

# G.I. Detox™ + Gentle Full Spectrum Binder

## Scientific Validation of Ingredients

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**Updated 2021;** Joseph Katzinger, ND

### **Ingredients:**

#### **Proprietary herbal blend**

Zeolite clay, Activated Charcoal, Aloe Vera Leaf extract (*Aloe barbadensis*), Apple pectin, Silica, Humic Powder

#### **Other Ingredients:**

Vegetable capsule (hydroxypropyl methylcellulose and water)

## **Zeolite Clay**

### **Biological Actions:**

Adsorbent, anti-inflammatory, antioxidant, immunomodulatory.<sup>1,2</sup>

### **Traditional Use:**

Zeolite is a collective name for minerals and chemical compounds within the group of silicates, known for their high absorbency. Due to the unique arrangement of the atoms and the water-binding capacities of the microporous structure, zeolite minerals act like a “rock-sponge”.<sup>1</sup>

Traditional applications of natural clay include skin conditions as well as gastrointestinal disorders such as diarrhea, irritable bowel syndrome, mercury poisoning, and nausea.<sup>3,4</sup> Medical applications of zeolites have been used in filtration systems for anesthesia and dialysis and as contrast materials in nuclear magnetic resonance imaging. Zeolite powders for external use include application as deodorants, antimycotic agents and wound dressings.<sup>5</sup>

### **Scientific Evidence:**

Zeolites are hydrated crystalline aluminosilicates of volcanic or synthetic origin with unique adsorption and dehydrating-rehydrating properties.<sup>2,5,6</sup> Zeolites can act as an inorganic

<sup>1</sup> Lamprecht M, Bogner S, Steinbauer K, et al. Effects of zeolite supplementation on parameters of intestinal barrier integrity, inflammation, redoxbiology and performance in aerobically trained subjects. *J Int Soc Sports Nutr.* 2015 Oct 20;12:40.

<sup>2</sup> Ivkovic S, Deutsch U, Silberbach A, et al. Dietary supplementation with the tribomechanically activated zeolite clinoptilolite in immunodeficiency: effects on the immune system. *Adv Ther.* 2004 Mar-Apr;21(2):135-47.

<sup>3</sup> Natural Medicines Comprehensive Database. Professional Monograph: Clay. 2015; <https://naturalmedicines.therapeuticresearch.com>. Accessed 09/07/2018.

<sup>4</sup> Williams LB, Haydel SE, Giese RF, et al. Chemical and mineralogical characteristics of French green clays used for healing. *Clays Clay Miner.* 2008 Aug;56(4):437-452.

<sup>5</sup> Boranić M. [What a physician should know about zeolites]. *Lijec Vjesn.* 2000 Nov-Dec;122(11-12):292-8.

<sup>6</sup> Montinaro M, Uberti D, Maccarinelli G, et al. Dietary zeolite supplementation reduces oxidative damage and plaque generation in the brain of an Alzheimer's disease mouse model. *Life Sci.* 2013 May 20;92(17-19):903-10.

cation-exchanger, adsorbent, detergent builder, and active reservoir for metal-catalyzed reactions. Zeolites are minerals and chemical compounds within the group of silicates with a microporous and distinctive three-dimensional structure which have a negative charge.<sup>1,2</sup> The three dimensional channel surfaces enables zeolites to trap molecules, with high exchange capacity for certain cations and capacity to adsorb contaminants.<sup>7</sup> Zeolite-clinoptilolite, used in G.I. Detox™, is one of the more abundant natural zeolites and has been used medically primarily for its antioxidant, anti-inflammatory, and detoxifying effects.<sup>8</sup> In one randomized and double blinded clinical trial, supplementation with zeolite-clinoptilolite was shown to beneficially affect intestinal barrier integrity, accompanied by mild anti-inflammatory effects in individuals undergoing regular aerobic exercise training. This included a statistically significant, nearly 30% reduction in stool zonulin levels; zonulin is the primary modulator of intercellular junctions, with increased concentrations directly associated with greater intestinal permeability.<sup>1</sup> Zeolite-clinoptilolite also binds heavy metals with high affinity, and has shown the greatest selectivity for lead and cadmium specifically.<sup>9</sup> In a second, randomized and placebo-controlled trial, supplementation with zeolite-clinoptilolite was shown to prevent as much as 90% of a tracer dose of 204Pb; importantly, the dose of lead used in this study met the upper limit of lead in drinking water, suggesting the potential to substantially reduce lead absorption at relevant real-world doses.<sup>10</sup> Preliminary data also indicates that clinoptilolite inhibits cholesterol absorption, in part by acting as a bile acid sequestrant, reducing cholesterol absorption into enterocytes.<sup>11</sup> In an uncontrolled study, supplementation improved the lipid profile of participants with dyslipidemia, including reductions in total cholesterol, and LDL-cholesterol.<sup>12</sup>

