INTEGRATIVE THERAPEUTICS®

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CURCUMAX™ PRO

CURCUMAX™ PRO
MOVEMENT SUPPORT FORMULA*†

There are many available options for occasional pain relief, but the safety of continuous use and the efficacy of low dose combinations remain questionable.

Curcumax Pro offers an affordable solution for occasional pain and stiffness that is well tolerated.*† Unlike many supplements in the professional channel, Curcumax Pro delivers clinically studied levels of two herbal extracts shown to improve patient comfort and mobility.*

Meriva® is a special turmeric extract with 18 times the bioavailability of curcumin and 29 times the bioavailability of total curcuminoids vs. other turmeric forms.[1]

AprèsFlex® is a fast-acting boswellia extract clinically shown to improve range of motion – with results as early as 5 days.*[2]

Alpha-Glycosyl Isoquercitrin is a novel form of quercetin that is nearly 18 times more bioavailable than ordinary quercetin.[3]

†occasional pain due to overuse or overexertion

Meriva® is a registered trademark of Indena S.p.A.
AprèsFlex® is a registered trademark of PL Thomas-Laila Nutra, LLC and is used under license. International Patents Pending.

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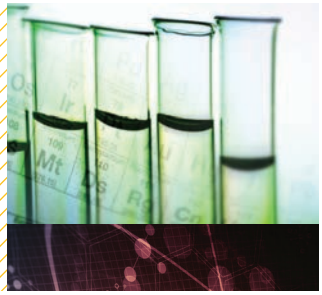
3. Makino T, Shimizu R, Kanemaru M, et al. *Biol Pharm Bull.* 2009;32(12):2034-2040.

wheat free · GF gluten free · dairy free · vegetarian



CURCUMAX™ PRO

Meriva® Turmeric

Background

Turmeric (*Curcuma longa*) is a traditional southeast Asian herb used historically as a culinary spice, a food, and medicine. It is widely used in the Indian Ayurvedic system of traditional medicine. Turmeric supplements are extracted from the roots and rhizomes of the plant, which is a member of the ginger (*Zingiberaceae*) family. There have been more than 2,500 scientific studies documenting the activity of curcumin, the main active constituent of turmeric. Its safety, efficacy, and modes of action in supporting many systems of the body has been extensively documented.[1,2]

Curcumin Mechanisms of Action

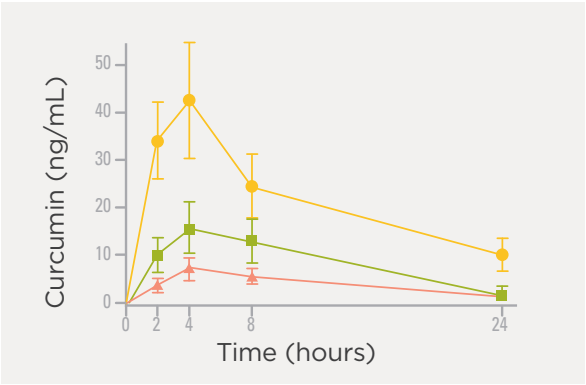
Curcumin has diverse therapeutic effects, such as modulating healthy cytokine and chemotactic pathways, antioxidant activity, and supporting normal cell proliferation.* The modulating activity of curcumin is particularly well characterized: it is known to down-regulate the activity of cyclooxygenase-2 (COX-2), lipoxygenase, and inducible nitric oxide synthase enzymes; it influences the production of various cytokines, including several interleukins and tumor necrosis factor-alpha (TNF-a).*[3,4] Curcumin has been shown to block cytokine-mediated NF-kappa B activation and gene expression by acting on inhibitory factor I-kappa B kinase.*[5] In animal in vitro models it has been shown to influence the activity of lipoxygenase and cyclooxygenase enzymes.*[6]

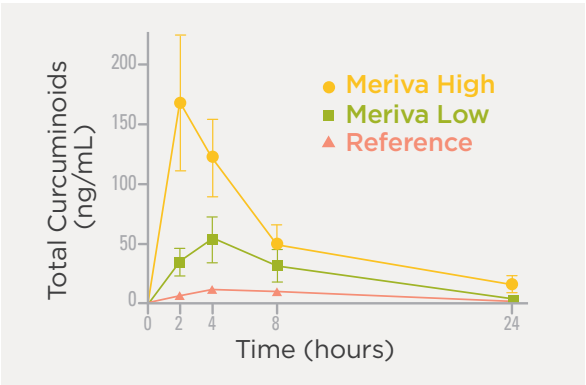
The vanilloid part of the curcumin molecule is important for activation of the transient receptor potential vanilloid 1 (TRPV1), which plays an important role in the perception of pain (nociception).* Among the several modes of action identified for turmeric, experimental research indicates that curcumin blocks TRPV1 activation and thereby inhibits TRPV1-mediated pain hypersensitivity.*[7]

Meriva Curcumin-Phosphatidylcholine Complex

The clinical utility of curcumin has been limited by its chemical instability at intestinal pH values, by its low water solubility, and by its poor oral bioavailability and quick conjugation and excretion.[8,9] These properties lead to less than ideal conditions for therapeutic utility. The consequence is that several human studies of non-complexed curcumin have failed, even at high doses,[10] and its full clinical potential remains unrealized.[11–13]

Meriva overcomes cucumin's absorption limitations through a proprietary technology that combines phosphatidylcholine with curcumin. This unique complex increases hydrolytic stability, thus shielding curcumin from water as well as improving oral absorption and bioavailability of curcuminoids. Preliminary pharmacokinetics (PK) research in animals demonstrated significant bioavailability advantages of Meriva over non-complexed powdered curcuminoids.[14] In a follow-up PK study in humans, bioavailability of curcuminoids as evaluated by the plasma area under the curve (AUC) was about 29-fold higher for those taking Meriva than in subjects taking conventional turmeric extract (95% curcumin).[15]





These data indicate that Meriva phytosome is 18 times more bioavailable for curcumin than non-complexed reference treatment; total curcuminoid bioavailability is about 29 fold higher for the phytosome formulation than the non-complexed reference.

Stability of Meriva

Comparative analysis of the hydrolytic stability of Meriva vs. conventional turmeric extract showed a dramatic advantage in stability at the pH range of the small intestine (pH 7-8), where the absorption of polyphenolic compounds takes place. In one study, turmeric extract revealed a half-life of <30 minutes in a phosphate buffer at pH 7.2; whereby only 45% of curcumin was still present in the buffer, and this value dropped to 33% after 240 minutes (4 hours). Under the same conditions, Meriva maintained 97% of its curcumin concentration after 30 minutes and 87% concentration after 4 hours. Repeated in a pH 8 buffer, curcumin content dropped to 10% of its initial time value in just 10 minutes, while curcumin in Meriva was maintained at 99% purity. At 60 minutes in pH 8 the curcumin content in the extract further dropped to 6% of its initial value, while curcumin in Meriva was still 31% of the starting value.[16]

It is well known that phosphatidylcholine complexes enhance polyphenols' capacity to cross the lipid-rich biomembranes and reach the circulation, but for this to occur the complexes must be stable at gastrointestinal pH values.[17] This study found that curcumin alone was unstable in the jejunum at pH 7-8, whereas Meriva was far more stable under the same conditions.

Efficacy of Meriva

In a 90-day clinical study (n=50), Meriva demonstrated significant improvements related to occasional pain, stiffness, physical function, and overall quality of life.* Occasional pain, stiffness, and physical function (impairment) decreased by 58% (as measured by the WOMAC scale).*[18] In the same group of subjects, Social and Emotional Index Score resulted in greater than 3-fold improvement. In a subpopulation with higher C-Reactive Protein (CRP), there was a decrease from increased values (168 mg/L) to healthier levels (11.3 mg/L).

AprèsFlex® Boswellia

Background

Frankincense is a resinous extract from the trees of the genus Boswellia, which are native to India and the Arabian peninsula. It has been used since antiquity in religious ceremonies and for perfume production, and its medicinal properties have been recognized and prized for millennia.[19] In modern times, the pharmacological characteristics and clinical efficacy of *Boswellia serrata* have been studied, with research published and systematically reviewed in the medical literature.[20]

Boswellia Mechanisms of Action

The main active constituents of Boswellia are the boswellic acids, most importantly acetyl-11-keto-beta boswellic acid (AKBA). AKBA has demonstrated many significant immunomodulatory and vascular response-modulating effects in preclinical research.* The best-documented action of boswellic acids is the inhibition of the mediator 5-lipoxygenase.* However, other factors such as cytokines (interleukins and TNF-alpha) and the complement system are likely molecular targets.[21,22] AKBA also naturally inhibits the transcription factor NF-kappaB.*[11,23]

AprèsFlex Boswellia serrata Extract

AprèsFlex is extracted from Boswellia, an ancient herb that is a potent lipoxygenase inhibitor. AprèsFlex is significantly better at supporting a healthy vascular mediator response compared to other Boswellia extracts presently available, even some with higher AKBA content. AprèsFlex makes use of a proprietary composition to improve the bioavailability and bioactivity of the AKBA, so less is to be required. The efficacy of AprèsFlex has been shown in two controlled clinical trials.

A 90-day, double-blind, randomized, placebo-controlled study was conducted to evaluate the comparative efficacy and tolerability of 5-Loxin® (30% AKBA) and AprèsFlex (20% AKBA).[25] Sixty subjects were included in the study. The subjects received either 100 mg (n=20) of 5-Loxin or 100 mg (n=20) of AprèsFlex or a placebo (n=20) daily for 90 days. Each subject was evaluated for comfort and physical function by using the standard tools (visual analog scale, Lequesne's Functional Index, and Western Ontario and McMaster Universities Index) at the baseline (day 0), and at days 7, 30, 60, and 90. A battery of biochemical parameters in serum, urine, and hematological parameters in citrated whole blood were performed to assess the safety of 5-Loxin and AprèsFlex in the subjects. Fifty-seven subjects completed the study. At the end of the study, both 5-Loxin and AprèsFlex conferred clinically and statistically significant improvements in comfort scores and physical function scores.* Interestingly, significant improvements were recorded as early as 7 days after initiation of the study in the treatment group supplemented with 100 mg AprèsFlex. Corroborating the improvements in scores in treatment groups, previous in vitro studies provide evidence that AprèsFlex is capable of inhibiting enzyme MMP-3 and has the potential to support a healthy vascular mediator via its influence on ICAM-1.* Although both Boswellia extracts were effective, AprèsFlex exhibited better efficacy compared to 5-Loxin.

A 30-day, double-blind, randomized, placebo-controlled study was conducted to validate the efficacy of AprèsFlex.[26] Sixty eligible subjects selected through screening were included in the study. The subjects received either 100 mg (n=30) of AprèsFlex

or placebo (n=30) daily for 30 days. Each subject was evaluated for comfort and physical functions by using the standard tools (visual analog scale, Lequesne's Functional Index, and Western Ontario and McMaster Universities Index) at the baseline (day 0), and at days 5, 15, and 30. A series of biochemical tests in serum, urine, and hematological parameters established the safety of AprèsFlex. The researchers found that AprèsFlex conferred clinically and statistically significant improvements in scores in as early as 5 days of treatment.* Researchers concluded AprèsFlex is a safe, fast-acting therapeutic intervention.

Another systematic review of data from randomized clinical trials showed Boswellia supports a healthy immune and vascular response and healthy range of motion in humans.*[20] Results of all trials meeting the inclusion criteria indicated that B. serrata extracts were clinically effective. No serious safety issues were noted.

Alpha-Glycosyl Isoquercitrin

Background

Rutin and isoquercitrin are the main glycoside forms of quercetin, and both occur widely in foods.[27] Alpha-glycosyl isoquercitrin is a glycoside form of quercetin with exceptional bioavailability. As an antioxidant and immune-modulator, alpha-glycosyl isoquercitrin is many more times more bioavailable than other forms of quercetin. It is 3 times more bioavailable than isoquercetin and nearly 18 times more bioavailable than ordinary quercetin (aglycone).[28] Animal research found that bioavailability was 2% for quercetin, 12% for isoquercetin, and 35% for alpha-glycosyl isoquercitrin. After oral administration of alpha-glycosyl isoquercitrin, quercetin hit its peak in the plasma after just 15 minutes. Alpha-glycosyl isoquercitrin has a further advantage over isoquercetin and quercetin aglycone of being freely soluble in water; the others are not.[29] Thus alpha-glycosyl isoquercitrin delivers quercetin benefits faster and more effectively, enhancing cellular antioxidant defenses and helping to modulate the body's healthy immune-response mechanisms.* Alpha-glycosyl isoquercitrin is Generally Recognized As Safe (GRAS).

Quercetin Mechanisms of Action

Glucosides of quercetin are more bioavailable than quercetin aglycone, and more stable against oxidative modification in the stomach.[30,31] Quercetin and its glucosides have demonstrated beneficial effects in animal models. Isoquercitrin demonstrated slightly better support for the body's natural vascular response than quercetin aglycone on the expression of COX-2 mRNA and cell exudation.*[27] Quercetin inhibits the generation of mediators such as leukotriene LTB4 and prostaglandin E2 in human neutrophils.[32] Therefore, quercetins, such as alpha-glycosyl isoquercitrin, are applicable when leukotriene modulation is the therapeutic goal.[33]

Supplement Facts

Serving Size 2 tablets

Ingredient	Amount
Active Relief Blend	1.3 g
Meriva® Curcuma longa Root and Rhizome Extract (phosphatidylcholine complex) providing 200 mg curcuminoids, AprèsFlex® Boswellia serrata Gum Extract providing 20 mg 3-O-acetyl-11-keto-beta-boswellic acid (AKBA), and Alpha-glycosyl isoquercitrin	

**Percent Daily Values (DV) are based on a 2,000 calorie diet.

***Daily Value not established.**Daily Value (DV) not established.

Recommendations: Two tablets daily following meals. Can be taken as 1 tablet twice daily or as directed by your healthcare professional.

Other ingredients: Cellulose, modified cellulose gum, silicon dioxide, modified cellulose, and glycerin

Contains No: Sugar, yeast, wheat, gluten, dairy products, artificial coloring, or ingredients of animal origin. This product contains natural ingredients; color variations are normal.

Caution: If pregnant, nursing, or taking prescription drugs, consult your healthcare professional prior to use.

Integrative Therapeutics™	Natural Partners	Emerson Ecologics
30 CT - 70668	30 CT - IT0089	30 CT - IT70668
60 CT - 70655	60 CT - IT0078	60 CT - T04511

Quercetin has been shown to inhibit cytokine and inducible nitric oxide synthase expression through inhibition of the NF-kappaB pathway.[34] Quercetins may also support healthy vascular response via systemic inhibition of TNF-α.*[35]

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