

C-NAG[®]

N' Acetyl Glucosamine + Vitamin C

Crohn's Disease: Genes, Bacteria and Innate Immunity

Crohn's disease is an inflammatory bowel disease characterized by damage to the gastrointestinal tract.

Although any part of the alimentary canal (from the mouth to the anus) can be affected, most cases of Crohn's disease involve the ileum and the colon.

Crohn's disease was once believed to be an autoimmune disease but it is now understood to be caused by impaired innate immunity.

The first step in the appearance of Crohn's disease is the increasing colonization of the gastrointestinal tract by bacteria such as *Mycobacterium avium subspecies paratuberculosis* and *Escherichia coli* as well as fungi such as *Candida albicans*.

To shut down the microbial activity in the gut and arrest the damage done to the mucosal surface, the immune system then mounts an attack directed at specific antigens produced by these microbes.

However, people at risk of Crohn's disease have a specific genetic variation that prevents their innate immune system from recognizing the specific markers in bacterial walls that differentiate host cells from the invading bacteria.

The result of this continuous microbial attack and impaired immune response is chronic inflammation in the gut and damage to the soft tissues of the gastrointestinal tract.

What is N-Acetyl Glucosamine (NAG)?

N-acetyl glucosamine (NAG) is a monosaccharide that is also related to glucose. However, unlike that simple sugar, N-acetyl glucosamine is not really a sugar but belongs to a class of compounds called amides although it is commonly described as a carbohydrate.

It is synthesized from the reaction between glucosamine and acetic acid.

N-acetyl glucosamine is pieced together to make a polymer known as chitin. Chitin is the compound that makes up the outer exoskeleton of insects and shellfish.

N-acetyl glucosamine is also found in cell walls of bacteria. Here, it is coupled with N-acetyl muramic acid by oligopeptide bridges to form a polymer known as peptidoglycan.

In humans, N-acetyl glucosamine couples with glucuronic acid to form hyaluronic, a major protective polymer found in joints and responsible for cushioning the grinding of bones against one another. In addition, N-acetyl glucosamine can be found in the mucosal layer of the gastrointestinal tract.

The protective mucosal of the gut is made of glycoproteins. These are proteins with carbohydrates attached to them. N-acetyl glucosamine accounts for half of the carbohydrates in these glycoproteins.

Uses of N-Acetyl Glucosamine

N-acetyl glucosamine is used to treat **osteoarthritis, multiple sclerosis and inflammatory bowel disease.**

Although, conclusive proofs for these indications are not available, the results of preliminary studies suggest that N-acetyl glucosamine is an effective healing agent. It is likely effective for diseases affecting the joints between bones because it can increase the production of hyaluronic.

N-acetyl glucosamine may also improve Crohn's disease because it forms a major part of the glycoproteins incorporated in the mucosal layer of the gastrointestinal tract. Therefore, it will serve as a healing factor in inflamed, damaged soft tissues of the gut.

Safety of N-acetyl Glucosamine

The results of current safety studies suggest that N-acetyl glucosamine is very safe.

Because it is commonly described as a carbohydrate that is related to glucose, there are concerns that N-acetyl glucosamine may raise blood sugar levels especially in people living with type 2 diabetes. However, studies show that this natural supplement does not affect blood sugar levels in diabetics. Clinical data obtained from diabetics placed on N-acetyl glucosamine also confirmed the safety of the supplement.

Another common concern with N-acetyl glucosamine supplementation is the risk of shellfish allergy.

Contrary to common belief, shellfish allergy is triggered by the meat of seafood and not by their shells. Therefore, shellfish allergy does not involve chitin or N-acetyl glucosamine. This means that Crohn's disease patients with shellfish allergy can safely take the supplement.

However, N-acetyl glucosamine is not recommended for pregnant and breastfeeding women as well as those who are about to undergo surgery.

It should be used cautiously by patients who also suffer from asthma, bleeding disorders and kidney problems.

N-acetyl glucosamine should not be combined with anticoagulant drugs such as warfarin.

N-Acetyl Glucosamine and Crohn's Disease

N-acetyl glucosamine is used in the repair of soft tissues all over the body. It is especially important in the gastrointestinal tract where it makes up the basic structure of the mucosa.

Therefore, N-acetyl glucosamine supplementation should speed up the repair of damaged, inflamed sections of the gut in Crohn's disease as well as protect the sections still untouched by bacterial attack and misguided immune response.