### **Safety Summary:**

Consumption of 1,845 mg/day of zeolite has been shown to be safe for 12 weeks in otherwise healthy endurance trained athletes.<sup>1</sup> Additionally, no side effects were reported at doses of clinoptilolite as high as 9 g/d for 8 weeks among participants with dyslipidemia.<sup>12</sup> When ingested, powdered zeolites (like almost all silicates), are inert and therefore do not react chemically with food or body fluids or their metabolites, suggesting that the risk of adverse effects is minimal.<sup>2</sup> Exercise caution during pregnancy and lactation as safety has not been established during these times

## **Activated Charcoal**

### **Biological Actions:**

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<sup>7</sup> Subramaniam MD, Kim IH. Clays as dietary supplements for swine: A review. *J Anim Sci Biotechnol.* 2015 Aug 22;6(1):38.

<sup>8</sup> Mastinu A, Kumar A, Maccarinelli G, et al. Zeolite Clinoptilolite: Therapeutic Virtues of an Ancient Mineral. *Molecules.* 2019 Apr 17;24(8):1517.

<sup>9</sup> Zamzow, M. J., Eichbaum, B. R., Sandgren, K. R., et al. Removal of heavy metal and other cations from wastewater using zeolites, *Sep. Sci. Technol.* 1990 25, 1555–1569.

<sup>10</sup> Samekova K, Firbas C, Irrgeher J, et al. Concomitant oral intake of purified clinoptilolite tuff (G-PUR) reduces enteral lead uptake in healthy humans. *Sci Rep.* 2021 Jul 20;11(1):14796.

<sup>11</sup> Kristo AS, Tzanidaki G, Lygeros A, et al. Bile sequestration potential of an edible mineral (clinoptilolite) under simulated digestion of a high-fat meal: an in vitro investigation. *Food Funct.* 2015 Dec;6(12):3818-27.

<sup>12</sup> Cutovic M, Lazovic M, Vukovic-Dejanovic V, et al. Clinoptilolite for Treatment of Dyslipidemia: Preliminary Efficacy Study. *J Altern Complement Med.* 2017 Sep;23(9):738-744.

Absorptive agent, adsorptive agent.<sup>13</sup>

### **Traditional Use:**

Charcoal has been used for thousands of years in Egyptian, Greek, Roman and Hindu cultures for medicinal purposes.<sup>14</sup> The activated form of charcoal has been used for the past century for gastric decontamination following the ingestion of toxic substances.<sup>14</sup> Activated charcoal is considered to be an effective remedy for the treatment of toxic ingestions with the exception of those caused by corrosive agents, cyanide, iron, mineral acids, organic solvents, and heavy metals.<sup>13</sup>

### **Scientific Evidence:**

Activated charcoal is considered to be among the most effective absorptive and adsorptive agents.<sup>13</sup> It helps prevent the absorption of substances within the gastrointestinal tract, thereby decreasing systemic absorption of potentially toxic chemicals.<sup>14</sup> Activated charcoal also enhances elimination by interrupting the reabsorption of chemicals excreted directly into the gastrointestinal tract from systemic circulation (enteroenteric recycling), or chemicals secreted in bile (enterohepatic recycling).<sup>15</sup> In the case of enteroenteric recycling, this effect has been termed “gastrointestinal dialysis”; the intestinal wall may be viewed as a semipermeable membrane, with toxins diffusing out of the blood from serosal to mucosal membranes, and onto the charcoal in the intestinal lumen.<sup>16</sup>

Activated charcoal is made from pulverized carbonaceous substances that produce charcoal. Charcoal is activated by a process called pyrolysis, which expands its surface area, causing the charcoal to develop millions of tiny pores between the carbon atoms. The pore structure of activated carbon makes the adsorbent suitable for adsorption, a process by which molecules are captured and trapped within the internal pores via electrostatic attractions. The average surface area of activated charcoal ranges between 200-800 m<sup>2</sup>/gram. The vast surface area provides activated charcoal with numerous bonding sites, which allows it to adsorb poisons and other substances, thereby preventing them from being absorbed or reabsorbed into the blood circulation.<sup>13</sup>

To date, there have been numerous animal and volunteer studies, as well as clinical studies (case series and reports) performed to assess the efficacy of activated charcoal in the treatment of acute poisoning. Research has demonstrated enhanced elimination and clinical benefits for the uses of

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<sup>13</sup> Karaman R. Novel Modified Bentonite-Montmorillonite and Activated Charcoal Complexes for Detoxification. *International Journal of Clinical Toxicology*. 2014;2(2):37-41.

