GI Repair SAP

Science-based formulation for GI support

Gastrointestinal (GI) health is a hallmark of overall well-being of an individual. Apart from its usual functions of food digestion and absorption, the GI tract plays a host of other roles including gut-microbiome crosstalk which regulates epithelial and immune functions. The gut-brain axis is responsible for communication between the gut and the central nervous system, influencing cognition, emotional and mental health. GI disorders such as irritable bowel syndrome (IBS), dyspepsia, ulcerative colitis and Crohn's disease can severely affect quality of life and mortality. Although general medical approaches to treating these ailments do help, natural therapeutic approaches provide a gentle healing mode of recovery, with minimal side effects. Many of these ingredients such as ginger, marshmallow, curcumin, and licorice have been used in traditional medicine since ancient times for their gut healing properties. New clinical evidence has established their therapeutic potential in mitigating GI disorders. Evidence suggests these ingredients can reduce mucosal inflammation, improve gastric emptying, and help promote beneficial gut microbial flora.

GI Repair SAP is a synergistic formulation of key evidence-based nutraceuticals that can help promote GI health by improving gut permeability, reducing gastric and intestinal inflammation, ameliorate peptic ulcers, promote gastric emptying, improve peristalsis and help gut microbial flora thrive.

ACTIVE INGREDIENTS

Each serving (~6.3 g) contains:

Quercetin	100 mg
Marshmallow (*Althaea officinalis*)	40 mg
Aloe vera leaf gel extract 8:1	300 mg
Deglycyrrhizinated licorice (*Glycyrrhiza glabra*)	400 mg
L-Glutamine	1500 mg
Boswellia (*Boswellia serrata*) extract, providing 70% organic acids, 35% boswellic acids	200 mg
N-Acetylglucosamine	1000 mg
Pectin (*Malus domestica*)	1000 mg
Slippery elm (*Ulmus rubra*)	250 mg
Zinc L-carnosine	75 mg
Ginger (*Zingiber officinale*) rhizome extract, 5% gingerols	50 mg
Turmeric (*Curcuma longa*) root extract, 95% curcuminoids	100 mg

Turmeric root extract is tested for curcumin I, demethoxycurcumin, and bisdemethoxycurcumin.

Other ingredients: Tropical punch flavour, lemon flavour, and *Stevia rebaudiana* leaf.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, preservatives, or artificial flavour or colour.

This product is non-GMO and vegan friendly.

GI Repair SAP contains 190 g per bottle.

DIRECTIONS FOR USE

Adults: Take 1 serving (Fill scoop up to the 10 ml mark) once daily or as directed by your healthcare practitioner. Mix in 8 oz. (235 ml) or more of water or natural unsweetened fruit juice.

INDICATIONS

GI Repair SAP helps improve impaired gut permeability, reduce gastric and intestinal mucosal inflammation, and can help:

- Ameliorate peptic ulcers.
- Improve stool consistency, gastric emptying efficiency and peristalsis.
- Promote beneficial gut flora.
- Reduce gall bladder volume and promote gall bladder health.

CAUTIONS AND WARNINGS

Consult a healthcare practitioner prior to use if you are pregnant or breastfeeding, or if symptoms persist or worsen, or have gallstones, bile duct obstruction, stomach ulcers or excess stomach acid, or if you are taking antiplatelet medication or blood thinners.

Known adverse reactions: Hypersensitivity, such as an allergy, has been known to occur; in which case, discontinue use.

Do not use if seal is broken. Keep out of reach of children.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **GI Repair SAP** lot number have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

NFH®

351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

For healthcare professional use only.

