

# GASTROINTESTINAL HEALTH

## Glutathione

Counteracts oxidative stress in the intestinal mucosa (gut wall); Recycles antioxidants such as vitamins C & E.<sup>1,2,3</sup>

## Selenium

Cofactor to glutathione peroxidase (GPx), which protects intestinal wall from inflammatory damage; Lower GPx activity due to selenium deficiency is very common in people with gut inflammation.<sup>3,4,5</sup>

## Glutamine

Preferred fuel for enterocytes (small intestine cells), which use the most glutamine in the entire body; Keeps the junctions between intestinal epithelial cells tight so foreign proteins cannot enter bloodstream.<sup>6,7,8</sup>

## Zinc

Decreases intestinal permeability; Maintains integrity of intestinal wall, especially when inflammatory chemicals (TNF $\alpha$ ) compromise epithelial lining; Works with vitamin A in regenerating cells that line the gut.<sup>9,10,11</sup>

## Vitamin A

Regulates growth of epithelial cells, including those that line the gastrointestinal (GI) tract; Reduces inflammatory proteins in the gut.<sup>12,13</sup>

## Lipoic Acid

Suppresses damaging chemicals (cytokines) in GI tract that cause an inflammatory immune response; Preserves glutathione levels and recycles vitamin C.<sup>35,36</sup>

## Vitamin C

An inflamed gut uses up the antioxidant vitamin C faster than a healthy gut; Promotes tissue healing in GI tract; Reduces gastrointestinal inflammation.<sup>14,15</sup>

## Magnesium

Deficiency affects the amount of good bacteria found in the gut; May help prevent stomach ulcers; Insufficient levels are very common in people with irritable bowel; Antacids induce magnesium deficiency.<sup>32,33,34</sup>

## Vitamin D

Keeps gut flora healthy by protecting good bacteria; Activates adaptive immunity that originates in GI tract; Promotes gut barrier integrity; Deficiency linked to inflammatory bowel disease flare-ups.<sup>16,17,18</sup>

## Choline

Maintains the barrier function of gastric epithelium (helps prevent stomach ulcers) via its role in building cell membranes and acting as a surfactant in the GI tract.<sup>30,31</sup>

## Vitamin K

Synthesized by intestinal bacteria; Deficiency common in chronic GI disorders; Bone demineralization that occurs with inflammatory bowel diseases (Crohn's, etc) is caused by vitamin K deficiency since it is a required cofactor for bone formation.<sup>19,20</sup>

## Folate

Deficiency alters genes in a way that makes colon cells more likely to become cancerous.<sup>28,29</sup>

## Vitamin B6

Deficiency is strongly linked with a higher risk of developing colon cancer.<sup>26,27</sup>

## Carnitine

May be therapeutically beneficial in people with colitis (inflammation of colon) due to its role in fatty acid metabolism, which is often impaired in GI disorders.<sup>23,24,25</sup>

## Vitamin B12

Improves gastrointestinal complaints in some patients with dyspepsia (indigestion); Antacids deplete B12.<sup>21,22</sup>

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Additional nutrients affect gastrointestinal health. This list is non-exhaustive.

