

## CURCUMAX™ PRO PROFESSIONAL STRENGTH PAIN 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 a safe and affordable solution for occasional pain and stiffness.\*\* 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 common turmeric and 29 times the bioavailability of total curcuminoids vs. other turmeric forms.<sup>1</sup>

**AprèsFlex®** is a fast-acting boswellia extract clinically shown to improve range of motion - with results as early as 5 days.\*<sup>2</sup>

**Alpha-Glycosyl Isoquercitrin** is a novel form of quercetin that is nearly 18 times more bioavailable than ordinary quercetin.<sup>3</sup>



†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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wheat free



gluten free



soy free



dairy free



vegan



# 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 efficacy and modes of action in supporting many systems of the body has been extensively documented.<sup>1,2</sup>

### Curcumin Mechanisms of Action

Curcumin has diverse therapeutic effects, such as modulating healthy cytokine and chemotactic pathways, and supporting normal cell signaling.\* 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.\*<sup>3,4</sup> In animal in vitro models it has been shown to influence the activity of lipoxygenase and cyclooxygenase enzymes.\*<sup>6</sup>

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.\*<sup>7</sup>

### 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.<sup>8,9</sup> 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,<sup>10</sup> and its full clinical potential remains unrealized.<sup>11-13</sup>

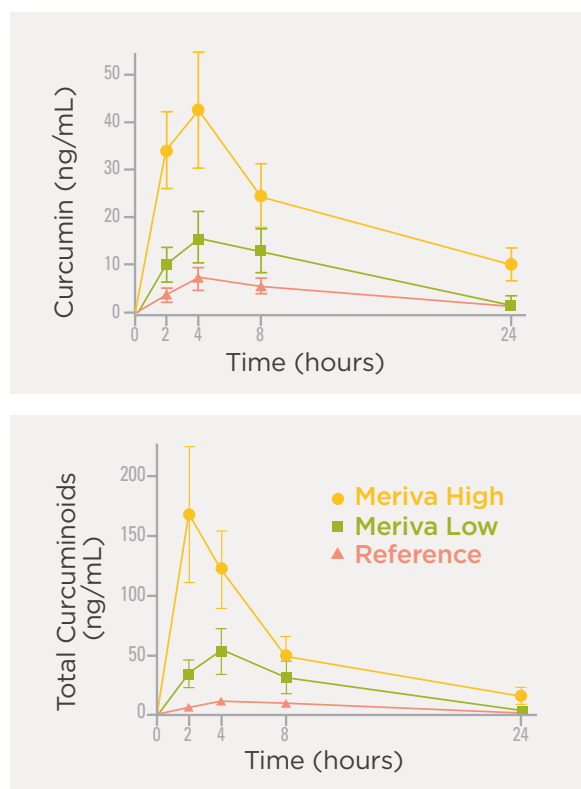
Meriva overcomes curcumin's absorption limitations through a proprietary technology that combines phosphatidylcholine with curcumin. This unique complex increases hydrolytic stability, thus shielding curcumin from water as well as improving oral absorption and bioavailability of curcuminoids. Preliminary pharmacokinetics (PK) research in animals demonstrated significant bioavailability advantages of Meriva over non-complexed powdered curcuminoids.<sup>14</sup> 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).<sup>15</sup>

### Stability of Meriva®

It is well known that phosphatidylcholine complexes enhance polyphenols' capacity to cross the lipid-rich membranes and reach the circulation, but for this to occur the complexes must be stable at gastrointestinal pH values.<sup>16</sup> 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



*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.*

function, and overall quality of life.\* Occasional discomfort, stiffness, and physical function (impairment) decreased by 58% (as measured by the WOMAC scale).<sup>\*17</sup> 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).

Another larger, eight-month, controlled study examined Meriva's efficacy in improving comfort and physical function (n=100).<sup>\*18</sup> Baseline function and comfort were assessed via the Karnofsky Performance Scale Index, WOMAC questionnaire and treadmill test. Subjects were divided into an active group (n=50) and control group (n=50) with the active group receiving daily oral administration of 1g of Meriva. After eight months, subjects in the active group reported significant improvement in the Karnofsky Scale vs at enrollment (92.2 vs. 73.3, p<0.05).<sup>\*</sup> WOMAC scores for the active group also decreased over 50 percent from baseline with significant reduction in scores (166 to 73, p<0.05), stiffness (7.4 to 3.2, p<0.05) and physical function (56.6 to 22.8, p<0.05). Meriva demonstrated a significant difference in relation to treadmill distance with a 345% improvement in distance in the active group compared to 89% improvement in the control group, p<0.05.<sup>\*</sup> Subjects receiving Meriva also experiences a 38% decrease in gastrointestinal complaints in contrast to a 15% decrease experienced by controls, p<0.05.<sup>\*</sup>