The gastrointestinal (GI) tract's function is not restricted to food digestion and subsequent nutrient and fluid uptake but profoundly contributes to health in many ways. This includes but is not limited to the gut-microbiome crosstalk to support food digestion, regulation of major epithelial and immune functions and the gut-brain axis: bidirectional communication between the central and the enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions that modulate mood and general well-being. [1] An individual's quality of life and mortality is significantly affected by an unhealthy GI tract which can result in symptoms associated with functional dyspepsia and irritable bowel syndrome (IBS) and comprise flatulence, bloating, regurgitation, heartburn, nausea, vomiting, constipation, diarrhea, food intolerance, incontinence, abdominal pain and cramps, loss of appetite, weight loss and blood in stools. Five key criteria are widely recognized for a healthy GI system: 1) Effective digestion and absorption of food, 2) Absence of GI illness, 3) Normal and stable intestinal microbiota, 4) Effective immune status and 5) Status of well-being. [1] Natural approaches to support the management of GI disorders and invigorate GI health exist, and substantial research evidence supports the therapeutic potential and efficacy of these nutraceutical ingredients.

NUTRACEUTICALS FOR GI REPAIR

L-Glutamine

Glutamine, the most predominant amino acid in the blood, the skeletal muscle, and the free amino acid pool is a key nutrient for the intestine, where 30% total glutamine is used. [2, 3] Tight junctions are dynamic structures comprising of various proteins that seal adjacent epithelial cells to produce a physical barrier between epithelial and endothelial cells. [3, 4] They are critical in modulating the transport of luminal molecules into mucosal cells by adjusting their tightness in response to various physiological stimuli and signal pathways. [3, 4] In various intestinal pathologies including inflammatory bowel disease (IBD) and celiac disease, maintenance of intestinal permeability by tight junction proteins has been proven to be essential for effective treatment. [3] Evidence from studies shows that glutamine supplementation was immensely helpful in individuals with an impaired gut permeability by enhancing the expression of tight junction proteins. It is well established that glutamine modulates the expression of tight junction proteins, in addition to its effect in suppressing NF-kB pathway activation, inhibiting STAT activation and expression of inflammatory cytokines such as IL-6 and IL-8 in intestinal tissues. [3] In a systematic review, glutamine-enriched diets were shown to significantly improve immunologic aspects in trauma patients and to alleviate mucositis in post-chemotherapy patients. [5, 6]

N-Acetylglucosamine

Glycosaminoglycans are long linear polysaccharides that have various physiological functions in the body, especially attached to mucin they help form a protective barrier separating bacteria from the intestinal epithelium. Inflammation at mucosal surfaces results in breakdown of glycosaminoglycans, specifically in individuals with IBD. *N*-acetylglucosamine (NAG) is a naturally occurring amino sugar precursor for epithelial glycosaminoglycan synthesis, directly incorporated into glycosaminoglycans and glycoproteins, as a substrate for tissue repair mechanisms. [7] This protective effect helps in mitigation of several symptoms of IBD, as was demonstrated in an open label clinical study. Patients suffering from IBD (n=64) upon being administered 6 g of NAG daily for 4 weeks reported significant improvement in IBD symptoms and lowered symptom scores for reduced abdominal pain, passage of mucus, rectal bleeding diarrhea, and nausea. [8] NAG also shows potential in amelioration of other inflammatory bowel conditions such as Crohn's disease and ulcerative colitis. Administration of 3-6 g daily of NAG to 12 children suffering from Crohn's disease (CD) and ulcerative colitis (UC) showed symptomatic improvement in eight patients, with increased glycosaminoglycans and intracellular NAG in histological evaluations. [9]

