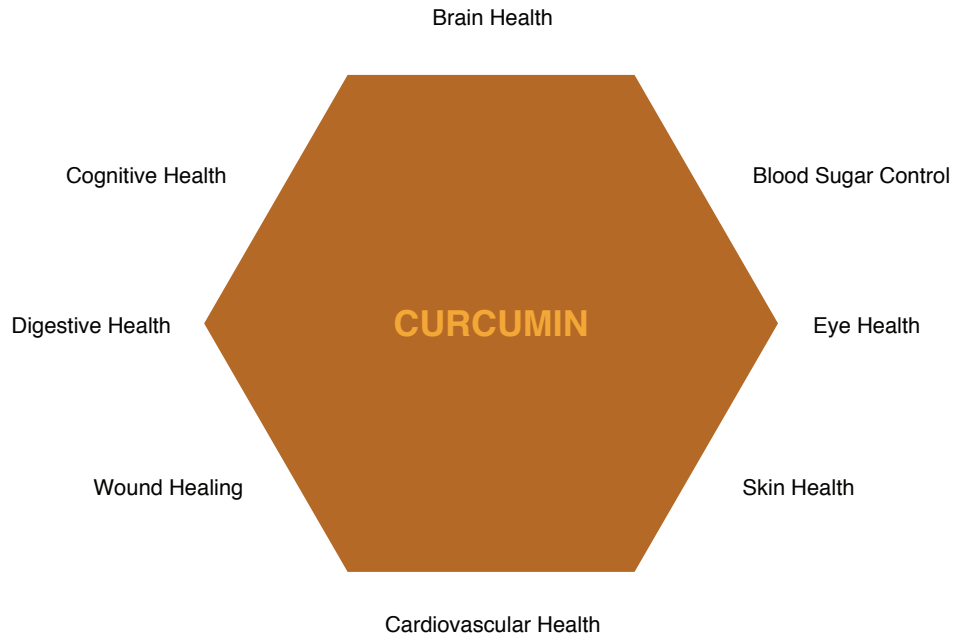
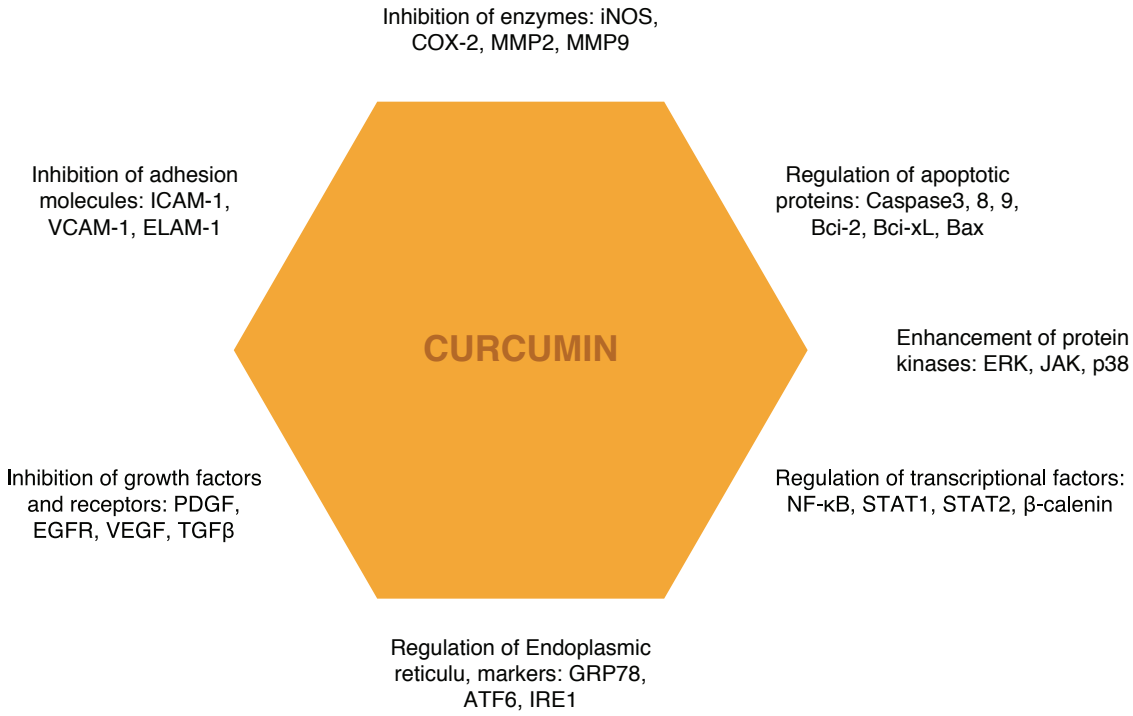
NuLivScience