N-acetyl glucosamine is synthesized from glucosamine in the body. The enzyme responsible for this synthesis simply transfers the acetyl group onto glucosamine.

Studies show that the determining step in the production of N-acetyl glucosamine is the synthesis of glucosamine-6-phosphate from which N-acetyl glucosamine is formed. The enzyme responsible for this key reaction is known as **glucosamine synthetase**.

Unfortunately, researchers found that the activity of this enzyme is considerably reduced in people suffering from inflammatory bowel diseases such as Crohn's disease.

Tissue biopsies taken from gastrointestinal tracts of these patients showed decreased glucosamine synthetase activity in the inflamed tissues. Because of the loss of this important structural carbohydrate, the inflamed tissues experience rapid loss of epithelial cells.

In contrast, studies show that the level of glucosamine synthetase is actually elevated in the soft tissues of the gut unaffected by the damage of Crohn's disease.

Knowing the importance of N-acetyl glucosamine to the structural integrity of the gastrointestinal mucosa, experts believe that taking N-acetyl glucosamine supplements can help make up for the reduced production of the compound in the damaged tissues of the gut.

Early data from preliminary studies confirm that this supplementation works. Healing of the mucosa and improvements of symptoms were recorded for most of the patients who received this supplement.

N-Acetyl Glucosamine vs. Glucosamine

N-acetyl glucosamine and glucosamine supplements are dietary supplements meant to treat the same medical conditions. They are especially useful in the management of autoimmune disease especially for those involving the depletion of glucosamine in the body.

There is an ongoing debate over which of the two supplements is better for dietary supplementation.

Some experts argue that glucosamine is the end-product needed in the body and that it is better absorbed than N-acetyl glucosamine. And they are right.

The absorption of glucosamine is much higher than N-acetyl glucosamine. In fact, the body absorbs most (98%) of the glucosamine obtained from the supplement. Once absorbed, glucosamine is distributed all over the body where it can be used to synthesize other important compounds like N-acetyl glucosamine.

The absorption of N-acetyl glucosamine is not only lower than that of glucosamine; the compound is actually broken down into glucosamine and acetic acid in the gut.

Effective supplements will provide NAG in enteric coated tablets or capsules or ideally in the new **DRCaps** to prevent destruction in the gut and deliver NAG directly to the small intestine for maximum absorption and bio-availability

Why N-acetyl Glucosamine is better for Crohn's Disease

In sharp contrast to the requirements of osteoarthritis and other autoimmune diseases affecting the joints, N-acetyl glucosamine and not glucosamine is actually the better supplement for Crohn's disease. Therefore, supplying this end product is better than giving its precursor (glucosamine).

Giving N-acetyl glucosamine saves the user several biochemical steps involved in the conversion of glucose-6-phosphate to N-acetyl glucosamine. In contrast, when glucosamine is given (as a sulfate salt, for example), it has to be first converted to glucose-6-phosphate and then taken through a number of steps before it is converted N-acetyl glucosamine.

Therefore, N-acetyl glucosamine supplements provide instantly available N-acetyl glucosamine while glucosamine supplements still need to be taken through several steps before they are converted into the compound needed to heal the gut.

Therefore, prescribing glucosamine sulfate or glucosamine hydrochloride to patients with inflammatory bowel disease is unwise.

In addition, the lower rate of absorption of N-acetyl glucosamine is really an advantage because this supplement is not rapidly absorbed, it spends more time in parts of the gut affected by Crohn's disease. Therefore, it is easily utilized to make the glycoproteins needed to repair the damaged sections of the gastrointestinal tract.

Studies on N-Acetyl Glucosamine and Crohn's Disease

N-Acetyl Glucosamine as a Structural Defense Unit of Gut Mucosa

A 1999 study published in the journal, *Medical Hypotheses*, identified glycosaminoglycan deficiency in the gut mucosa as the root cause of inflammatory bowel diseases such as Crohn's disease.

The researchers identified that defects in the glycosaminoglycan layer allows the entry of toxins (both bacterial toxins and free radicals) into the gastrointestinal mucosa. The immune response to the continuous exposure of the mucosa to these toxins is believed to be responsible for the inflamed lesions of Crohn's disease.

They also noted that this theory is supported by the fact that N-acetyl glucosamine, a supplement known to repair the glycosaminoglycan layer, improves the symptoms of Crohn's disease.

The glycosaminoglycan layer does more than simply provide mechanical defense against toxins and bacteria, it also provides an electrostatic barrier that repels charged toxins. N-acetyl glucosamine contributes significantly to both the physical and electrostatic defense provided by the glycosaminoglycan layer.