<sup>14</sup> Lapus RM. Activated charcoal for pediatric poisonings: the universal antidote? *Current opinion in pediatrics*. 2007;19(2):216-222.

<sup>15</sup> Wang X, Mondal S, Wang J, et al. Effect of activated charcoal on apixaban pharmacokinetics in healthy subjects. *Am J Cardiovasc Drugs*. 2014 Apr;14(2):147-54.

<sup>16</sup> Zellner T, Prasa D, Färber E, et al. The Use of Activated Charcoal to Treat Intoxications. *Dtsch Arztebl Int*. 2019 May 3;116(18):311-317.

both single and multiple doses of activated charcoal.<sup>17,18</sup> In a clinical trial, administration of activated charcoal significantly reduced exposure to Rivaroxaban (an anticoagulant agent), suggesting that it could be used in overdose and accidental ingestion to antagonize absorption.<sup>19</sup> While human studies are lacking, animal models also suggest activated charcoal may also protect against exposure to some environmental toxins, specifically against dioxin-mediated changes to the gut microbiome.<sup>20</sup> Animal studies have also shown that it prevents dioxin-induced immune suppression, by sequestering these toxins, thereby limiting their bioavailability.<sup>21</sup>

### **Safety Summary:**

Considered safe when used orally short term.<sup>22</sup> Therapeutic doses are 25-100 grams for adolescents and adults, and 25-50 grams (or 0.5-1 gram/kg body weight) for children aged 1 to 12 years.<sup>23</sup> Administration of 50 grams of activated charcoal has been safely used without serious adverse events in otherwise healthy volunteers.<sup>19</sup> Activated charcoal is contraindicated in patients with unprotected airways and decreased levels of consciousness who are not intubated.<sup>14</sup> It is also contraindicated in therapeutic doses if its use increases the risk or severity of aspiration, particularly in cases of ingestion of hydrocarbons (such as kerosene, lighter fluid and lamp oil).<sup>14</sup> Adverse reactions following the ingestion of corrosives (acids or alkalis) may lead to vomiting, obscure endoscopic visualization,<sup>14</sup> constipation, black stools, gastrointestinal obstruction, and pulmonary aspiration.<sup>22</sup> Administration following the ingestion of corrosives may also cause charcoal leaking into the peritoneum in cases of perforation.<sup>14</sup> Caution should be exercised when administering charcoal in therapeutic doses in patients who are at risk of gastric hemorrhage or perforation. Caution is also advised in patients who have ingested a substance that puts them at risk for sudden onset of seizures, or sudden decrease of mental status (e.g. clonidine or tricyclic antidepressants).<sup>14</sup>

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<sup>17</sup> Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol.* 1999;37(6):731-51.

<sup>18</sup> Bond GR. The role of activated charcoal and gastric emptying in gastrointestinal decontamination: a state-of-the-art review. *Ann Emerg Med.* 2002 Mar;39(3):273-86.

<sup>19</sup> Ollier E, Hodin S, Lanoiselée J, et al. Effect of Activated Charcoal on Rivaroxaban Complex Absorption. *Clin Pharmacokinet.* 2017 Jul;56(7):793-801.

<sup>20</sup> Stedtfeld RD, Brett Sallach J, Crawford RB, et al. TCDD administered on activated carbon eliminates bioavailability and subsequent shifts to a key murine gut commensal. *Appl Microbiol Biotechnol.* 2017 Oct;101(19):7409-7415.

<sup>21</sup> Boyd SA, Sallach JB, Zhang Y, et al. Sequestration of 2,3,7,8-tetrachlorodibenzo-p-dioxin by activated carbon eliminates bioavailability and the suppression of immune function in mice. *Environ Toxicol Chem.* 2017 Oct;36(10):2671-2678.

<sup>22</sup> Natural Medicines Comprehensive Database. Professional Monograph: Activated Charcoal. 2012; <https://naturalmedicines.therapeuticresearch.com/>. Accessed 13/10/2015.

<sup>23</sup> Chyka PA, Seger D, Krenzelo EP, et al. Position paper: Single-dose activated charcoal. *Clin Toxicol (Phila).* 2005;43(2):61-87.

Considered safe during pregnancy and breastfeeding when used orally short term.<sup>22</sup>

## **Aloe Vera (*Aloe barbadensis*)**

### **Biological Actions:**

Antifungal, anti-inflammatory, antimicrobial, antioxidant, antiviral, demulcent, emollient, immune enhancing, vulnerary.<sup>24,25,26</sup>

### **Traditional Use:**

Aloe vera has traditionally been used internally as a general tonic, anti-inflammatory, carminative, laxative, and anthelmintic agent.<sup>24</sup> In Ayurvedic medicine, aloe gel has been used as a tonic for the liver, spleen and the blood due to its bitter, astringent, pungent, sweet and cooling properties.<sup>27</sup>

### **Scientific Evidence:**

The key phytochemical compounds of aloe gel include anthraquinones (aloin and emodin), enzymes (catalase, amylase), fatty acids (lupeol and campesterol), polysaccharides (glucomannans) and glycoproteins.<sup>28</sup> Aloe resin, the solid residue obtained from the latex, consists of mainly hydroxyanthracene derivatives.<sup>29</sup> The aloe inner parenchyma, known as the fillet or leaf, also contains 4 tocopherol isoforms (primarily a, but also d, b, and g), as well as mannans, and a diverse variety of polyphenols, antioxidants, and antimicrobial compounds.<sup>30</sup> Aloe vera has been reported to improve parameters of gastrointestinal function including colonic bacterial activity, gastrointestinal pH, stool specific gravity, and gastrointestinal motility.<sup>24</sup> Animal models have shown that aloe polysaccharides improve intestinal permeability, as assessed by the lactulose/mannitol ratio, via an upregulation of the tight junction protein zonula occludens (ZO)-1.<sup>31</sup> Animal studies also suggest that glucomannan from aloe vera increases intestinal epithelial cell regeneration via upregulation of the Wnt/ $\beta$ -catenin signaling pathway.<sup>32</sup>

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<sup>24</sup> Braun L, Cohen M. Herbs and Natural Supplements an Evidenced Based Guide. Vol 2. 4th ed. Chatswood, NSW: Elsevier Australia; 2015.

<sup>25</sup> Bone K. A Clinical Guide to Blending Liquid Herbs: Herbal Formulations for the Individual Patient. Edinburgh, Scotland: Churchill Livingstone; 2003.

<sup>26</sup> Kumar R, Singh AK, Gupta A, et al. Therapeutic potential of Aloe vera-A miracle gift of nature. Phytomedicine. 2019 Jul;60:152996.

<sup>27</sup> Frawley D, Lad V. The Yoga of Herbs. WI, USA: Lotus Press; 1986.

<sup>28</sup> Sánchez M, González-Burgos E, Iglesias I, et al. Pharmacological Update Properties of Aloe Vera and its Major Active Constituents. Molecules. 2020 Mar 13;25(6):1324.

<sup>29</sup> Fisher C. Materia Medica of Western Herbs. Nelson, New Zealand: Vitex Medica; 2009.

<sup>30</sup> Añibarro-Ortega M, Pinela J, Barros L, et al. Compositional Features and Bioactive Properties of Aloe vera Leaf (Fillet, Muclage, and Rind) and Flower. Antioxidants (Basel). 2019 Oct 1;8(10):444.

<sup>31</sup> Le Phan TH, Park SY, Jung HJ, et al. The Role of Processed Aloe vera Gel in Intestinal Tight Junction: An In Vivo and In Vitro Study. Int J Mol Sci. 2021 Jun 17;22(12):6515.

<sup>32</sup> Zhang D, Zhou X, Liu L, et al. Glucomannan from Aloe vera Gel Promotes Intestinal Stem Cell-Mediated Epithelial Regeneration via the Wnt/ $\beta$ -Catenin Pathway. J Agric Food Chem. 2021 Sep 15;69(36):10581-10591.

Several clinical trials have reported the beneficial effects of aloe vera administration. Aloe gel has been shown to reduce histological disease activity in patients with ulcerative colitis.<sup>33,34</sup> Supplementation with *Aloe barbadensis* extract (AVH200®) has demonstrated improvement in pain severity, pain frequency and bloating in adult patients with irritable bowel syndrome (IBS).<sup>35</sup> Similarly, two randomized and double-blinded trials found that an aloe inner leaf extract improved symptoms of IBS-D specifically, with significant improvements in abdominal pain severity and frequency.<sup>36</sup> Analysis of multiple randomized trials also indicates that aloe may help to improve both glycemic and lipid control, particularly among participants with metabolic abnormalities.<sup>37</sup> Although the mechanisms are unclear, aloe inner leaf gel has been shown to significantly improve the bioavailability of both vitamin C and vitamin B12 in healthy human volunteers when given simultaneously.<sup>38</sup>

Oral administration of aloe vera gel has also been found to reduce the growth of *Candida albicans* in the spleen and kidney (animal research), with *in vitro* data suggesting similar efficacy to standard antifungal treatments.<sup>39,40</sup> *In vitro* experiments also show that aloe possesses antimicrobial activity against several pathogens including *Helicobacter pylori*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Staphylococcus aureus* (methicillin-resistant strains), *Escherichia coli*, *Shigella flexneri*, *Enterobacter cloacae* and *Enterococcus bovis*, and to inhibit *Staphylococcus aureus* (methicillin resistant) biofilm formation, with components of aloe blocking the initial adhesion and proliferation of biofilms.<sup>24,41,42,43</sup>

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- <sup>33</sup> Langmead L, Feakins RM, Goldthorpe S, et al. Randomized, double-blind, placebo-controlled trial of oral aloe vera gel for active ulcerative colitis. *Aliment Pharmacol Ther.* 2004 Apr 1;19(7):739-47.
- <sup>34</sup> Foster M, Hunter D, Samman S. Evaluation of the Nutritional and Metabolic Effects of Aloe vera. In: Benzie IFF, Wachtel-Galor S, editors. *Herbal Medicine: Biomolecular and Clinical Aspects*. 2nd ed. Boca Raton (FL): CRC Press/Taylor & Francis; 2011. Chapter 3.
- <sup>35</sup> Størsrud S, Pontén I, Simrén M. A Pilot Study of the Effect of Aloe barbadensis Mill. Extract (AVH200®) in Patients with Irritable Bowel Syndrome: a Randomized, Double-Blind, Placebo-Controlled Study. *J Gastrointest Liver Dis.* 2015 Sep;24(3):275-80.
- <sup>36</sup> Ahluwalia B, Magnusson MK, Böhn L, et al. Aloe barbadensis Mill. extract improves symptoms in IBS patients with diarrhoea: post hoc analysis of two randomized double-blind controlled studies. *Therap Adv Gastroenterol.* 2021 Oct 8;14:17562848211048133.
- <sup>37</sup> Zhang Y, Liu W, Liu D, et al. Efficacy of Aloe Vera Supplementation on Prediabetes and Early Non-Treated Diabetic Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrients.* 2016 Jun 23;8(7):388.
- <sup>38</sup> Yun JM, Singh S, Jialal R, et al. A randomized placebo-controlled crossover trial of aloe vera on bioavailability of vitamins C and B(12), blood glucose, and lipid profile in healthy human subjects. *J Diet Suppl.* 2010 Jun;7(2):145-53.
- <sup>39</sup> Im SA, Lee YR, Lee YH, et al. In vivo evidence of the immunomodulatory activity of orally administered Aloe vera gel. *Arch Pharm Res.* 2010 Mar;33(3):451-6.
- <sup>40</sup> Nabila VK, Putra IB. The effect of Aloe vera ethanol extract on the growth inhibition of *Candida albicans*. *Med Glas (Zenica).* 2020 Aug 1;17(2):485-489.
- <sup>41</sup> Saddiq AA, Al-Ghamdi H. Aloe vera extract: A novel antimicrobial and antibiofilm against methicillin resistant *Staphylococcus aureus* strains. *Pak J Pharm Sci.* 2018 Sep;31(5(Supplementary)):2123-2130.
- <sup>42</sup> Xiang H, Cao F, Ming D, et al. Aloe-emodin inhibits *Staphylococcus aureus* biofilms and extracellular protein production at the initial adhesion stage of biofilm development. *Appl Microbiol Biotechnol.* 2017 Sep;101(17):6671-6681.
- <sup>43</sup> Cataldi V, Di Bartolomeo S, Di Campli E, et al. In vitro activity of Aloe vera inner gel against microorganisms grown in planktonic and sessile phases. *Int J Immunopathol Pharmacol.* 2015 Dec;28(4):595-602.

