



AstraGin[®]

A full spectrum gut health nutraceutical
absorption, healing, microbiota, and immune

16 *in-vitro* and 8 *in-vivo* studies

Published in Journal of Agricultural and Food Chemistry, Molecular Nutrition & Food Research, Scientific Reports

Patents US8197860 B2, Patent pending US 13/444765, US 13/444770, US 12/424193
US 12/345218

NPN 80094882



FOUNDATION FOR HEALTHY GUT FUNCTIONS



The human gut has a huge impact on the entire health of the body. A healthy gut contributes to better absorption, a healthy gut ecosystem, stronger immune functions, heart health, brain health, improved mood, healthy sleep, and more.

Nutrients in the foods, once digested, may enter the human body from the gut lumen by passive diffusion and osmosis. But many nutrients such as amino acids, do require active transporters located on the intestinal epithelial cell membrane to transport them from the gut lumen to circulation, such as SGLT1 for glucose absorption. These active transporters are activated by mRNA.

Disruption of normal barrier function is a fundamental factor in inflammatory bowel disease, which includes increased epithelial cell death, modified mucus configuration, altered tight junctions, along with decreased expression of antimicrobial peptides.

Gut microbiota is a dynamic “organ” of critical importance for human health. In healthy conditions the symbiotic microorganisms in the intestinal tract participate in the normal nutrient metabolism and immunity regulation of the host. Gut mucosal integrity is absolutely important for the adhesion and growth of gut microbiota.

The lymphoid elements of the gut comprise organized lymphoid tissues such as the Peyer’s patches (PP), and the mesenteric lymph nodes (MLN). The effector sites of the intestine are the mucosal epithelium and underlying lamina propria (LP). Here there are many different immune cells including activated T cells, plasma cells, mast cells, dendritic cells and macrophages. Inflamed intestinal epithelial cell and lamina propria reduce these immune cells and weaken the immune functions.

ASTRAGIN® PROMOTES ABSORPTION, INTESTINAL WALL REGENERATION, MICROBIOTA POPULATION AND IMMUNE FUNCTIONS



AstraGin® is NuLiv Science's proprietary gut nutraceutical composed of highly purified and fractionated *Panax notoginseng* and *Astragalus membranaceus* produced by a proprietary pharmaceutical extraction and processing technology.

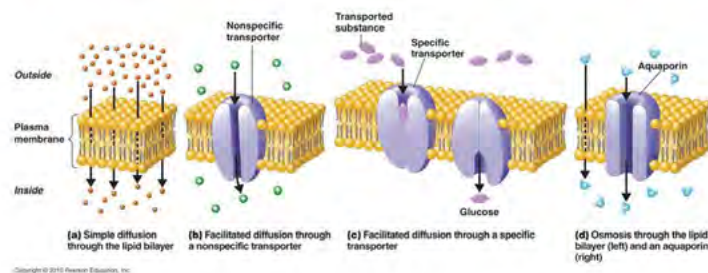
AstraGin® has shown in 16 *in-vitro* and 8 *in-vivo* studies that are published in the Journal of Agricultural and Food Chemistry, Molecular Nutrition & Food Research and Scientific Reports to:

- increase the absorption of peptides, amino acids, fatty acids, vitamins and phytonutrients by up-regulating the absorption specific mRNA and transporters, such as SGLT1, CAT1, and GLUT4.
- repair ulcerated and damaged intestinal walls and reduce intestinal submucosa inflammation. AstraGin® was shown in a hematoxylin-eosin stain and a MPO assay to reduce ulceration and unclear surfaces of intestinal epithelial cells and sub-mucosal edema in TNBS-induced colitis rats.
- may help maintain a healthy microbiota population by mending ulcerated and damaged intestinal epithelial cell surfaces for the microbiota to populate.
- may help support stronger immune functions by mending ulcerated epithelial cells and reducing the inflammation in intestinal mucosal lamina propria that hosts the gut-associated lymphoid tissue (GALT1), T cells, plasma cells, mast cells, dendritic cells, and macrophages.

ASTRAGIN® INCREASES ABSORPTION & BIOAVAILABILITY OF AMINO ACIDS, PEPTIDES, FATTY ACIDS, VITAMIN, AND PHYTONUTRIENTS

Types of Transport Proteins

- Non-specific transporter
- Specific transporter

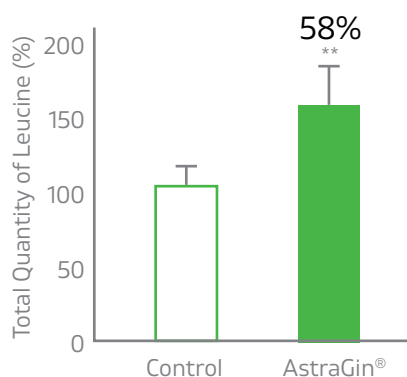


Many nutrients, such as glucose and amino acids, are absorbed through special absorption sites on intestinal lumen by special transport proteins.

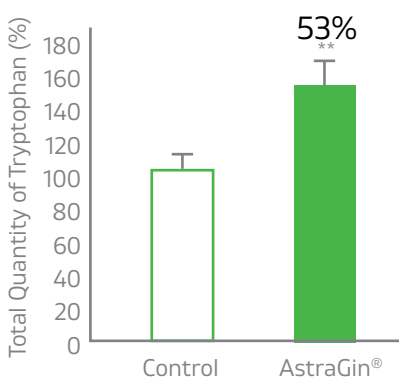
AstraGin® has shown in 16 *in-vitro* in Caco-2 cell and 8 *in-vivo* in normal and TNBS-induced colitis rat to increase the absorption of amino acids, peptides, fatty acids, folate, and phyto nutrients by up-regulating the expression level of special mRNA and transport proteins, such as SGLT1 and CAT1.