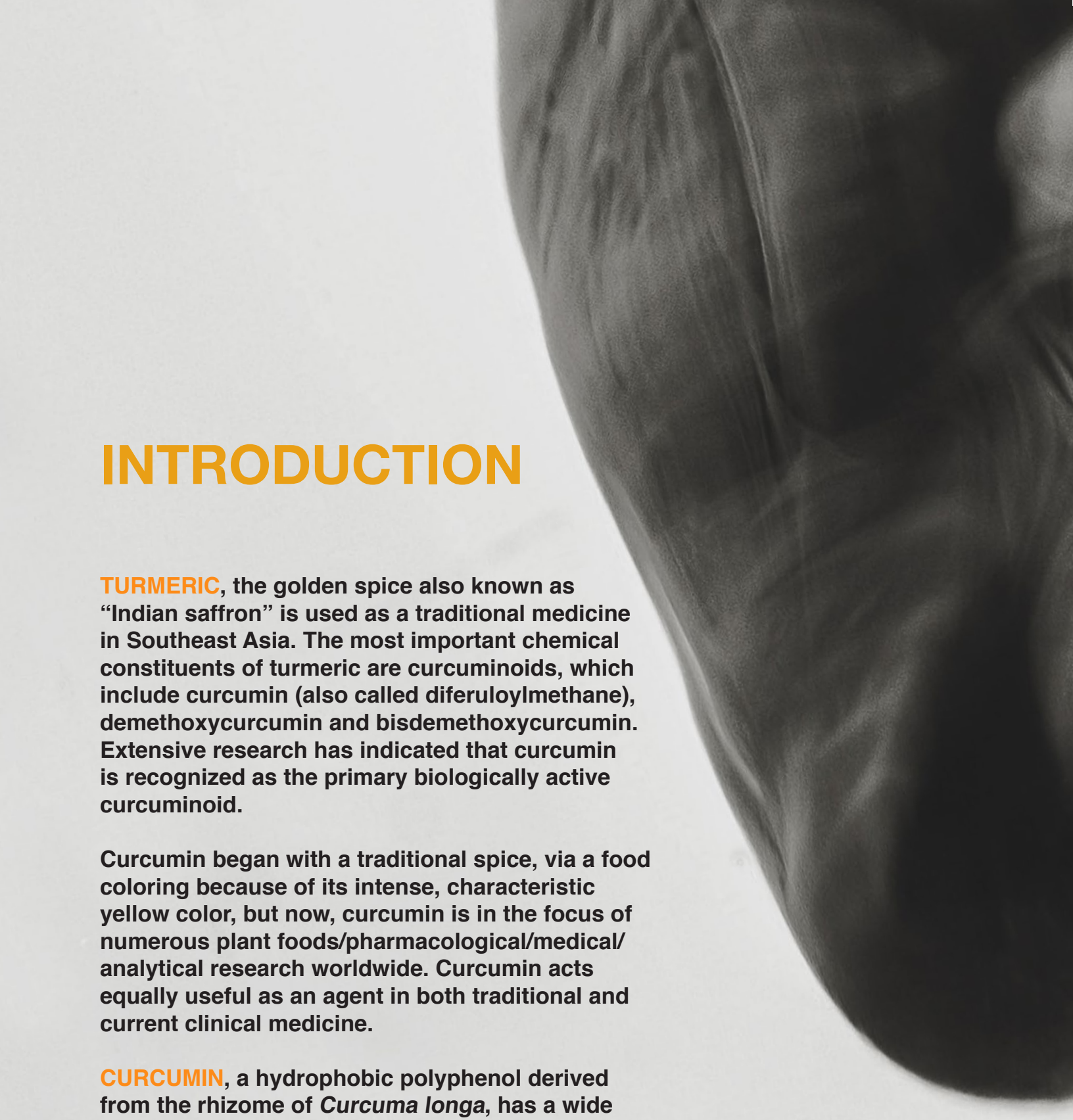
AstraGin®

ASTRAGIN® INCREASES ABSORPTION AND BIOAVAILABILITY OF CURCUMIN IN THE GUT


Brain Health
Cognitive Health
Blood Sugar Control
CURCUMIN
Digestive Health
Eye Health
Wound Healing
Skin Health
Cardiovascular Health


Inhibition of enzymes: iNOS, COX-2, MMP2, MMP9
Inhibition of adhesion molecules: ICAM-1, VCAM-1, ELAM-1
Regulation of apoptotic proteins: Caspase3, 8, 9, Bci-2, Bci-xL, Bax
CURCUMIN
Enhancement of protein kinases: ERK, JAK, p38
Inhibition of growth factors and receptors: PDGF, EGFR, VEGF, TGFβ
Regulation of transcriptional factors: NF-κB, STAT1, STAT2, β-calenin
Regulation of Endoplasmic reticulu, markers: GRP78, ATF6, IRE1

CONTENT



INTRODUCTION