Pectin

Pectin is a soluble dietary fiber present in many fruits and vegetables, more commonly apples, potatoes, sugar beets as well as citrus fruits. Structurally pectin fibers consist of branched segments of rhamnogalacturonans and linear homogalacturonan (1,4-D-galacturonan) segments. [10] Animal studies have demonstrated the protective effects of pectin on the intestinal barrier. Pectin supplementation reduced the production of proinflammatory cytokines such as IL-1β, IL-6 and TNF-α; as well as upregulated proteins responsible for intestinal integrity such as zonula, occludin and antimicrobial peptides β-defensin-1 (DEFB1). [11] These modulating parameters have in turn shown reduction in fat accumulation and improved weight gain in obese animal models. [12] A randomized controlled trial showed that administration of 24g pectin for 6 weeks in 46 IBD patients showed reduced IBD symptom scores and improved fecal bacterial composition, indicating the prebiotic benefits of pectin. [13] Pectin supplementation (enteral formula:liquid pectin 2:1) for 4 weeks to 18 children suffering from cerebral palsy significantly reduced gastric reflux and improved esophageal pH. [14]

Deglycyrrhizinated licorice (DGL) (*Glycyrrhiza glabra*)

The roots and rhizomes of licorice have been used in the treatment of GI disorders for centuries in traditional medicine. Glycyrrhiza glabra is known for its antimicrobial, hepatoprotective, antioxidant and laxative properties. [15] Animal studies have shown that in addition to glycyrrhizin, certain flavonoids in DGL also have bactericidal effect on Helicobactor pylori, which helps explain the mechanism of action behind its anti-ulcer properties. DGL may contribute to increased number of mucous secreting cells, thereby increasing levels of mucin. [16, 17] Supplementation with 75 mg twice a day of DGL for 30 days in 25 dyspepsia patients showed significant improvement of dyspepsia symptoms and was well tolerated. [15]

Slippery elm (*Ulmus rubra muhle*)

Slippery elm is a species of elm purported to have beneficial effects on GI distress. In a pilot study looking at herbal formulation containing slippery elm administered to 31 IBD patients for 3 weeks, the formulation appeared to ease some symptoms of IBD. [18] A further specific in vitro study showed that slippery elm has a dose dependent anti-inflammatory effect on colonic cells isolated from patients suffering with ulcerative colitis. The response of slippery elm was comparable to that of 5-aminosalicylic acid. [19] Further studies, especially human clinical trials should help to fully elucidate the beneficial effects of slippery elm.

Boswellia (*Boswellia serrata*)

Boswellic acids are the active therapeutic constituents of Boswellia serrata, which has been used for its anti-inflammatory properties since ancient times. Various in vitro and animal studies have demonstrated the potential of boswellia as an anti-inflammatory agent in the treatment of IBD. [20] Administration of 350 mg thrice a day for 6 weeks to ulcerative colitis patients showed an improvement in stool properties, scan microscopy of rectal biopsies and histopathology. [21] Therapeutic effects of boswellia in the management of Crohn's disease were comparable with mesalazine (5-aminosalicylic acid [5ASA] derivative, the standard treatment for CD), when boswellia extract was administered to 44 Crohn's disease patients and compared with 39 patients treated with mesalazine. [22] Another randomized, placebo-controlled, double blind study found that administration of 400 mg of boswellia extract thrice per day for 6 weeks to 25 collagenous colitis patients appeared to show clinical improvement of collagenous colitis. [23]

Curcumin (*Curcuma longa*)

Curcumin has been known to promote colon health by playing a key role by modulating NF-κB proinflammatory cytokines and the IL-6/STAT3 signaling pathway and could be therapeutically useful in several colonic inflammatory diseases, such as IBD. [24] Two clinical studies have evaluated the use of curcumin in IBD in 99 patients with UC and CD. [24, 25] As an adjunct to mainstream therapy (sulfasalazine or mesalamine or corticosteroids), curcumin dosed at 1100-2000 mg/day over 2-6 months duration has been shown to significantly improve symptoms in UC/CD patients compared to the placebo and enabled dosage reduction of corticosteroids or 5-ASA derivatives. [24, 25] Researchers reported that in the small study of 10 patients, some patients even stopped taking corticosteroids or 5-ASA. [24] Researchers also noted that curcumin had better clinical efficacy over placebo in the prevention of relapse and was welltolerated. [25] Based on this evidence, curcumin could be a promising and safe therapy for maintaining remission in patients with IBD and can be used as a steroidsparing induction agent in mild to moderate colitis or as an adjunct to maintain remission in patients nonresponsive to immunomodulators. An additional benefit of curcumin on gall bladder health and function has been observed. Supplementation with 20 mg curcumin showed significant reduction in gall bladder volume observed by ultrasound over 2 hours post administration, a positive indicator in promoting gall bladder health and preventing gall bladder stones. [26]