ABSORPTION

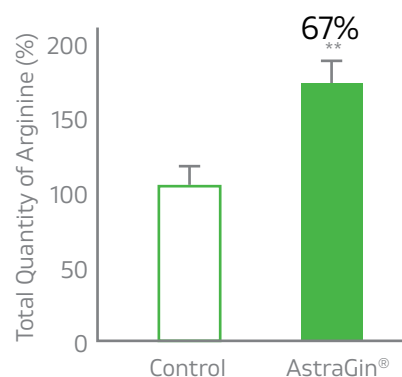
ASTRAGIN® INCREASES AMINO ACIDS AND PEPTIDES ABSORPTION IN CACO-2 CELL



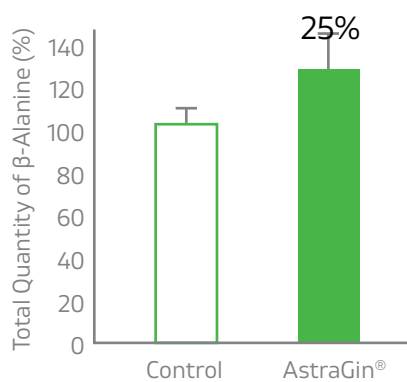
Leucine



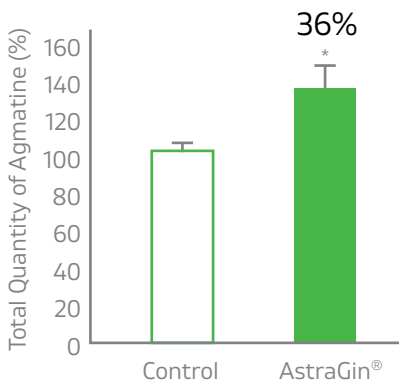
Tryptophan



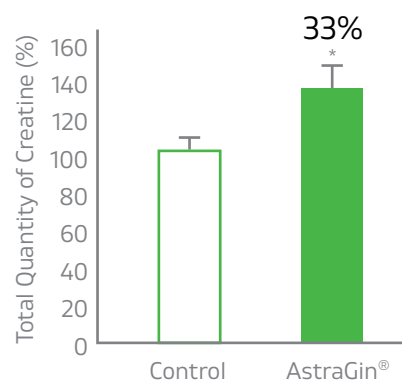
Arginine



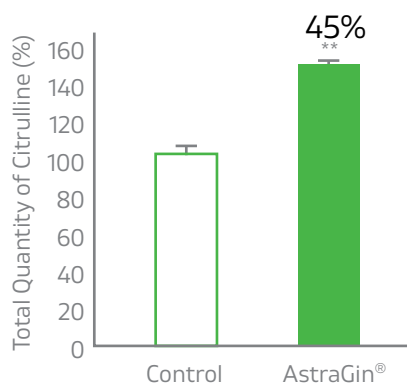
β-Alanine



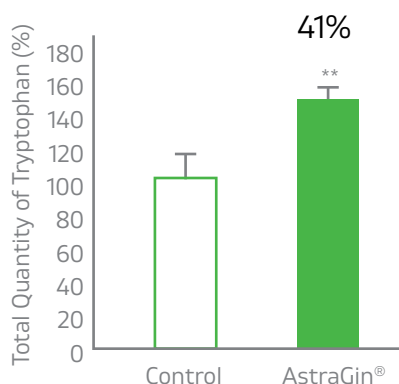
Agmatine



Creatine



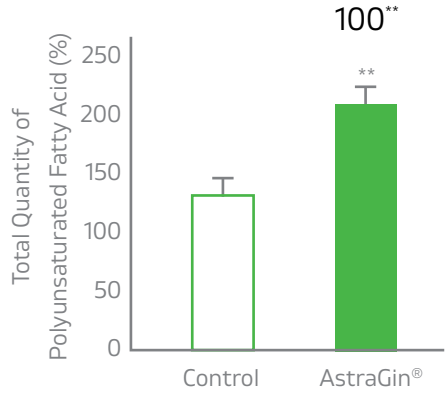
Citrulline



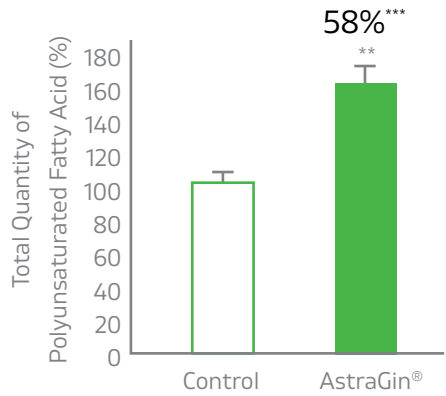
Peptides

ABSORPTION

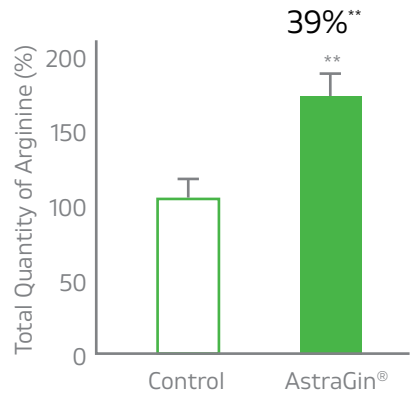
ASTRAGIN[®] INCREASES FATTY ACIDS ABSORPTION



Fish Oil

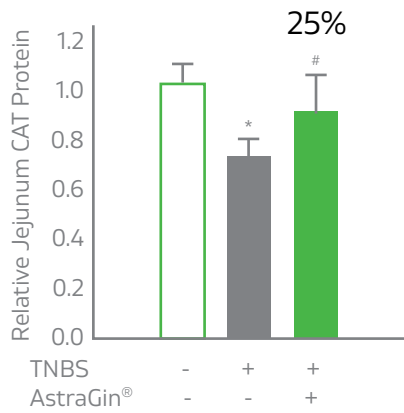


Flax Seed Oil

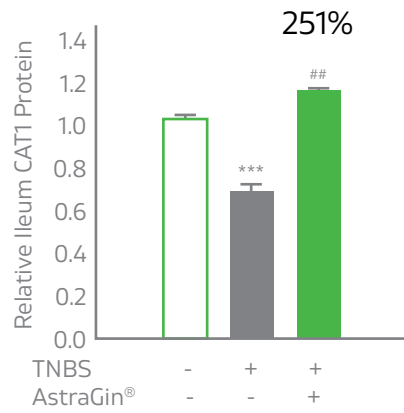


Omega-7 Fatty Acids

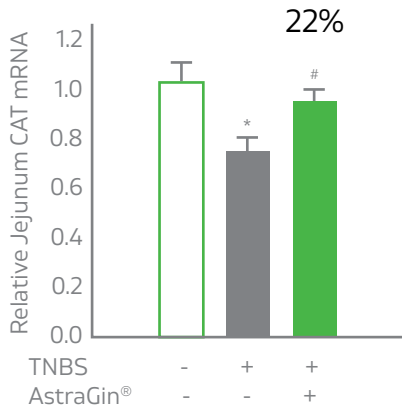
ASTRAGIN® INCREASES PROTEIN TRANSPORTER CAT1 IN RATS