TURMERIC, the golden spice also known as "Indian saffron" is used as a traditional medicine in Southeast Asia. The most important chemical constituents of turmeric are curcuminoids, which include curcumin (also called diferuloylmethane), demethoxycurcumin and bisdemethoxycurcumin. Extensive research has indicated that curcumin is recognized as the primary biologically active curcuminoid.

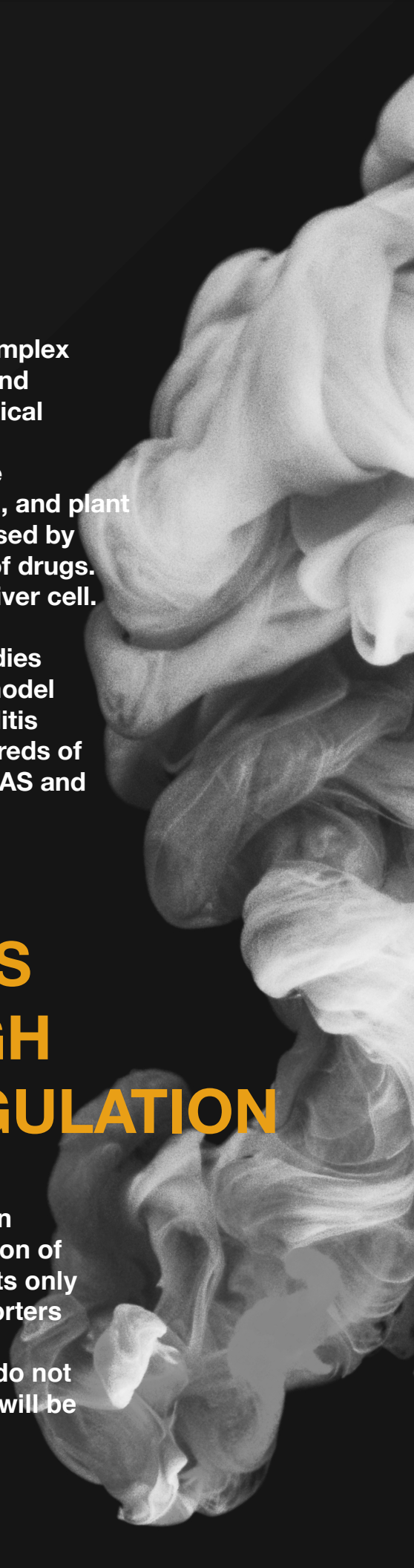
Curcumin began with a traditional spice, via a food coloring because of its intense, characteristic yellow color, but now, curcumin is in the focus of numerous plant foods/pharmacological/medical/ analytical research worldwide. Curcumin acts equally useful as an agent in both traditional and current clinical medicine.

