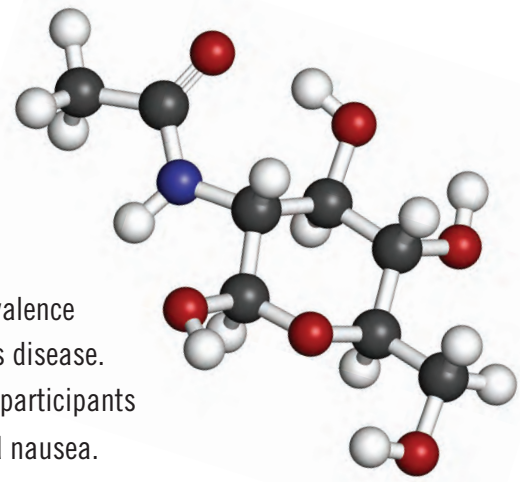
N-Acetylglucosamine:

A Gastrointestinal Protector for Inflammatory Bowel Disease



People with gluten sensitivity and celiac disease tend to have a high prevalence of inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease. In a clinical trial, N-acetylglucosamine (NAG) was shown to help 88 percent of participants with their IBD symptoms, including reducing abdominal pain, diarrhea, and nausea.

N-acetylglucosamine (also known as N-acetyl-D-glucosamine, GlcNAc or NAG) is classified as an amino sugar. It is closely related to glucosamine; however, from a biological standpoint, it has a significantly different scope of activities as compared to glucosamine.

By
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Functions of NAG in the Gastrointestinal Tract

NAG is a critical component in gastrointestinal mucin production and therefore can be classified as a gastrointestinal protector. Mucins are molecules that protect the epithelial surface of the gastrointestinal tract from damage.

NAG regulates production of biofilms that populate the gastrointestinal tract and positively influences the integrity of the gastrointestinal microbiome. Biofilms are a group of microorganisms such as a virus, bacteria, or fungi that forms a colony to shield treatments from penetrating its surface.

NAG protects mucosal cells from the toxic effects of gliadin peptides, gliadin being one of the main proteins in gluten.

NAG serves as a natural precursor for epithelial glycosaminoglycan synthesis. It is well recognized that IBD is associated with a widespread breakdown of glycosaminoglycans (complex carbohydrates). Glycosaminoglycans attach to mucin, helping to form a protective barrier separating bacteria from the intestinal epithelium. Taking NAG can alleviate IBD-related inflammation by increasing the amount of glycosaminoglycan attachments to the mucin layer.

Dosage, Safety, and Efficacy

To assess the efficacy and safety of NAG as an adjunct therapy for IBD, 34 adult IBD patients were recruited into an open-label clinical trial. A daily dose of 6 g NAG was taken orally for four weeks. Self-reported IBD symptom scores were assessed at baseline and after four weeks of treatment.

Overall, 88.1 percent (30 out of 34) patients reported that NAG helped with their IBD symptoms: 58.8 percent of patients reported improvement in abdominal pain with a 49 percent reduction in symptom score (P=0.00022); 64.7 percent of patients reported improvement in diarrhea with a 47 percent reduction in symptom score (P=0.0003)

Significant reductions in symptom score were also observed for nausea, passage of mucus, and rectal bleeding (effect size=41%-55%, all $P<0.05$)

In another clinical trial, NAG was used in children with difficult-to-treat IBD. NAG (total daily dose 3 to 6 g) was administered orally as adjunct therapy to 12 children with severe treatment resistant IBD (10 Crohn's disease, 2 ulcerative colitis).

Seven of these children suffered from symptomatic strictures (narrowing of the intestines caused by scar tissue). In addition, similar doses were administered rectally as sole therapy in nine children with distal ulcerative colitis or proctitis resistant to steroids and antibiotics.

Eight of the children given oral NAG showed clear improvement, while four required resections. Of the children with symptomatic Crohn's stricture, only three of seven have required surgery over a mean follow-up of over 2.5 years, and endoscopic or radiological improvement was detected in the others.

Rectal administration induced remission in two cases, clear improvement in three, and no effect in two. In all cases biopsied, there was evidence of histological improvement, and a significant increase in glycosaminoglycans in the epithelial and lamina propria as well as NAG within cells. (Lamina propria is a thin layer of connective tissue that is part of the mucosa.) It was concluded that NAG shows promise as an inexpensive and nontoxic treatment in chronic inflammatory bowel disease, with a mode of action which is distinct from conventional treatments.

Typically, the daily dose of NAG varies from 2,000 to 6,000 mg a day. The majority of NAG comes from shellfish; therefore, individuals who have an allergy to shellfish should only use NAG of plant origin, not animal origin.

For greater effectiveness, NAG can be combined with prebiotics and probiotics. For those with increased intestinal permeability (leaky gut syndrome), NAG can be successfully used in combination with butyrate and/or propionate salts.

Surprisingly, the research on NAG and its derivatives has not received a lot of attention from the medical community. As NAG has a strong safety profile and is well tolerated, it could be an efficacious adjunctive treatment for IBD.

References:

"Association of a Marker of N-Acetylglucosamine with Progressive Multiple Sclerosis and Neurodegeneration." *JAMA Neurology.* July 1, 2021;78(7):842-852. Brandt, A., Sy, M., et al.

"N-Acetylglucosamine for Treatment of Inflammatory Bowel Disease. A real-world pragmatic clinical trial." *Natural Medicine Journal*, April 1, 2015. Zhu, A.

"N-acetylglucosamine inhibits T-helper 1 (Th1)/T-helper 17 (Th17) cell responses and treats experimental autoimmune encephalomyelitis." *The Journal of Biological Chemistry.* November 18, 2011;286(46):40133-41. Grigorian, A., Araujo, L., et al.

"N-acetylglucosamine drives myelination by triggering oligodendrocyte precursor cell differentiation." *The Journal of Biological Chemistry.* December 18, 2020;295(51):17413-17424. Sy, M., Brandt, A., et al.

"Mannan and oligomers of N-acetylglucosamine protect intestinal mucosa of celiac patients with active disease from in vitro toxicity of gliadin peptides." *Gastroenterology.* October 1990;99(4):973-8. Auricchio, S., De Ritis, G., et al.

"A pilot study of N-acetyl glucosamine, a nutritional substrate for glycosaminoglycan synthesis, in paediatric chronic inflammatory bowel disease." *Alimentary Pharmacology & Therapeutics.* December 2000;14(12):1567-79. Salvatore, S., Heuschkel, R., et al. GFM

As always, consult a medical professional before beginning any new protocol.