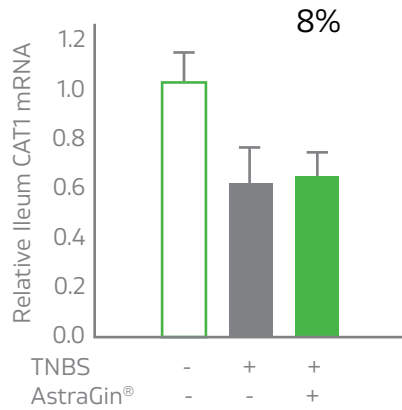
Jejunum CAT1 Protein



Ileum CAT1 Protein



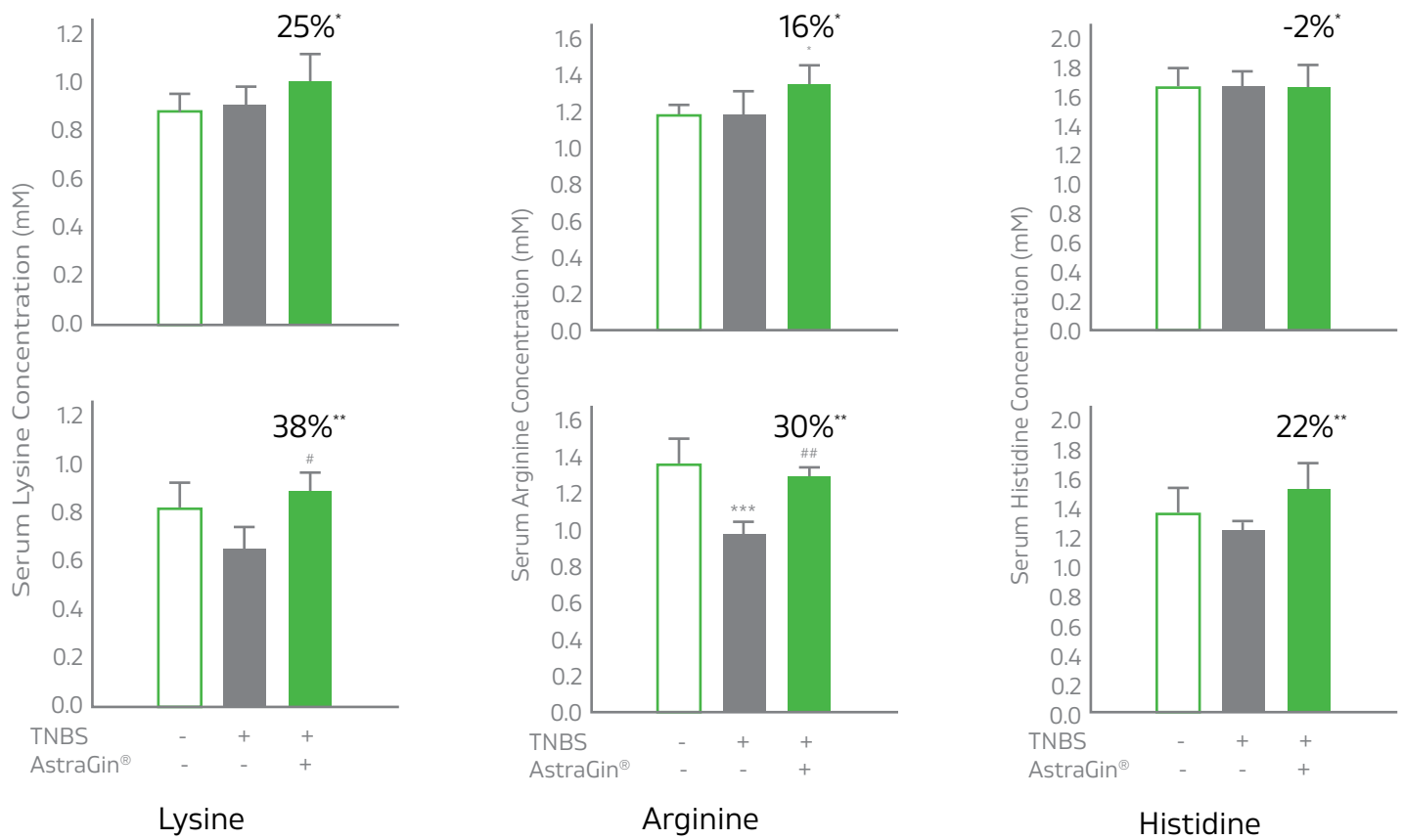
Jejunum CAT1 Transcript



Ileum CAT1 Transcript

ABSORPTION

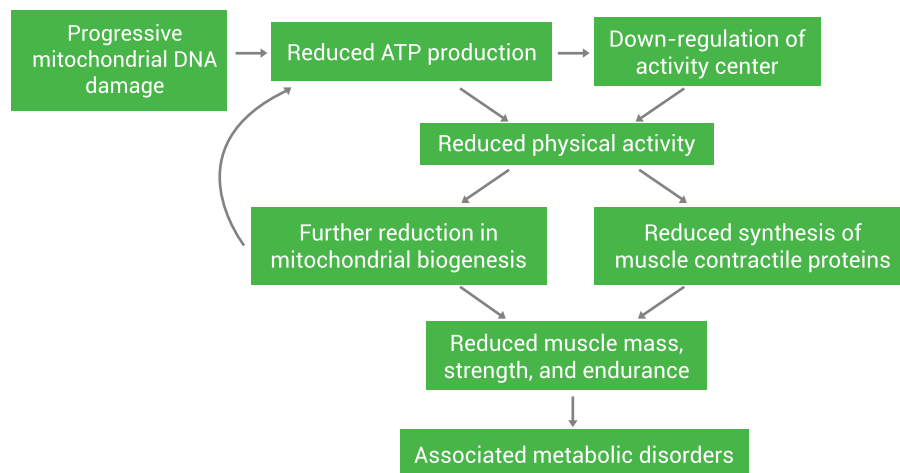
ASTRAGIN® INCREASES LYSINE, HISTIDINE AND ARGININE ABSORPTION IN NORMAL AND TNBS-INDUCED RATS