CURCUMIN, a hydrophobic polyphenol derived from the rhizome of *Curcuma longa*, has a wide spectrum of biological and pharmacological activities. Curcumin is a natural anti-inflammatory compound. Curcumin has been shown to exhibit antioxidant, anti-inflammatory, antimicrobial, and anti-carcinogenic activities. [1]

INTRODUCING ASTRAGIN®

ASTRAGIN® is a proprietary plant derived compound complex extracted from highly fractionated *Panax notoginseng* and *Astragalus membranaceus* by a proprietary pharmaceutical extraction and processing technology. AstraGin® has demonstrated in multiple *in-vitro* studies to increase the absorption of peptides, amino acids, fatty acids, vitamin, and plant compound in Caco-2 intestinal cell, the gold standard used by pharmaceutical companies to measure the absorption of drugs. AstraGin® also increased the ATP production in HepG2 liver cell.

AstraGin® has also demonstrated in multiple *in-vivo* studies in a normal and IBD (Inflammatory Bowel Disease) rat model to increase the absorption of peptides in normal and colitis rats. Human uses began in late 2010 and is now in hundreds of supplements worldwide. AstraGin® is a self-affirmed GRAS and NDI nutraceutical ingredient.



ASTRAGIN® INCREASES ABSORPTION THROUGH TRANSPORTER UPREGULATION

AstraGin® upregulates the mRNA and protein expression levels of nutrient transporters that regulate the absorption of nutrients and plant compounds in the gut. Most nutrients only enter human body through active absorption by transporters that are transported by portal vein to liver and through circulation to the rest of the body. Those nutrients that do not enter into the intestinal cells through active absorption will be excreted from the human body.

BENEFITS OF ASTRAGIN®

1

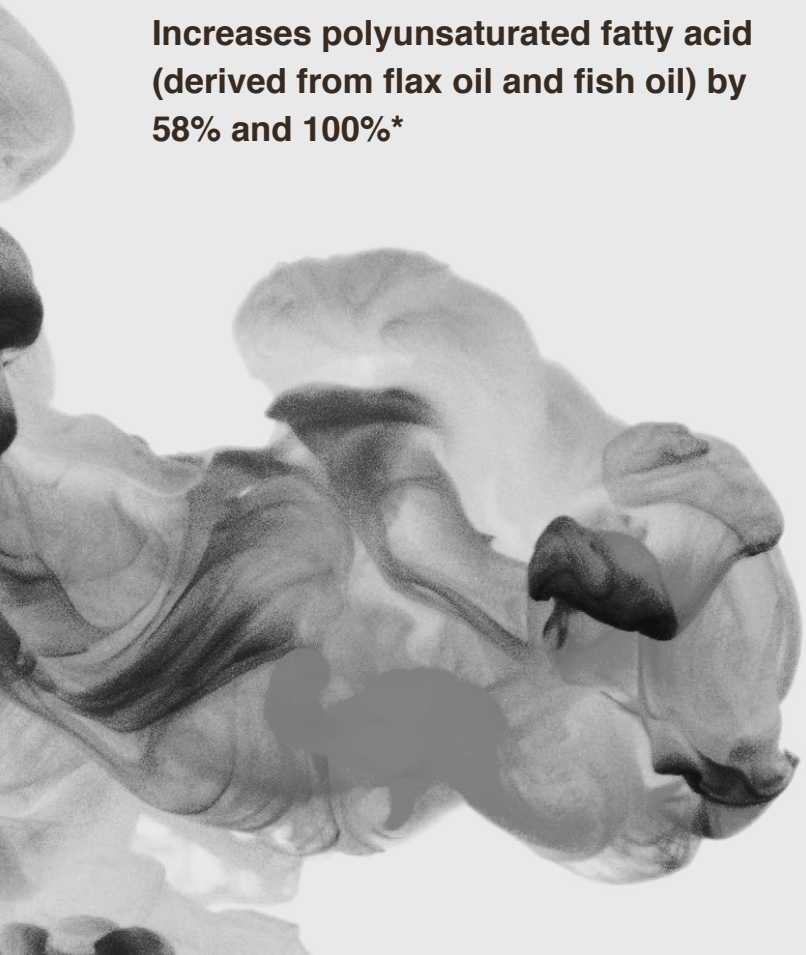
Increase curcumin absorption by 92% (in this special report)