Glucosamine or N-Acetyl Glucosamine?

A 1983 study published in *The American Journal of Gastroenterology* compared the uptake of glucosamine against that of N-acetyl glucosamine in the intestinal mucosa of patients with inflammatory bowel diseases.

The researchers recruited 9 patients with Crohn's disease, 9 patients with ulcerative colitis and 26 controls.

By incubating the soft tissues of the intestinal mucosa obtained from the participants in solutions of glucosamine and N-acetyl glucosamine, the researchers found that the incorporation of glucosamine relative to N-acetyl glucosamine was much lower in patients with inflammatory bowel disease than controls.

This study showed that the conversion of glucosamine to N-acetyl glucosamine is impaired in Crohn's disease. Specifically, the step involving the N-acetylation of glucosamine was blocked.

This means that glucosamine supplementation for people with Crohn's disease will not improve the synthesis of glycoprotein, repair the glycosaminoglycan layer or improve the symptoms of Crohn's disease.

Therefore, N-acetyl glucosamine is the better supplement for Crohn's disease.

Glucosamine Synthetase Activity in Crohn's disease

A 1977 study published in the journal, *Gut*, provided a unique insight into how the activity of glucosamine synthetase is related to the severity of Crohn's disease. Glucosamine synthetase is the most important enzyme in the synthesis of the glycoproteins incorporated in the intestinal mucosa. It converts glucosamine to glucosamine-6-phosphate. N-acetyl glucosamine is then produced from this phosphorylated glucosamine.

This study found that the level of glucosamine synthetase was lower in the colon mucosa of Crohn's disease patients than healthy controls.

In addition, the researchers found that the level of this enzyme dropped when epithelial cells were lost from the mucosa. Patients who were quickly recovering from Crohn's disease, however, have elevated levels of this enzyme.

The researchers believed this increase in glucosamine synthetase production was due to

- The synthesis of glycosaminoglycans to repair the gastrointestinal mucosa
- Immunoglobulins (especially IgA) released during recovery

Lastly, the researchers noted that both immunoglobulin and glycosaminoglycans are rich in N-acetyl glucosamine.

Glucosamine Synthetase Activity in Crohn's Disease

N-Acetyl Glucosamine Supplementation

The most commonly quoted study in the discussion of N-acetyl glucosamine supplementation in Crohn's disease was published in 2000 in the journal, *Alimentary Pharmacology and Therapeutics*.

In this study, the researchers aimed to use N-acetyl glucosamine as a tissue repair agent by determining whether it will be incorporated into the glycoproteins and glycosaminoglycans used by the body to make gastrointestinal mucosa.

For this study, they recruited 12 (10 with Crohn's disease and 2 with ulcerative colitis) children with severe inflammatory bowel diseases who were unresponsive to treatment. These children were given 3 – 6 g of oral N-acetyl glucosamine daily in 3 divided doses as adjunct therapy.

Of the 12 children with inflammatory bowel disease, 8 recovered with no further intervention and 4 needed surgeries.

Of the 10 children with Crohn's disease, 7 had abnormal narrowing of the gastrointestinal tract before the study. N-acetyl glucosamine supplementation rectified the condition in 4 of the children.

The researchers found that N-acetyl glucosamine supplementation raised the concentration of N-acetyl glucosamine in the mucosal cells and also increased the production of glycosaminoglycans in the gastrointestinal epithelium.

They concluded that N-acetyl glucosamine was safe, inexpensive and an effective supplement for treating Crohn's disease especially when other treatment options have failed.

Even though further studies are needed to confirm and fully explain the benefits of N-acetyl glucosamine supplementation in Crohn's disease therapy, this study provided solid preliminary evidence to confidently recommend the supplement for people living with Crohn's disease.

Summary:

C-NAG, to be most effective, is provided in **DRCaps** to ensure delivery to the small intestine for maximum bio-availability and with concomitant supply of vitamin C to facilitate the biosynthesis of NAG and to address the symptoms of subclinical scurvy common in up to 70% of Crohn's patients.

Sources

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<http://altmedicine.about.com/od/glucosamine/a/N-Acetyl-Glucosamine.htm>

<http://www.umm.edu/altmed/articles/crohns-disease-000043.htm>

Scurvy and vitamin C deficiency in Crohn's disease.