* 1 week after AstraGin® in normal rats

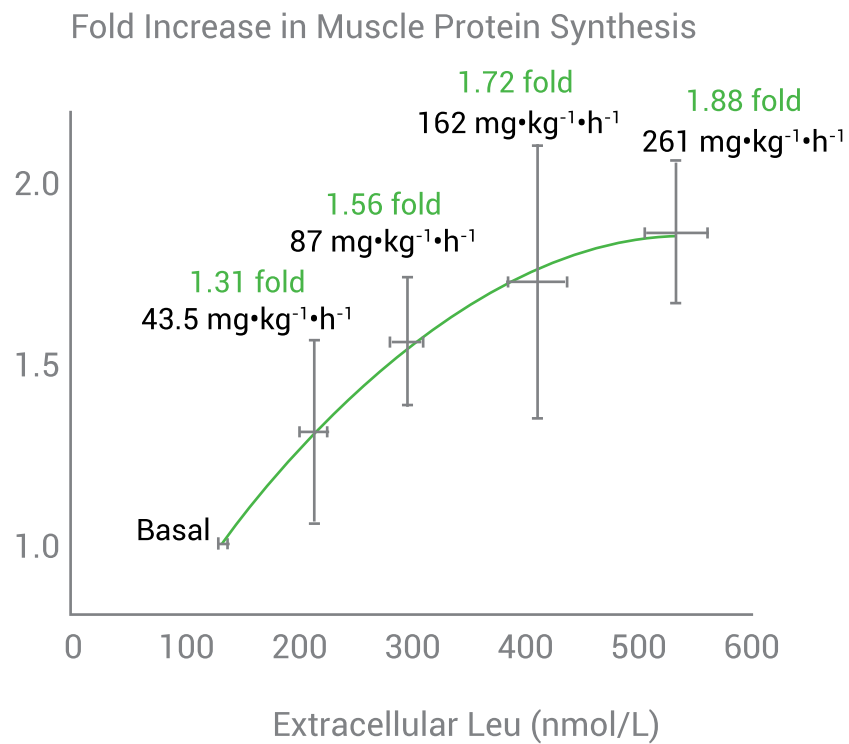
** 1 week after AstraGin® in TNBS-induced colitis rats

ASTRAGIN[®] INCREASES PROTEIN SYNTHESIS THROUGH MITOCHONDRIAL FUNCTION DERIVED SIGNALING PATHWAYS



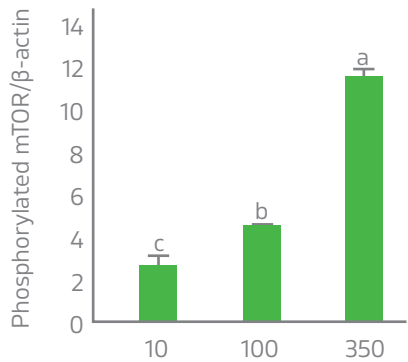
Mitochondrial dysfunction inhibits muscle mass growth. AstraGin[®] has shown to increase liver ATP production by 18% and elevated mitochondrial function.

PLASMA CONCENTRATION LEVEL OF LEUCINE AND HUMAN MUSCLE PROTEIN SYNTHESIS

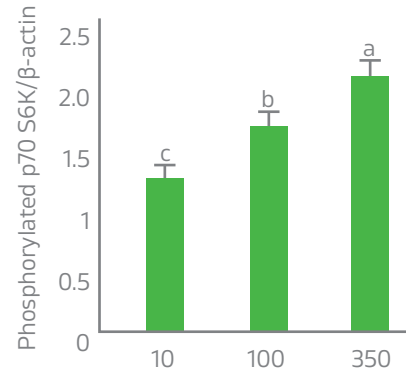


Muscle protein synthesis is influenced by the availability of leucine.

ARGININE CONCENTRATION AND mTOR PATHWAYS



L-Arginine Concentration in Culture Medium (μM)



L-Arginine Concentration in Culture Medium (μM)

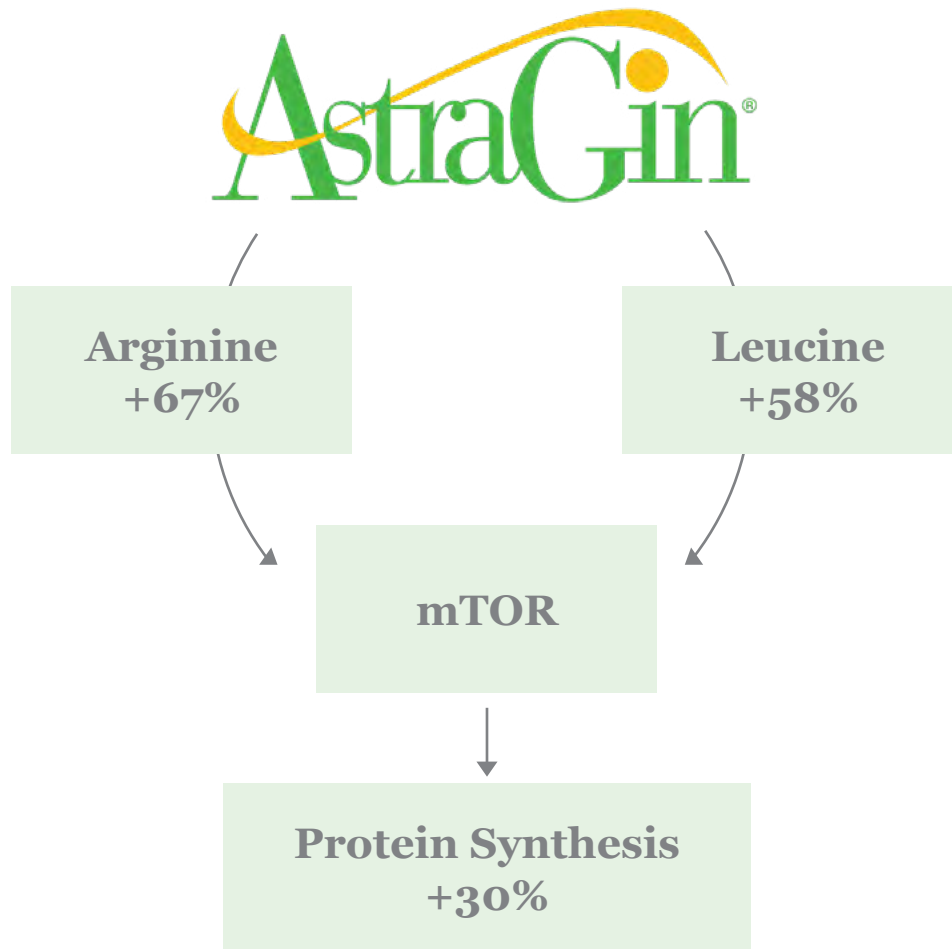
mTOR

mTOR (Mammalian target of rapamycin) is an enzyme that is stimulated by nutrients and growth factors and inhibited by stress to ensure that cells grow only during favorable conditions.

p70S6K

p70S6K (S6K1) is a kinase that acts downstream of mTOR signaling in response to growth factors and plays a role in protein synthesis and in cell growth control.