## REFERENCES

- <sup>1</sup>Sido B, Hack V, Hochlehnert A et al. Impairment of intestinal glutathione synthesis in patients with inflammatory bowel disease. *Gut*. 1998;42:485-492.
- <sup>2</sup>Pinto M, Soares-Mota S, Lopes M et al. Does active Crohn's disease have decreased intestinal antioxidant capacity? *J Crohns Colitis* 2013;7:e358-e366.
- <sup>3</sup>Esworthy R, Binder S, Doroshov J et al. Microflora trigger colitis in mice deficient in selenium-dependent glutathione peroxidase and induce Gpx2 gene expression. *Biol Chem*. 2003;384:597-607.
- <sup>4</sup>Nagy D, Fülesdi B, Hallay J. Role of selenium in gastrointestinal inflammatory diseases. *Orv Hetil* 2013;154:1636-1640.
- <sup>5</sup>Brigelius-Flohé R, Kipp A. Physiological functions of GPx2 and its role in inflammation-triggered carcinogenesis. *Ann N Y Acad Sci*. 2012;1259:19-25.
- <sup>6</sup>Li N, Neu J. Glutamine deprivation alters intestinal tight junctions via a PI3K/Akt mediated pathway in Caco-2 cells. *J Nutr* 2009;139:710-714.
- <sup>7</sup>Lecleire S, Hassan A, Marion-Letellier R et al. Combined glutamine and arginine decrease proinflammatory cytokine production by biopsies from Crohn's patients in association with changes in nuclear factor-kappaB and p38 mitogen-activated protein kinase pathways. *J Nutr* 2008;138:2481-2486.
- <sup>8</sup>Li J, Langkamp-Henken B, Suzuki K et al. Glutamine prevents parenteral nutrition-induced increases in intestinal permeability. *J Parent Enteral Nutr* 1994;18:303-307.
- <sup>9</sup>Ranaldi G, Ferruzza S, Canali R et al. Intracellular zinc is required for intestinal cell survival signals triggered by the inflammatory cytokine TNF $\alpha$ . *J Nutr Biochem* 2013;24:967-976.
- <sup>10</sup>El Tawil A. Zinc supplementation tightens leaky gut in Crohn's disease. *Inflamm Bowel Dis* 2012;18:E399.
- <sup>11</sup>Zhong W, McClain C, Cave M et al. The role of zinc deficiency in alcohol-induced intestinal barrier dysfunction. *Am J Physiol Gastrointest Liver Physiol* 2010;298:G625-633.
- <sup>12</sup>Long K, Santos J et al. Vitamin A supplementation reduces the monocyte chemoattractant protein-1 intestinal immune response of Mexican children. *J Nutr* 2006;136:2600-2605.
- <sup>13</sup>Bai A, Lu N, Guo Y et al. All-trans retinoic acid down-regulates inflammatory responses by shifting the Treg/Th17 profile in human ulcerative and murine colitis. *J Leukoc Biol*. 2009;86:959-969.
- <sup>14</sup>Aghkassi E, Wendland B, Steinhart H et al. Antioxidant vitamin supplementation in Crohn's disease decreases oxidative stress: a randomized controlled trial. *Am J Gastroenterol* 2003;98:348-353.
- <sup>15</sup>Cevikel MH, Tuncyurek P, Ceylan F et al. Supplementation with high-dose ascorbic acid improves intestinal anastomotic healing. *Eur Surg Res*. 2008;40:29-33.
- <sup>16</sup>Palmer M, Weaver C. Linking vitamin D deficiency to inflammatory bowel disease. *Inflamm Bowel Dis* 2013;19:2245-2256.
- <sup>17</sup>Ulitsky A, Ananthakrishnan AN, Naik A et al. Vitamin D deficiency in patients with inflammatory bowel disease: association with disease activity and quality of life. *J Parenter Enteral Nutr*. 2011 May;35:308-316.
- <sup>18</sup>Blanck S. Vitamin D deficiency is associated with ulcerative colitis disease activity. *Dig Dis Sci*. 2013;58:1698-1702.
- <sup>19</sup>Nakajima S, Iijima H, Egawa S et al. Association of vitamin K deficiency with bone metabolism and clinical disease activity in inflammatory bowel disease. *Nutrition*. 2011 Oct;27:1023-1028.
- <sup>20</sup>Schoon E, Muller M, Vermeer C et al. Low serum and bone vitamin K status in patients with longstanding Crohn's disease: another pathogenic factor of osteoporosis in Crohn's disease? *Gut* 2001;48:473-477.
- <sup>21</sup>Gumurdulu Y, Serin E, Ozer B et al. The impact of B12 treatment on gastric emptying time in patients with *Helicobacter pylori* infections. *J Clin Gastroenterol* 2003;37:230-233.
- <sup>22</sup>Oh S. Proton pump inhibitors – uncommon adverse effects. *Aust Fam Physician* 2011;40:705-708.
- <sup>23</sup>Sonne S, Shekhawat PS, Matern D et al. Carnitine deficiency in OCTN2 $^{-/-}$  newborn mice leads to a severe gut and immune phenotype with widespread atrophy, apoptosis and a pro-inflammatory response. *PLoS One*. 2012;7:e47729.
- <sup>24</sup>Mikhailova T, Sishkova E, Poniewierka E et al. Randomised clinical trial: the efficacy and safety of propionyl-L-carnitine therapy in patients with ulcerative colitis receiving stable oral treatment. *Aliment Pharmacol* 2011;34:1088-1097.
- <sup>25</sup>Shekhawat P, Srinivas S, Matern D et al. Spontaneous development of intestinal and colonic atrophy and inflammation in the carnitine-deficient jvs (OCTN2 $^{-/-}$ ) mice. *Mol Genet Meta*. 2007;92:315-324.
- <sup>26</sup>Larsson S, Orsini N, Wolk A. Vitamin B6 and Risk of Colorectal Cancer: A Meta-analysis of Prospective Studies. *JAMA* 2010;303:1077-1083.
- <sup>27</sup>Lee J, Li H, Giocannucci E et al. Prospective study of plasma vitamin B6 and risk of colorectal cancer in men. *Cancer Epidemiol Biomarkers Prev* 2009;18:1197-1202.
- <sup>28</sup>Crott J, Liu Z et al. Moderate folate depletion modulates the expression of selected genes involved in cell cycle, intracellular signaling and folate uptake in human colonic epithelial cell lines. *J Nutr Biochem* 2008;19:328-335.
- <sup>29</sup>Knock E, Deng L, Wu Q et al. Low dietary folate initiates intestinal tumors in mice, with altered expression of G2-M checkpoint regulators polo-like kinase 1 and cell division cycle 25c. *Cancer Res* 2006;66:10359-10356.
- <sup>30</sup>Mourelle M, Guarner F, Malagelada J. Polyunsaturated phosphatidylcholine prevents stricture formation in a rat model of colitis. *Gastroenterology* 1996;110:1093-1097.
- <sup>31</sup>Dunjic B, Axelson J. Gastroprotective capability of exogenous phosphatidylcholine in experimentally induced chronic gastric ulcers in rats. *Scand J Gastroenterol* 1993;28:89-94.
- <sup>32</sup>Pachikian BD, Neyrinck AM, Deldicque L et al. Changes in intestinal bifidobacteria levels are associated with the inflammatory response in magnesium-deficient mice. *J Nutr*. 2010;140:509-514.
- <sup>33</sup>Mackay J, Bladon P. Hypomagnesaemia due to proton-pump inhibitor therapy: a clinical case series. *QJM*. 2010;103:387-395.
- <sup>34</sup>Henrotte J, Aymard N, Allix M et al. Effect of pyridoxine and magnesium on stress-induced gastric ulcers in mice selected for low or high blood magnesium levels. *Ann Nutr Metab* 1995;39:285-290.
- <sup>35</sup>Trivedi P, Jena G. Role of  $\alpha$ -lipoic acid in dextran sulfate sodium-induced ulcerative colitis in mice: Studies on inflammation, oxidative stress, DNA damage and fibrosis. *Food Chem Toxicol*. 2013;59:339-55.
- <sup>36</sup>Kolgazi M, Jahovic N, Yüksel M et al. Alpha-lipoic acid modulates gut inflammation induced by trinitrobenzene sulfonic acid in rats. *J Gastroenterol Hepatol*. 2007;22:1859-1865.