Quercetin

The antioxidant and anti-inflammatory effects of quercetin are well known. Recent studies have successfully established the gastroprotective benefits of these properties. In a randomized, double-blind clinical study conducted with 60 participants for 8 weeks, supplementation with 500 mg quercetin and vitamin C significantly reduced oxidative stress and inflammatory biomarkers including C-reactive protein and interleukin-6. [27] A population-based study conducted in Sweden with 505 patients showed that high intake of quercetin through diet was associated with less risk of developing abnormal cell growth in the gastric lining; quercetin particularly exerted a protective effect against oxidative stress. [28]

Zinc-L-Carnosine

Zinc-L-carnosine (ZnC) is a chelated compound that contains L-carnosine and zinc. ZnC is perhaps best known for its approved use in Japan for the management of stomach ulcers. In a randomized, controlled, double-blind study, 258 subjects with confirmed stomach ulcers were randomly assigned to receive 150 mg ZnC per day, a placebo, 800 mg of cetraxate hydrochloride (a known mucosal protection agent), or a placebo for 8 weeks. Endoscopy was done before and after treatment and subjective measures of symptoms were collected. Symptoms were 61% better in the marked improvement category in the ZnC group and 61.5% in the cetraxate group at 4 weeks. At 8 weeks, the ZnC group increased to 75% markedly improved compared to 72% for the cetraxate group. The endoscopic cure rate was 26.3% in the ZnC group and 16.2% in the cetraxate group at 4 weeks and 60.4% in the ZnC group and 46.2% in the cetraxate group at 8 weeks. This suggests that ZnC can provide superior relief of symptoms and improvement in gastric ulcers compared to a known mucosal protection agent. [29] Another study by the same group using 50, 75, or 100 mg twice daily showed improvement in symptoms and the endoscopic healing rate at all three doses. [30]

Ginger (*Zingiber officinale*)

Ginger has been used as a traditional herbal remedy since ancient times for its therapeutic potential against dyspepsia, flatulence and diarrhea. Recent clinical trials also show the impact of ginger on gastric emptying and motility. When gastric emptying and antral contractions were measured in 24 healthy individuals over 90 minutes following ingestion of 1200 mg of ginger capsule, it was found that gastric half emptying decreased significantly, accompanied with greater antral contractions. [31] Similar results were observed in a randomized double-blind trial conducted with 11 functional dyspepsia patients, where 1200 mg ingestion of ginger showed increased rate of gastric emptying and improved antral contractions. [32]

Marshmallow (*Althaea officinalis*)

Marshmallow root has been used in traditional medicine for relief from GI disorders and treatment of ulcers. [33] Marshmallow is rich in pectins, mucilage (colloidally soluble polysaccharides, particularly of acid arabinogalactans, galacturonic rhamnans and glucans) and flavonoids. [33] Supplementation of marshmallow extract (100 mg/kg/day) for 14 days significantly improved macroscopic, biochemical and histological condition of peptic ulcer pathology in rats. [34] Clinical studies of marshmallow on GI disorders are lacking and are warranted to evaluate its therapeutic potential given the traditional and preclinical evidence.