EFFECTS OF ASTRAGIN® ON mTOR PATHWAY



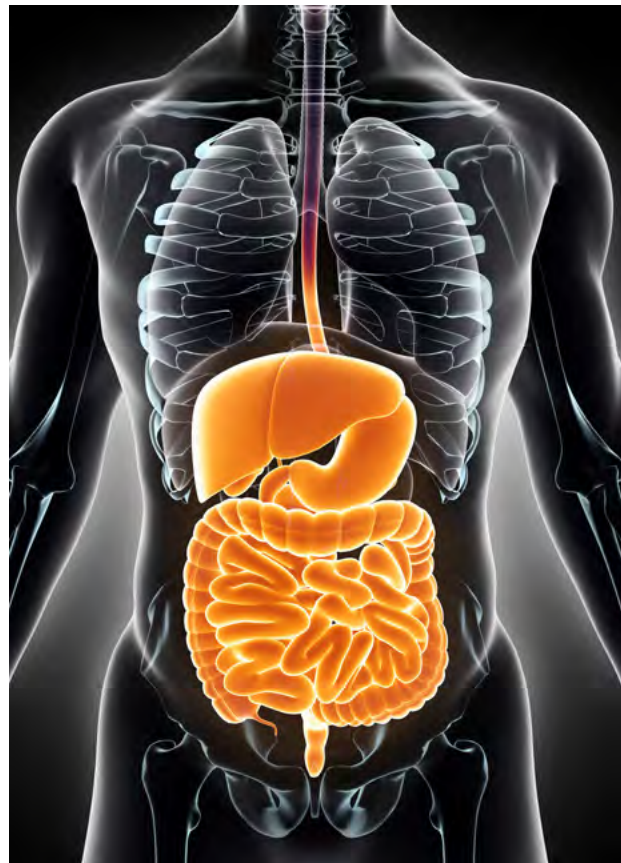
Based on the difference in extracellular concentration of leucine from 130nM to 210nM.

INTESTINAL LUMEN PERMEABILITY ON HEALTH AND DISEASE

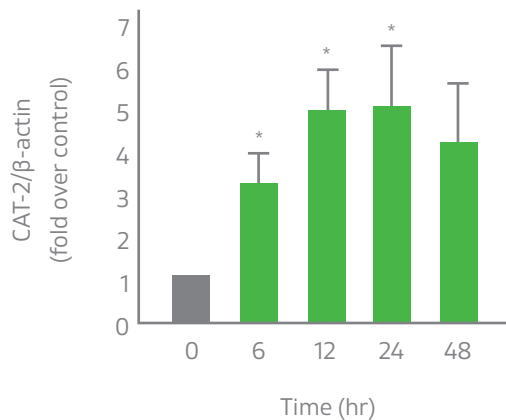
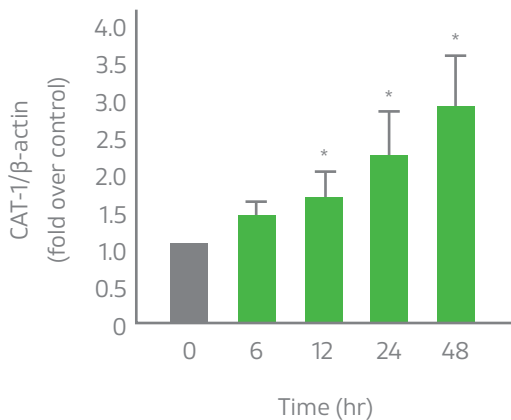
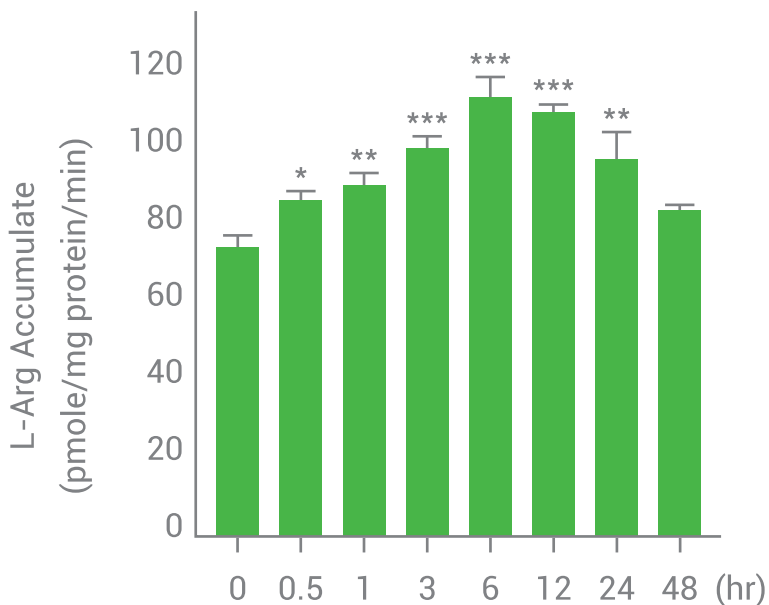
Healthy epithelial cells of the villi transport nutrients (amino acids and carbohydrates) and lacteals (lipids) from the lumen of the intestine to the blood stream. When epithelial barrier integrity is compromised due to inflammation, medications or other factors, harmful substances get into our body.

Precise mechanisms of this condition is still unknown. Most studies concur that it is associated with hereditary, infectious, environmental, and auto-immune factors. The integrity of the intestinal epithelial barrier plays a critical role in human health.

Restoration of the epithelial barrier integrity is an important healing response in intestinal disorders. Medications such as non-steroidal anti-inflammatory drugs, steroids, and immunomodulators, are limited in their application because of poor efficacy and adverse effects.