[Postgrad Med J.](#) 1979 Jan;55(639):26-9
[Linaker BD.](#)

Abstract

A case of scurvy presenting in a patient with Crohn's disease is reported. A normal response to replacement therapy is seen. Vitamin C (ascorbic acid) deficiency was found in 7 out of 10 patients with clinically quiescent Crohn's disease, 4 of who had an adequate oral intake of vitamin C. There was no significant difference in oral intake between patients with Crohn's disease and matched controls but there was a significant difference (P less than 0.001) in leucocyte ascorbic acid levels. **It is recommended that patients with Crohn's disease be screened for vitamin C deficiency and receive prophylactic vitamin C supplements daily.**

Vitamin C status in 137 outpatients with Crohn's disease. Effect of diet counseling.

[J Clin Gastroenterol.](#) 1986 Aug;8(4):443-6.

[Imes S,](#) [Dinwoodie A,](#) [Walker K,](#) [Pinchbeck B,](#) [Thomson AB.](#)

Abstract

Vitamin C intake, and serum and leukocyte ascorbate levels were assessed serially over 6 months in 137 outpatients with Crohn's disease. Vitamin C intake was low in 18% of males and 37% of females. Serum ascorbate levels were suboptimal in 11% of males and 18% of females. Leukocyte ascorbate levels were low in 26% of males and 49% of females. Serum ascorbate levels were more frequently below the reference range in patients who smoked, but neither the serum nor the leukocyte ascorbate levels were affected by Crohn's disease activity, the use of an oral contraceptive agent, or by taking prednisone or sulfasalazine. Monthly diet counseling sessions significantly increased vitamin C intake, led to more patients consuming a normal ascorbate intake, and to a normalization of serum ascorbate values. We did not establish the importance of these ascorbate abnormalities on the clinical course of Crohn's disease. We conclude that low serum or leukocyte ascorbate levels are relatively common in patients with active or inactive Crohn's disease; these abnormalities are due in part to the reduced intake of dietary ascorbate; and **the ascorbate status in patients with Crohn's disease may be normalized by improving the dietary intake of vitamin C.**

Vitamin C, Inflammatory Bowel Disease and Polymorphisms

By Julia Bird

As our understanding of human genetics has grown, we are starting to appreciate the effect of how genes and environment interact. Researchers [Shaghghi and associates](#) published an article on the effect that variations in a vitamin C transporter have on two forms of inflammatory bowel disease. Vitamin C is a major water-soluble antioxidant. It has been shown to reduce inflammation by scavenging reactive oxygen species to prevent cellular damage according to a review by [Traber and Stevens](#). [Buffinton and Doe](#) found that levels of vitamin C were lower in people with inflammatory bowel disease, and this could hinder recovery of the intestinal lining.

The gene [SLC23A1](#) produces one of two vitamin C transporters located in cells in the lining of the intestine. It is required for the body to absorb vitamin C. Various polymorphisms within this gene have been shown to affect levels of ascorbic acid. In the current study, the polymorphisms in position [rs6596473](#), [rs33972313](#) (reported on previously by [TalkingNutrition](#)) and [rs10063949](#) were investigated.

The authors compared polymorphism types between 162 Crohn's disease patients, 149 patients with ulcerative colitis, and 146 ethnicity-matched controls. They found that the rs10063949G allele was associated with increased risk of Crohn's disease, with a stronger risk found when patients had two rather than one copy of the G-variant. There was also a significant association between haplotype CGG in the rs6596473, rs33972313, and rs10063949 single nucleotide polymorphisms and Crohn's disease, **which could indicate that general deficiencies in the vitamin C transporter increase risk of this disease.**

These results show that reduced absorption of vitamin C into intestinal cells increases risk of Crohn's disease. The authors suggest that dietary supplements containing an oxidized form of vitamin C, dehydroascorbate, could be tested in an intervention study as a possible therapy for Crohn's disease. This form of vitamin C uses another means of entering the cell and the SLC23A1 protein is not involved. This could potentially help intestinal cells repair damage done by inflammatory bowel disease, and also [correct low vitamin C levels](#) that are frequently found in people with Crohn's disease.

Main Citation:

Mandana Amir Shaghghi, Charles N Bernstein, Alejandra Serrano León, Hani El-Gabalawy, and Peter Eck. Polymorphisms in the sodium-dependent ascorbate transporter gene SLC23A1 are associated with susceptibility to Crohn disease. *Am J Clin Nutr* 2014 *ajcn*.068015; First published online November 27, 2013. [doi:10.3945/ajcn.113.068015](https://doi.org/10.3945/ajcn.113.068015)

Supporting Citations:

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