2

Increases vitamins absorption such as folate by 50%*

3

Increases polyunsaturated fatty acid (derived from flax oil and fish oil) by 58% and 100%*



4

Increase glucosamine absorption by 23%*

5

Increases omega-7 fatty acid (Palmitoleic acid) by 39%*

6

Increase ATP production in liver by 18%*

7

Increases the steady-state absorption rate of arginine, agmatine, β-alanine, citrulline, creatine, leucine, peptides and tryptophan by 67%, 36%, 25%,45%, 33%, 58%, 41% and 53%*

*See the complete product dossier

MANY WAYS TO USE ASTRAGIN®

Weight Management

Protein powders, meal replacements, dietary supplements

Medical Food

Nutrition supplements

Sports Nutrition

Bodybuilding, fitness and energy formulas, protein supplements, energy bars, ready-to-drink supplements

Functional Beverages

Energy drinks, smoothies, powder drink mixes

Baked Goods

Breads, cereals, pastas, snacks

Nutraceuticals

All categories of dietary supplements in capsule, liquid, powder, soft gel, and tablet forms

Animal Nutrition and Natural Feed Supplement Products

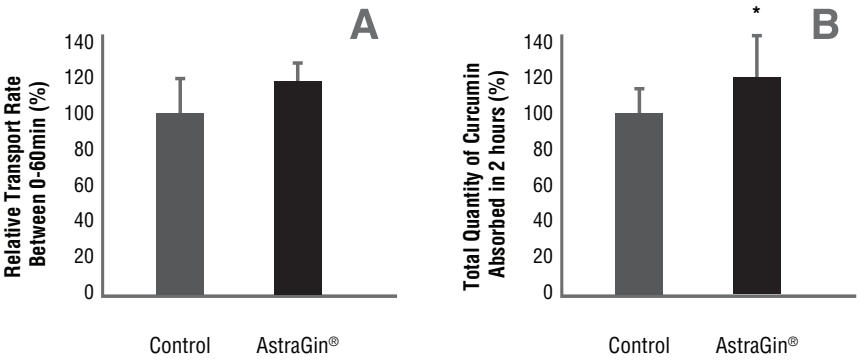
6. CURCUMIN UPTAKE ASSAYS
6.1 CURCUMIN UPTAKE ASSAY

MATERIALS AND METHODS

After TEER measurement, the differentiated Caco-2 monolayers were gently rinsed twice with Hank's balanced salt solution (HBSS) and equilibrated for 30 min at 37°C. Then the medium was replaced with fresh HBSS containing the curcumin solution. The transwells were incubated at 37°C for 180 min and the basolateral medium were sampled at the designated time intervals and analyzed via fluorescence (Ex: 450 nm; Em: 540 nm; Enspire 230, Perkin Elmer). During and at the end of the experiments, TEER was measured and data were recorded only from experiments in which TEER was higher than 250Ω·cm²

RESULTS

A. Effect of AstraGin® on Curcumin absorption in Caco-2 cells



Relative transport rate (A); total quantity of curcumin absorbed by AstraGin® in Caco-2 cells.

Analysis of the effect of AstraGin® on curcumin transport rate and total quantity absorption.

Groups	Relative curcumin transport rate in 60min (%)	Total quantity of curcumin absorption in 2hours (%)
Control	100.00±20.12	100.00±12.68
AstraGin®	116.02±12.30	118.06±22.30