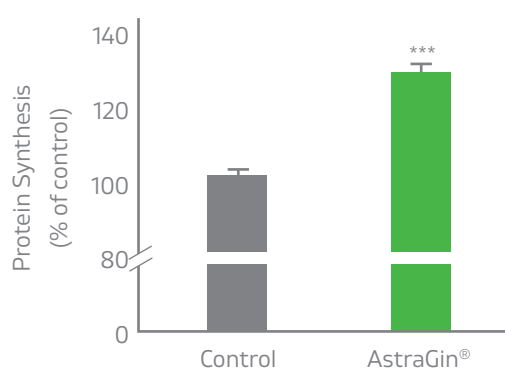
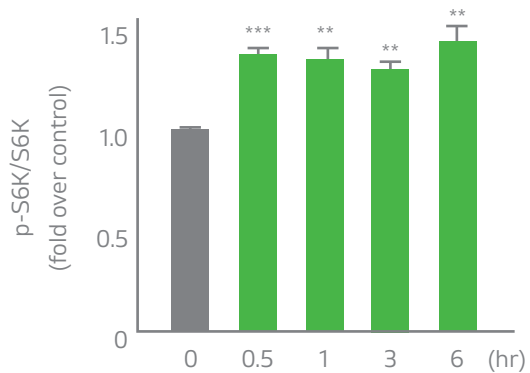
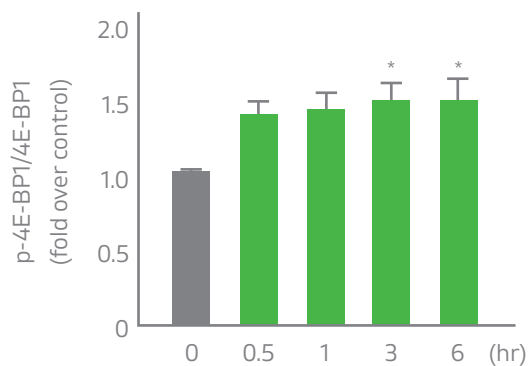
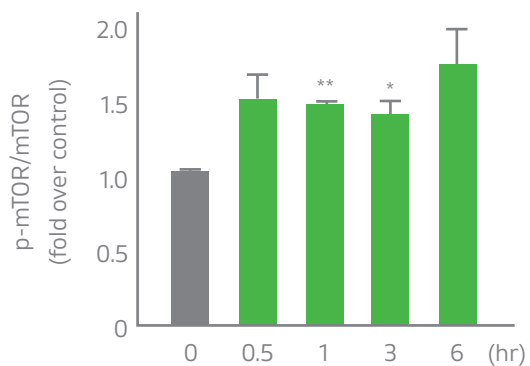


ASTRAGIN® INCREASES L-ARGININE UPTAKE AND CAT TRANSPORTER LEVELS IN CACO-2 CELLS



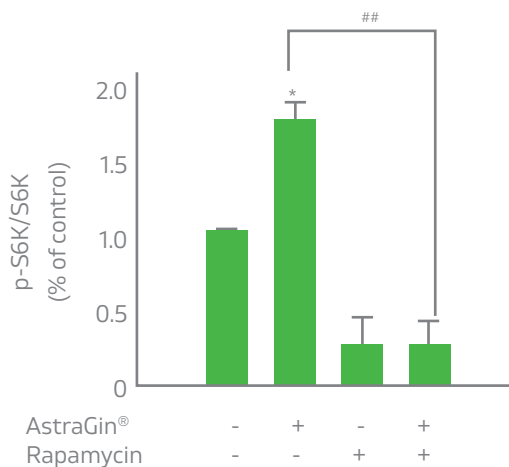
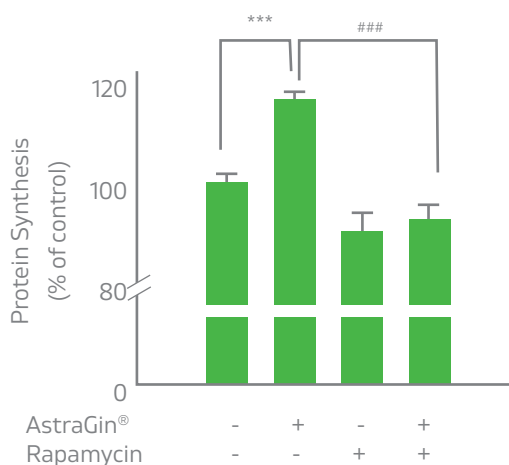
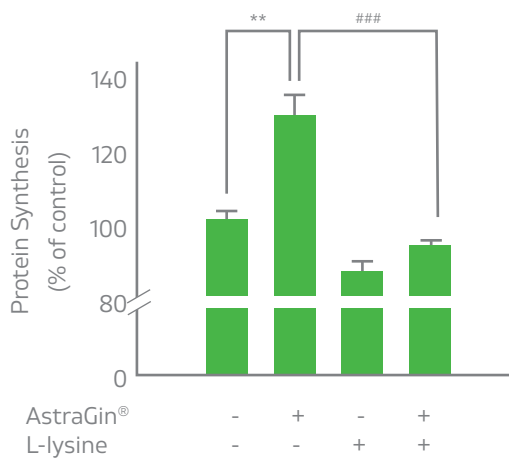
*p<0.05, **p<0.01, and ***p<0.001 versus the untreated control.