SYNERGISM FOR OPTIMAL EFFICACY

GI Repair SAP contains ingredients specifically chosen to target mucosal inflammation, manage stomach ulcers, improve gastric motility, and help beneficial gut bacteria thrive. Research evidence suggests that supplementing a combination of key ingredients such as slippery elm, licorice, marshmallow, and ginger can together provide a comprehensive approach to healing the digestive tract and promote smooth functioning of the gut. [18, 34]

REFERENCES:

1. Bischoff, S.C. "Gut health': a new objective in medicine?" *BMC Med.* (2011): 9-24.
2. Wu, G. "Intestinal mucosal amino acid catabolism". *J. Nutr.* Vil. 128, (1998): 1249–1252.
3. Kim, H. and Kim, M.H. "The Roles of Glutamine in the Intestine and Its Implication in Intestinal Diseases". *Int. J. Mol. Sci.* Vol. 18, (2017): 1051.
4. Gonzalez-Mariscal, L., et al. "Tight junction proteins. Prog. Biophys." *Mol. Biol*. Vol. 81 (2003): 1-44.
5. García-de-Lorenzo, A., et al. "Clinical evidence for enteral nutritional support with glutamine: A systematic review". *Nutrition.* Vol. 18 (2003): 805–811.
6. Benjamin, J., et al. "Glutamine and whey protein improve intestinal permeability and morphology in patients with Crohn's disease: A randomized controlled trial". *Dig. Dis. Sci.* Vol. 57 (2012): 1000–1012.
7. Murch, S.H., et al. "Disruption of sulphated glycosaminoglycans in intestinal inflammation". *Lancet.* Vol. 8847, No. 4 (*1993 Mar 20*): 341-711.
8. Zhu, A.Z.X. et al. "*N*-Acetylglucosamine for the Treatment of Inflammatory Bowel Disease: A real-world pragmatic clinical trial". *Natural medicine Journal.* Vol. 7, issue 4 (*April 2015*).
9. Salvatore, S. et al. "*A pilot study of N-acetyl glucosamine, a nutritional substrate for glycosaminoglycan synthesis, in paediatric chronic inflammatory bowel disease*". *Pharmacol Ther.* Vol. 12 (2000 Dec;14):1567-79.
10. Beukema et al. "The effects of different dietary fiber pectin structures on the gastrointestinal immune barrier: impact via gut microbiota and direct effects on immune cells". *Experimental & Molecular Medicine.* Vol. 1376 (2020): 52-1364.
11. Sun Y., et al. "Low-methoxyl lemon pectin attenuates inflammatory responses and improves intestinal barrier integrity in caerulein-induced experimental acute pancreatitis". *Mol Nutr Food Res.* Vol. 4 (*2017 Apr*): 61.
12. Jiang T., et al. "Apple-Derived Pectin Modulates Gut Microbiota, Improves Gut Barrier Function, and Attenuates Metabolic Endotoxemia in Rats with Diet-Induced Obesity". *Nutrients.* Vol. 3 (*2016 Feb 29*): 8-126.
13. Xu L., et al. "Efficacy of pectin in the treatment of diarrhea predominant irritable bowel syndrome". *Zhonghua Wei Chang Wai Ke Za Zhi.* Vol. 71, No. 3 (*2015 Mar*): 18-267.
14. Miyazawa R., et al. "Effects of pectin liquid on gastroesophageal reflux disease in children with cerebral palsy". *BMC Gastroenterol.* (*2008 Apr 16*): 8-11.
15. Raveendra K.R., et al. "An Extract of Glycyrrhiza glabra (GutGard) Alleviates Symptoms of Functional Dyspepsia: A Randomized, Double-Blind, Placebo-Controlled Study". *Evid Based Complement Alternat Med.* (2012): 2012-216970.
16. Fukai T., et al. "Anti-Helicobacter pylori flavonoids from licorice extract". *Life Sci.* Vol. 12, No. 1463 (2002): 71-1449.