*** p<0.05, when compared to control group.**

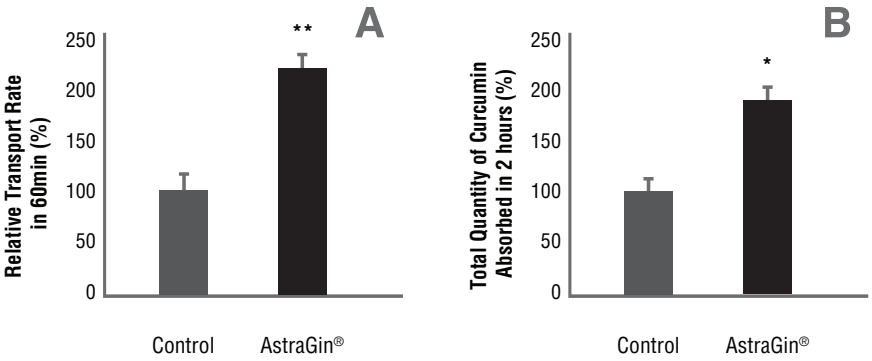
In this study, AstraGin® demonstrated a modest effect in improving the absorption of curcumin as a stand alone single compound at the transport rate of 16% in 60 min and a total of 18% in 2 hours.

6.2 CURCMIN-PIPERINE UPTAKE ASSAY

MATERIALS AND METHODS

After TEER measurement, the differentiated Caco-2 monolayers were gently rinsed twice with Hank's balanced salt solution (HBSS) and equilibrated for 30 min at 37°C. Then the medium was replaced with fresh HBSS containing the curcumin-piperine solution (Curcumin and piperine are in 1:2 weight ratio). The transwells were incubated at 37°C for 180 min and the basolateral medium were sampled at the designated time intervals and analyzed via fluorescence (Ex: 450 nm; Em: 540 nm; Enspire 230, Perkin Elmer). During and at the end of the experiments, TEER was measured and data were recorded only from experiments in which TEER was higher than 250Ω·cm²

RESULTS



Relative transport rate (A); total quantity of curcumin-piperine absorbed by AstraGin® in Caco-2 cells

Analysis of the effect of AstraGin® on curcumin-piperine transport rate and total quantity absorption.

Groups	Relative curcumin transport rate in 60min (%)	Total quantity of curcumin absorption in 2hours (%)
Control	100.00±13.67	100.00±12.89
AstraGin®	221.73±13.67**	189.77±13.94*

*** p<0.05, when compared to control group**
**** p<0.01, when compared to control group**

In this study, AstraGin® demonstrated to improve the absorption of a blend of curcumin and piperine compound at the transport rate of 121% in 60 min and a total of 190% in 2 hours. The curcumin-piperine blend with AstraGin® is the best documented compound to show in human bioavailability of curcumin.

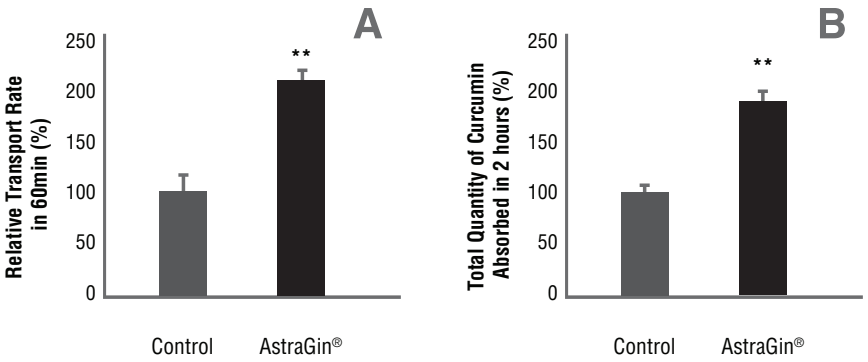
6.3 CURCUMIN-LECITHIN UPTAKE ASSAY

MATERIALS AND METHODS

After TEER measurement, the differentiated Caco-2 monolayers were gently rinsed twice with Hank's balanced salt solution (HBSS) and equilibrated for 30 min at 37°C. Then the medium was replaced with fresh HBSS containing the curcumin-lecithin solution (Curcumin and lecithin are in 1:2 weight ratio). The transwells were incubated at 37°C for 180 min and the basolateral medium were sampled at the designated time intervals and analyzed via fluorescence (Ex: 450 nm; Em: 540 nm; Enspire 230, Perkin Elmer). During and at the end of the experiments, TEER was measured and data were recorded only from experiments in which TEER was higher than 250Ω·cm²

RESULTS

C. Effect of AstraGin® on Curcumin-Lecithin absorption in Caco-2 cells



Relative transport rate (A); total quantity of curcumin-lecithin absorbed by AstraGin® in Caco-2 cells

Analysis of the effect of AstraGin® on curcumin-lecithin transport rate and total quantity absorption.