ASTRAGIN® ACTIVATES THE mTOR PATHWAY AND ENHANCES PROTEIN SYNTHESIS IN CACO-2 CELLS



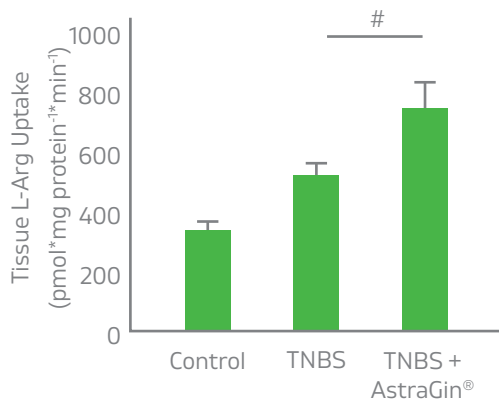
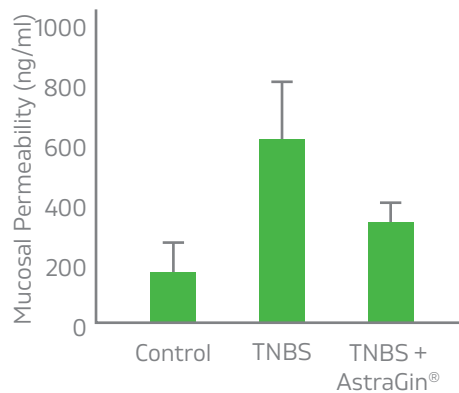
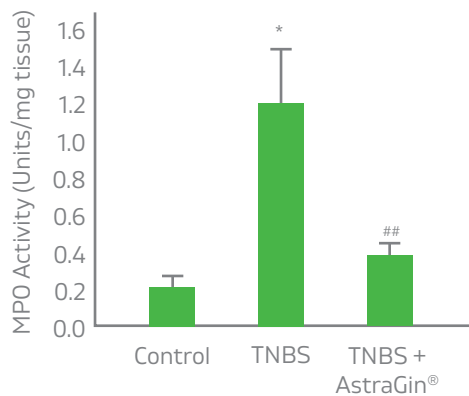
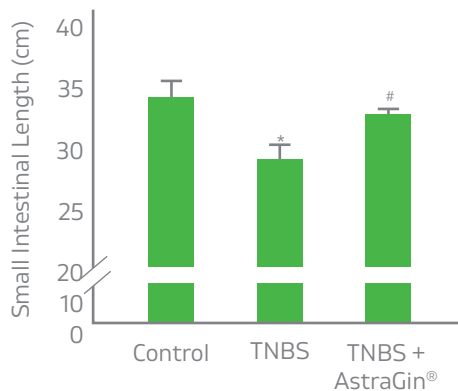
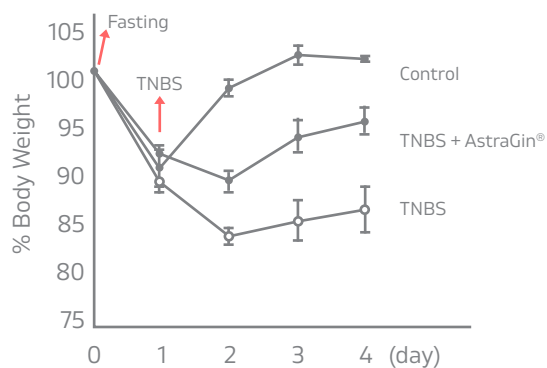
* $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$ versus the untreated control.

LYSINE AND RAPAMYCIN SUPPRESS THE EFFECTS OF ASTRAGIN® ON *mTOR* SIGNALING PATHWAY

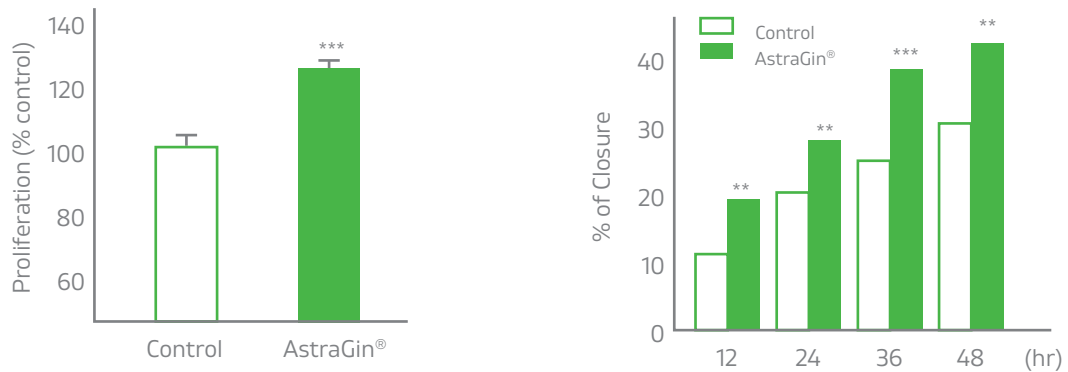


*p < 0.05, **p < 0.01, and ***p < 0.001 versus the untreated control.
p < 0.01, and ### p < 0.001 versus the AstraGin®-treated.

ASTRAGIN[®] REDUCES INFLAMMATION IN TNBS-INDUCED COLITIS MICE



ASTRAGIN[®] PROMOTES CELL PROLIFERATION AND SCRATCH WOUND CLOSURE IN CACO-2 CELLS



The mTOR pathway, a central regulator of human metabolism and physiology, regulates cell growth, cell proliferation, cell motility, cell survival, protein synthesis, autophagy, and transcription.

p<0.01, and *p<0.001 versus the untreated control.