17. Van Marle J., et al. "Deglycyrrhizinised liquorice (DGL) and the renewal of rat stomach epithelium". *Eur J Pharmacol.* Vol. (2-3), No. 225 (1981): 72-219.
18. Hawrelak J.A., Myers S.P. "Effects of two natural medicine formulations on irritable bowel syndrome symptoms: a pilot study". *J Altern Complement Med.* Vol. 10, No. 71 (*2010 Oct*): 16-1065.
19. Langmead L., et al. "Antioxidant effects of herbal therapies used by patients with inflammatory bowel disease: an in vitro study". *Aliment Pharmacol Ther.* Vol. 12, No. 205 (*2002 Feb*): 16-197.
20. Ammon H.P. "Boswellic Acids and Their Role in Chronic Inflammatory Diseases". *Adv Exp Med Biol.* No. 327 (2016): 928-291.
21. Gupta I., et al. "Effects of Boswellia serrata gum resin in patients with ulcerative colitis". *Eur J Med Res.* Vol. 1, No. 43 (*1997 Jan*): 2-37.
22. Gerhardt H., et al. "Therapie des aktiven Morbus Crohn mit dem Boswellia-serrata-Extrakt H 15 [Therapy of active Crohn disease with Boswellia serrata extract H 15]". *Z Gastroenterol.* Vol. 1, No. 7 (*2001 Jan*): 39-11. German.
23. Madisch A., et al. "Boswellia serrata extract for the treatment of collagenous colitis. A double-blind, randomized, placebo-controlled, multicenter trial". *Int J Colorectal Dis.* Vol. 12, No. 51 (*2007 Dec*): 22-1445.
24. Holt, P.R.; et al. "Curcumin therapy in inflammatory bowel disease: A pilot study". *Dig. Dis. Sci.* Vol. 50 (2005): 2191–2193.
25. Hanai, H., et al. "Curcumin maintenance therapy for ulcertive colitis: Randomized, multicenter, double-blind, placebo-controlled trial". *Clin. Gastroenterol. Hepatol.* Vol. 4 (2006): 1502–1506.
26. Rasyid A., Lelo A. "The effect of curcumin and placebo on human gall-bladder function: an ultrasound study". *Aliment Pharmacol Ther.* Vol. 2, No. 9 (*1999 Feb*): 13-245.
27. Askari G., et al. "The effect of quercetin supplementation on selected markers of inflammation and oxidative stress". *J Res Med Sci.* Vol. 7, No. 41 (*2012 Jul*): 17-637.
28. Ekström A.M., et al. "Dietary quercetin intake and risk of gastric cancer: results from a population-based study in Sweden". *Ann Oncol.* Vol. 2, No. 43(*2011 Feb*): 22-438.
29. Miyoshi, A.; et al. "Clinical Evaluation of Z-103 on Gastric Ulcer–A Multicenter Double-Blind Comparative Study with Cetraxate Hydrochloride". *Jpn. Pharm. Ther.* No. 20 (1992): 199–223.
30. Miyoshi, A. "Clinical evaluation of Z-103 in the treatment of gastric ulcer, a multicenter double-blind dose finding study". *Yakuri Chiryo* No. 20 (1992): 181–197.
31. Wu K.L., et al. "Effects of ginger on gastric emptying and motility in healthy humans". *Eur J Gastroenterol Hepatol.* Vol. 5, No. 40 (*2008 May*): 20-436.
32. Hu M.L., et al. "Effect of ginger on gastric motility and symptoms of functional dyspepsia". *World J Gastroenterol.* Vol. 1, No. 10 (*2011 Jan 7*): 17-105.
33. Esmail and AL-Snafi. "The Pharmaceutical Importance of Althaea officinalis and Althaea rosea : A Review". *Int.J.PharmTech Res.* Vol. 3 (2013): 1378-1385.
34. Zaghlool S.S., et al. "Protective effects of ginger and marshmallow extracts on indomethacin-induced peptic ulcer in rats". *J Nat Sci Biol Med.* Vol. 2, No. 8 (2015 Jul-Dec): 6-421.

For healthcare professional use only.