Groups	Relative curcumin transport rate in 60min (%)	Total quantity of curcumin absorption in 2hours (%)
Control	100.00±9.18	100.00±5.87
AstraGin®	205.32±12.79**	192.43±9.96**

** p<0.01, when compared to control group

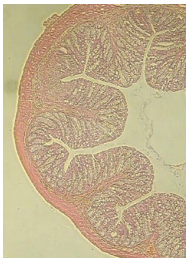
In this study, AstraGin® demonstrated to improve the absorption of curcumin-lecithin compound at the transport rate of 105% in 60 min and a total of 92% in 2 hours.

7. HISTOLOGY ASSAY (*IN-VIVO*)
7.1 HEMATOXYLIN-EOSIN STAIN

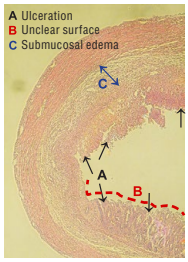
MATERIALS AND METHODS

Colons were removed immediately from animals after they were euthanized by cervical dislocation. The specimens were fixed in 10% buffered formalin and embedded in paraffin. Two sections of 4µm in thickness were cut and stained with hematoxylin–eosin (H&E) for histological evaluation.

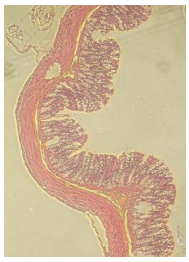
RESULTS



Normal colon cells



TNBS induced colon cells



After supplemented with AstraGin®

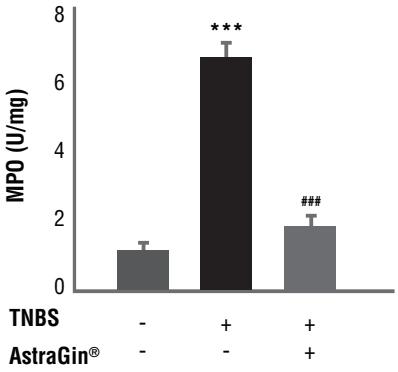
7.2 MPO ACTIVITY ASSAY

MATERIALS AND METHODS

Colon samples obtained longitudinally from a site of macroscopically detectable inflammation were homogenized in 0.5% (w/v) hexadecyltrimethylammonium bromide in potassium phosphate buffer, pH 6.0. For the myeloperoxidase (MPO) assay, 50µL of each sample were added to 200µL of o-dianisidine solution in phosphate buffer, pH 6.0 immediately prior to reading the change in absorbance at 460nm over 5 min using a microplate reader.

RESULTS

		Relative MPO activity (%)
Normal Placebo	100.00	-
TNBS Placebo	592.2***	100.0
TNBS+AstraGin®	158.7	26.8###



***p<0.001, when compared to Normal Placebo
###p<0.001, when compared to TNBS Placebo

MPO activity was significantly lower in TNBS placebo group after TNBS induction but recovered in TNBS+AstraGin® group.

8. ASTRAGIN® IS GRAS AND NDI

The Expert Panel at ABIMR has independently and collectively critically evaluated the safety assessment of AstraGin®, and unanimously concludes that the intended use of AstraGin® as a food ingredient, produced in accordance with Good Manufacturing Practice (GMP), and meeting the specifications presented in the document that is the basis for the GRAS determination, is generally recognized as safe. The Expert Panel further concludes that the intended use of GRAS based upon scientific procedures and corroborated by an extensive history of safe use (exposure). The Expert Panel believes that other experts qualified by training and experience to evaluate the safety of food ingredients would concur with this GRAS conclusion.

9. DISCUSSION

The wide spectrum of pharmacological properties of curcumin is attributed to its numerous effects on several targets including transcription factors, growth regulators, adhesion molecules, apoptotic genes, angiogenesis regulators, and cellular signaling molecules. Curcumin exerts anti-cancer activity mainly through blocking cell cycle progression and triggering tumor cell apoptosis [2].