In a 2016 study, Meriva also demonstrated effects in subjects encountering age-related changes in muscle strength and endurance.<sup>\*19</sup> Healthy subjects over 65 years of age either received standard management of diet and exercise (n=33) or standard management of diet and exercise along with daily oral administration of 1g of Meriva. Evaluations and mean values of hand grip, weight lifting, time and distance before fatigue for cycling, walking and climbing stairs, as well as general mobility scores were recorded at baseline and at conclusion of the study 3 months later. Significant improvement was seen in all categories for the group receiving Meriva, compared to baseline: handgrip (31.kg, SD=1.5 baseline vs. 33.9kg, SD=1.8 at 3 months), weight lifting (13 repetitions, SD=1 at baseline vs. 16 repetitions, SD=2 at 3 months), cycling (2'29", SD=18 at baseline vs. 3'11", SD=11 at 3 months), walking (251, SD=11 baseline vs. 311, SD=14 at 3 months), climbing stairs (54", SD=6" baseline vs. 75", SD=3" at 3 months), and general mobility scores (1.2 baseline v. 2.2 at 3 months).<sup>\*</sup> Calculated probability for a II values was p<0.05. No significant improvements were seen in the standard diet and exercise group. The authors conclude that Meriva is effective at supporting strength and function in healthy elderly subjects.<sup>\*</sup> Meriva has also been studied at a dose of 2g per day.<sup>20,21</sup>

## 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.<sup>22</sup> 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.<sup>23</sup>

### 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.<sup>\*</sup> The best-documented action of boswellic acids is the inhibition of the mediator 5-lipoxygenase.<sup>\*</sup> However, other factors such as cytokines (interleukins and TNF-alpha) and the complement system are likely molecular targets.<sup>\*24,25,26</sup>

### 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).<sup>27</sup> 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 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.<sup>\*</sup> Interestingly, significant improvements were recorded as early as 7 days after initiation of the study in the treatment group supplemented with 100 mg AprèsFlex.<sup>\*</sup> 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.<sup>28</sup> 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 efficacy 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 fast-acting therapeutic intervention.\*<sup>26</sup>

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.\*<sup>23</sup> Results of all trials meeting the inclusion criteria indicated that B. serrata extracts were clinically effective.

## Alpha-Glycosyl Isoquercitrin

### Background

Rutin and isoquercitrin are the main glycoside forms of quercetin, and both occur widely in foods.<sup>29</sup> 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 has been found to be 3 times more bioavailable than isoquercetin and nearly 18 times more bioavailable than ordinary quercetin (aglycone).<sup>30</sup> 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.<sup>31</sup> 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.\*

### Quercetin Mechanisms of Action

Glucosides of quercetin are more bioavailable than quercetin aglycone, and more stable against oxidative modification in the stomach.<sup>32,33</sup> 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

## Supplement Facts

Serving Size 2 tablets		Servings per container 30
Amount per 2 tablets		%DV
Total Carbohydrate	1g	<1%**
Dietary Fiber	1g	4%**
Active Relief Blend:	1.2g	**
Meriva® Curcuma longa Root and Rhizome Extract (phospholipid complex providing 200 mg curcuminoids, AprèsFlex® <i>Boswellia serrata</i> Gum Extract standardized to 20% 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.

**Recommendations:** Two tablets daily with food. Can be taken as 1 tablet twice daily or as directed by your healthcare professional.

**Other ingredients:** Cellulose, sodium carboxymethyl cellulose, silicon dioxide, hydroxypropyl methylcellulose, glycerin

**Contains No:** Sugar, salt, yeast, wheat, gluten, soy, dairy products, artificial coloring, or ingredients of animal origin.

**Warning:** Do not use if pregnant or nursing. If taking prescription drugs, consult your healthcare professional prior to use.

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and cell exudation.\*<sup>29</sup> Quercetin inhibits the generation of mediators such as leukotriene LTB4 and prostaglandin E2 in human neutrophils.<sup>34</sup> Therefore, quercetins, such as alpha-glycosyl isoquercitrin, are applicable when leukotriene modulation is the therapeutic goal.\*<sup>35</sup>

Quercetin has been shown to affect cytokine and inducible nitric oxide synthase expression.\*<sup>36</sup> Quercetins may also support healthy vascular response.\*<sup>37</sup>

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\*THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THESE PRODUCTS ARE NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE.