabolites, including salicylic acid (SA), are detected in the bloodstream. After a single dose of willow bark extract (equivalent to 240 mg salicin), a peak concentration of SA is reached after one hour (Figure 1).

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

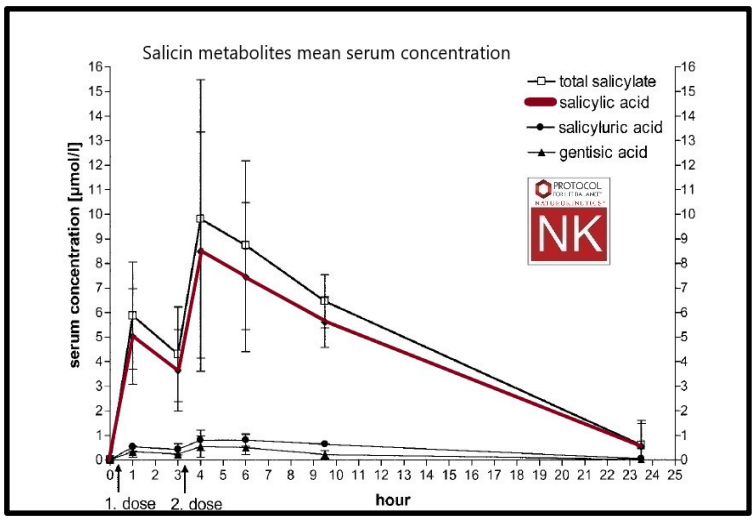


Figure 1: Mean serum levels of salicylic acid, gentisic acid, and salicyluric acids of ten healthy volunteers after ingestion of willow bark extract equivalent to 240 mg salicin.

Gingerols: After ingestion of ginger, no free 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol can be detected in human plasma, indicating that ginger constituents are highly metabolized after oral ingestion of ginger.

AKBA: AKBA is a highly lipophilic compound that is known for its relatively poor absorption in generic *Boswellia* extracts. The unique extraction process used to manufacture Aprèsflex® allows increased bioavailability of AKBA as demonstrated in a pharmacokinetic study performed in laboratory animals. In this experiment, AKBA peak concentration was obtained 3.5 h after ingestion and the overall bioavailability, as measured by the area under the curve (AUC), was 50% higher than AKBA from a standard *Boswellia* extract. (figure 2). Clinical data suggest that boswellic acids including AKBA are better absorbed when taken with a fat-containing meal.

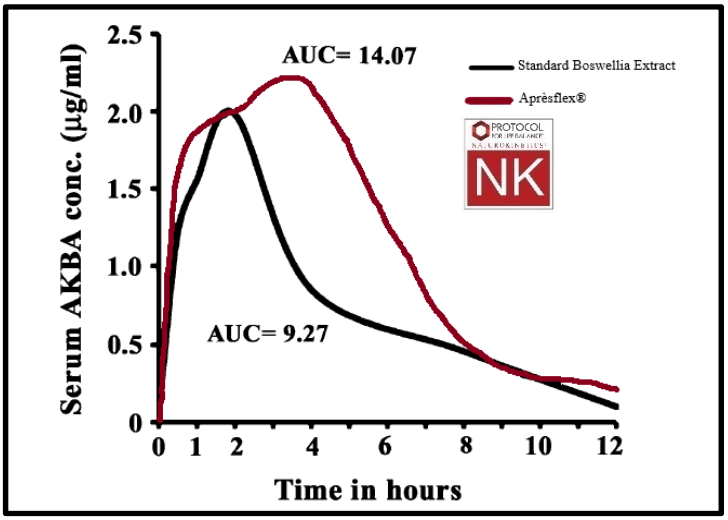


Figure 2: Comparative bioavailability of AKBA in a standard *Boswellia* extract and Aprèsflex® supplemented lab animals. Line diagram represents mean AKBA concentration (mcg/ml) in serum samples of tested animals.

Distribution: Since after oral intake, salicin and major constituents of ginger are extensively metabolized and typically undetectable in the peripheral blood stream, information about their tissular distribution is irrelevant.

Limited information is available regarding the distribution of AKBA in the body. Pre-clinical data suggest that it can pass the blood-brain barrier. In experimental models, the other tissues where AKBA can be found are the eyes, liver, kidney, and skeletal muscle.

Metabolism: Salicin: After oral ingestion, salicin is hydrolyzed to salicyl alcohol, which his oxidized to salicylic acid. Subsequently, salicylic acid is converted to salicyluric acid and gentisic acid.

Gingerols: Laboratory studies have shown that gingerols are subjected to a complex multistep metabolism involving the gut flora and the liver. After oral ingestion of ginger the majority of metabolites identified in the serum are glucuronide conjugates.

AKBA: Preclinical data suggest that AKBA is not subjected to phase I metabolism. A small portion of AKBA is metabolized into 11-keto-beta-boswellic acid (KBA).

Elimination: Salicin: Salicyluric acid and gentisic acid are excreted in urine intact or after glucuronidation. The average elimination half-life of SA is about 2.45 h after ingestion of willow bark extract. It is estimated that 95% of renally eliminated salicylates are excreted within 24 hours of ingestion. In urine, glucuronide metabolites are hydrolyzed. Salicyluric acid is the dominant metabolite (71% of total metabolites).

Gingerols: Pre-clinical data suggest that gingerol are partially eliminated via urine.

AKBA: The outcome of AKBA after it reaches the bloodstream is currently unknown.

CLINICAL VALIDATION

- Willow bark and ginger extracts have a long history of use in alleviating occasional minor aches and pains due to overexertion, and this traditional use has been confirmed by a multitude of randomized clinical trials.*
- Aprèsflex® has been evaluated in well-designed double-blind, randomized, placebo-controlled clinical trials. In these studies, 50 mg Aprèsflex® used twice daily resulted in a significant pain reduction vs. placebo and improved joint function as early as 5 days after the beginning of supplementation as evaluated on a visual analog scale for pain and a functional index questionnaire. It remained statistically significant for pain and joint function up to 90 days.* (figure 3)

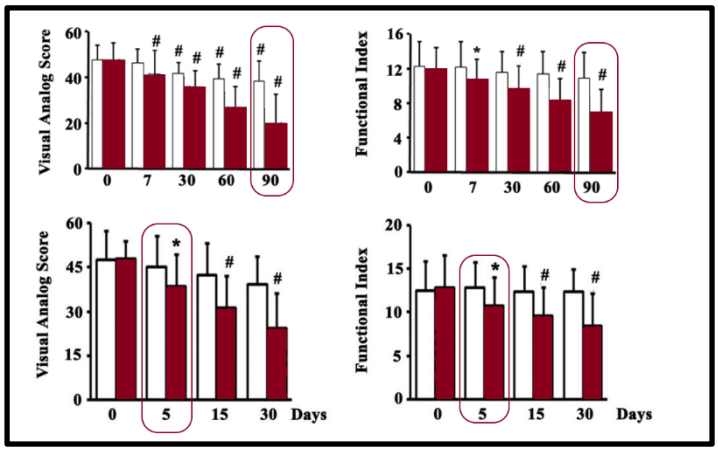


Figure 3: Red bar: 100 mg/d Aprèsflex®; white bar: placebo. *p<0.05 #p<0.01. n=57

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SAFETY INFORMATION

Tolerability: In clinical studies, up to 90 days of supplementation, Aprèsflex® is well tolerated.

Ginger is typically well tolerated.

Willow bark extract may cause GI discomfort in sensitive individuals.

Contraindications: Allergy to aspirin.

INTERACTIONS

Drug Interactions: Aprèsflex® may theoretically interact with drugs metabolized through CYP450. Aprèsflex® may theoretically interact with drugs whose metabolism is affected by P-glycoprotein.

Ginger and willow bark extract may interact with anti-coagulant/antiplatelet medications.

Supplement Interactions: Ginger and willow bark extract may interact with supplements having anti-coagulant/antiplatelet properties.

Interaction with Lab Tests: None known.

STORAGE

Store at ambient temperature (59°F -80°F) and in dry conditions in sealed container.

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