Although curcumin has a potential to support numerous human health challenges, it has poor in vivo bioavailability, as evidenced by its extremely low concentrations in blood plasma, urine, and peripheral tissues even after oral ingestion of heroic doses [3,4]. Major factors are the undesirable physicochemical and pharmacokinetic properties such as low aqueous solubility, chemical instability at neutral and slightly alkaline pH, susceptibility to autoxidation, its avid metabolism by reduction and conjugation in vivo, and poor absorption in the gastrointestinal tract [1, 5, 6, 7]. A previous report suggested that approximately 75% of ingested curcumin (1 g/kg of body weight) was excreted in the feces and that curcumin was poorly absorbed from the intestine of rats [16]. An animal study demonstrated that the oral bioavailability of curcumin was about 1% in the rat [17].

Despite the lower bioavailability, therapeutic efficacy of curcumin against various human conditions, including neurodegenerative [8], atherosclerosis [9], cardiovascular [10], cancer [11], pulmonary, autoimmune and neoplastic diseases [12], biliary and hepatic disorders [13], diabetes [14], and skin diseases [15] has been documented.* Enhanced bioavailability of curcumin in the near future is likely to bring this promising natural product to the forefront of therapeutic agents for supporting human health conditions.*

Two major strategies have been pursued to improve the bioavailability of curcumin. The first is a combination with adjuvants capable of increasing the absorption of curcumin, like piperine, quercetin, or turmeric oil. The second strategy has been the inclusion of curcumin in a lipophilic matrix (liposomes, phytosomes, and lipid micro- and nanoparticles) or encapsulation with micellar surfactants or casein.

AstraGin® has shown in the three assays in section 6 to have modest effect in the absorption of curcumin and better effect than adding piperine to curcumin. Overly processed foods, stress, medication all contribute to different degree of compromised gut function, even in healthy people. The saponins of AstraGin® have sugar moiety (mainly glucose) attached to the steroid skeleton, so they are amphiphilic compounds in nature. These saponins can be used as pharmaceutical excipients to enhance the bioavailability of bioactives with low solubility and permeability, such as curcumin.

One study has demonstrated that ginsenoside can exert beneficial effect on the stabilization of the lipid carrier matrices which are composed of phospholipids/fats and are prone to problems associated with stability during the storage period [18]. In another aspect, ginsenosides in nanostructured lipid carrier dispersion containing curcumin can inhibit curcumin crystal formation both immediately after preparation and during an extended storage period. Most saponins all share similar these properties. We speculate these factors are also the possible mechanisms of AstraGin® on different curcumin formulations absorption. So considering the effect of AstraGin® in reducing inflammation and repairing damaged gut wall (section 7) where most absorption occurs, it may be a good strategy to incorporate AstraGin® in a curcumin supplement not for its demonstrated effect in increasing the absorption of curcumin but to also assure optimum gut function so the baseline absorption performance is not compromised.

10. NUTRITION FACTS

Nutrient	UOM	Per 100 g
Calories (Kcal)	Kcal	377
Calories from Fat	g	3
Total Fat (by GC)	g	0.35
Monounsaturated Fat	g	0.03
Polyunsaturated Fat	g	0.12
Saturated Fat	g	0.19
Trans Fat	g	0.00
Cholesterol	mg	<2.0
Sodium	mg	35
Carbohydrates	g	91.2
Total Dietary Fiber (TDF)	g	0.3
Total Sugar		
Fructose	g	0.8
Glucose	g	0.5
Lactose	g	<0.5
Maltose	g	2.1
Sucrose	g	6.4
Protein (Combustion)	g	2.2
Vitamin A (Retinol+Carotene)	IU	<20
Vitamin C	mg	<0.5
Calcium	mg	11
Iron	mg	0.60
Moisture	g	5.8
Ash	g	0.43

Analysis performed by OMIC USA Inc. Portland, Oregon, USA 97210

11. REFERENCE

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*The contents of this publication have not been evaluated by the Food and Drug Administration. They are not presented here to provide information and advice that in any way is intended to diagnose, treat, cure or prevent disease.

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