ASTRAGIN® REDUCES INTESTINAL MUCOSA INFLAMMATION AND PERMEABILITY

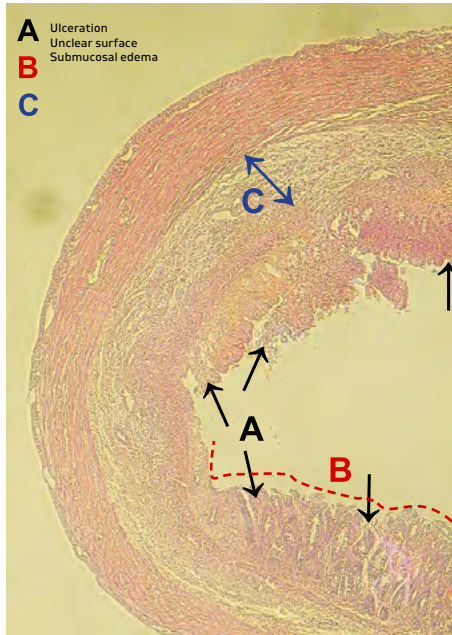


CONTROL



Normal healthy colon cells

IBD MODEL



Inflamed TNBS induced colon cells

ASTRAGIN® UNDER IBD MODEL

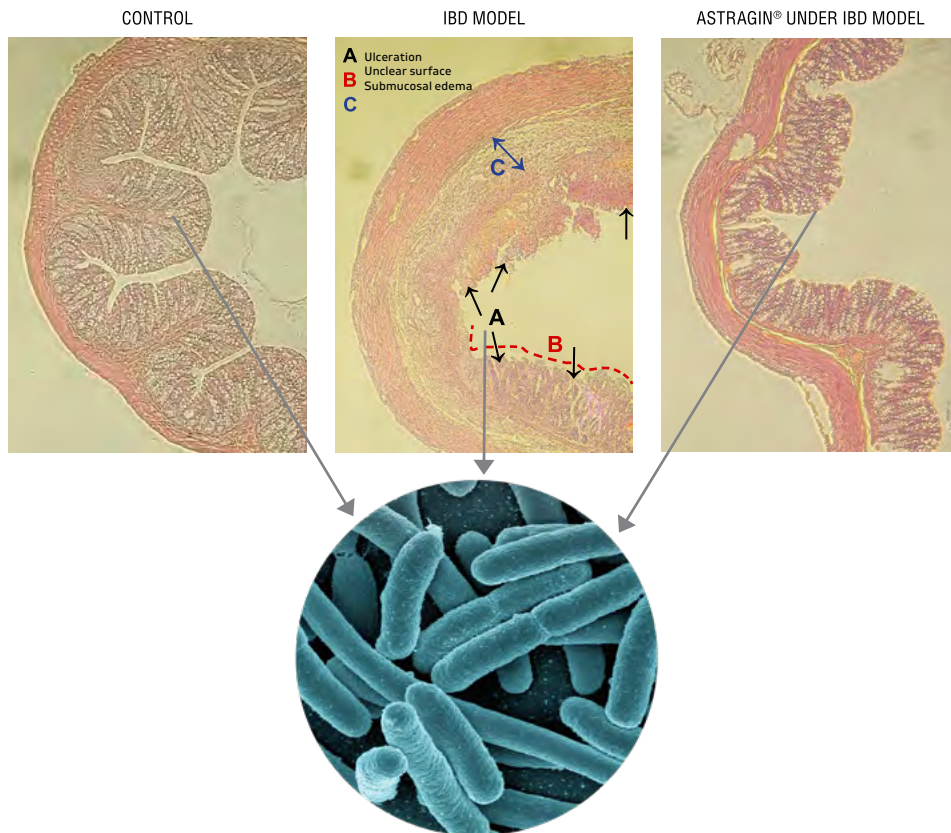


AstraGin®-treated TNBS-induced colon cell

AstraGin® was shown in a hematoxylin-eosin stain and a MPO assay to reduce ulceration and unclear surface of intestinal epithelial cells and sub-mucosal edema in TNBS-induced colitis rats. It is suggested from the many *in-vitro* studies that this effect may be due to AstraGin®'s ability to up-regulate the mTOR pathway to increase the protein synthesis and cell proliferation.

ASTRAGIN[®] MAY SUPPORT A HEALTHY GUT FLORA POPULATION

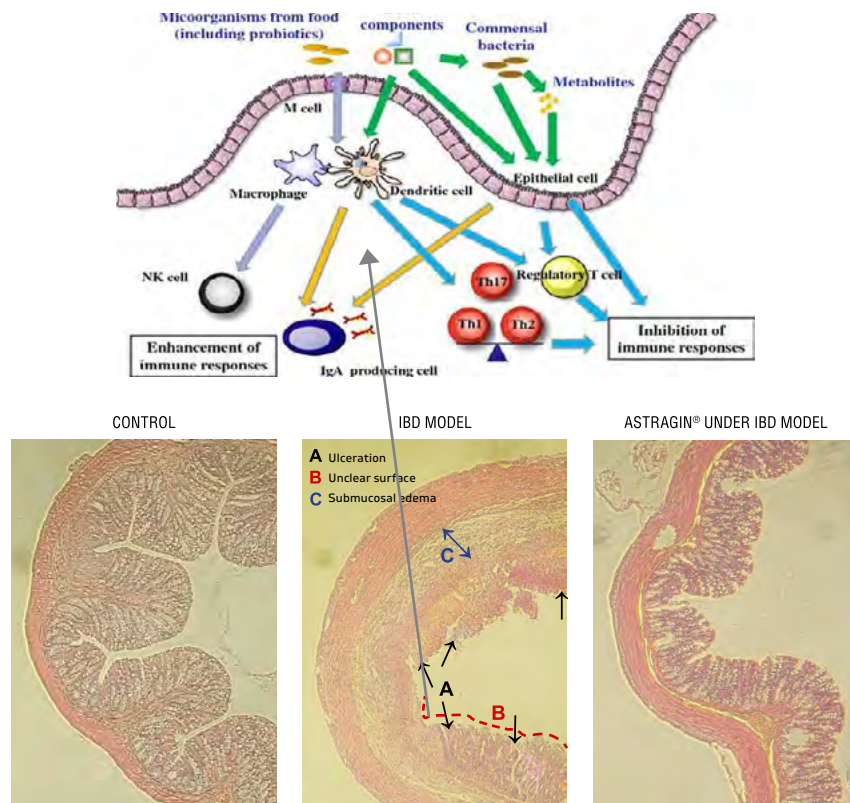
Gut microbiota is a dynamic “organ” of critical importance for human health. In healthy conditions, the symbiotic microorganisms in the intestinal tract participate in the normal nutrient metabolism and immunity regulation of the host. Gut mucosal integrity is absolutely important for the adhesion and growth of gut microbiota.



AstraGin[®] may help populate good gut microbiota by mending ulcerated and damaged intestinal epithelial cells for the microbiota to live.

ASTRAGIN® MAY SUPPORT STRONGER IMMUNE FUNCTIONS

Intestinal epithelial cells and sub-mucosa (lamina propria (LP)) host gut-associated lymphoid tissue (GALT), T cells, plasma cells, mast cells, dendritic cells, and macrophages. Inflamed intestinal epithelial cells and lamina propria reduce these immune cells and weaken the immune functions.



AstraGin® has shown to repair ulcerated epithelial cells and reduce inflammation in lamina propria that host many immune cells, such as gut-associated lymphoid tissue (GALT), T cells, plasma cells, mast cells, dendritic cells, and macrophages.

PUBLICATIONS

1. T.C. Chang, etc. Effect of ginsenosides on glucose uptake in human Caco-2 cells is mediated through altered Na⁺/glucose cotransporter 1 expression. *J. Agric. Food Chem.* (2007)
2. T.C. Chang, etc. A gut microbial metabolite of ginsenosides, compound K, induces intestinal glucose absorption and Na⁽⁺⁾ /glucose cotransporter 1 gene expression through activation of cAMP response element binding protein. *Mol Nutr Food Res.* (2015)
3. T.C. Chang, etc. Astragaloside II promotes intestinal epithelial repair by enhancing L-arginine uptake and activating the mTOR pathway. *Scientific Reports.* (2017)

PATENTS

Title	Country	Patent No.	Application No.
Method for Regulating Nutrient Absorption with Astragalus Fraction	USA	US 8, 197, 860 B2	US 13/444765 & US 13/444770 CIP of US 12/424, 193
	China	CN 200610090113.0	
	Taiwan	TW I271195	
Method for Regulating Nutrient Absorption with Notoginseng Fraction	USA		US 12/345, 218
	China	CN 200610090114.5 CN 200910178493.7 CN 200910178492.2	
	Taiwan	TW I317280	



PRODUCT INNOVATION NOTES



For questions and additional information please contact



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