**Safety Summary:**

Contraindicated in persons with a known hypersensitivity to aloe vera.<sup>44</sup> Considered safe and well tolerated at the dose recommended, with no known interactions.<sup>25</sup> No adverse effects expected during pregnancy and breastfeeding.<sup>25</sup>

## Silica

**Biological Actions:**

Adsorptive agent<sup>45</sup>

**Traditional Use:**

Silicon is the third most abundant trace element within the human body, it can be found in higher concentrations in the skin, as well as mucous membranes and connective tissues.<sup>46</sup> Silicon rarely occurs as a pure free element, rather it forms strong bonds with oxygen and mainly exists as silica or silicate compounds.<sup>47</sup> Silicon is an essential mineral for bone formation, it improves bone matrix quality, facilitates bone mineralization and plays a role in optimal connective tissue health.<sup>48</sup> Silicon, in the form of monomethyl silanetriol (MMST) has been used for decades as an oral silica supplement for bone and connective tissue health, with a higher intake of silica associated with greater bone mineral density in both men and women.<sup>49,50</sup>

**Scientific Evidence:**

MMST is a monomeric, organosilicon molecule that is stable in aqueous solution at high concentrations when compared to its naturally occurring inorganic analogue.<sup>49</sup> Supplementation with silica in the form of Silicea Gastrointestinal Gel (a gel comprised of silicon dioxide and water), has been shown to significantly improve gastrointestinal symptoms associated with functional gastrointestinal disorders.<sup>45</sup> Due to its extremely hydroscopic nature, silicic acid readily binds with water, resulting in very large surface areas (i.e. a surface area of 300 m<sup>2</sup>/g has been measured from a particle size of approximately 4 µm). When mixed with water, silicon dioxide forms a gel, allowing

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<sup>44</sup> Ferreira M, Teixeira M, Silva E, et al. Allergic contact dermatitis to Aloe vera. *Contact Dermatitis*. 2007 Oct;57(4):278-9.

<sup>45</sup> Uehleke B, Ortiz M, Stange R. Silicea gastrointestinal gel improves gastrointestinal disorders: a non-controlled, pilot clinical study. *Gastroenterol Res Pract*. 2012;2012:750750.

<sup>46</sup> Araújo LA, Addor F, Campos PM. Use of silicon for skin and hair care: an approach of chemical forms available and efficacy. *An Bras Dermatol*. 2016 May-Jun;91(3):331-5.

<sup>47</sup> Price CT, Koval KJ, Langford JR. Silicon: a review of its potential role in the prevention and treatment of postmenopausal osteoporosis. *Int J Endocrinol*. 2013;2013:316783.

<sup>48</sup> Jugdaohsingh R. Silicon and bone health. *J Nutr Health Aging*. 2007 Mar-Apr;11(2):99-110.

<sup>49</sup> Jugdaohsingh R, Hui M, Anderson SH, et al. The silicon supplement 'Monomethylsilanetriol' is safe and increases the body pool of silicon in healthy Pre-menopausal women. *Nutr Metab (Lond)*. 2013 Apr 26;10(1):37.

<sup>50</sup> Rondanelli M, Faliva MA, Peroni G, et al. Silicon: A neglected micronutrient essential for bone health. *Exp Biol Med (Maywood)*. 2021 Jul;246(13):1500-1511.

various molecules (bacteria, acids, ions, organic poisons and gas) to be adsorbed into its structure, thereby aiding in their elimination from the body.<sup>45</sup> Silica in the form of silicic acid may also provide protection to the gastrointestinal mucous membrane. Clinical evidence suggests silica gel can help reduce abdominal pain, distension, and nausea as well as decrease stool frequency and the duration in subjects with diarrhea.<sup>45</sup>

### **Safety Summary:**

MMST silica is considered safe as it does not contain nano-silica particles unlike some silicon supplements, over which safety concerns have been expressed.<sup>51,52</sup> Supplementation with 10.5 mg of MMST per day for 4 weeks has been shown to be safe with no adverse effects or serum biochemical changes in otherwise healthy pre-menopausal women.<sup>49</sup> Considered safe during pregnancy and breastfeeding when used in amounts commonly found in food.<sup>53</sup> The estimated dietary intake of silicon in the U.S. and Europe ranges between 12-62 mg/day.<sup>50</sup>

## **Apple Pectin**

### **Biological Actions:**

Anti-inflammatory,<sup>54</sup> antioxidant,<sup>55</sup> prebiotic<sup>56</sup>

### **Traditional Use:**

Pectin is a type of soluble fiber found in cell walls of all higher plants.<sup>57</sup> Traditionally apple pectin was primarily used in the treatment of digestive disorders due to its high fiber content and the ability to regulate bowel movements. Pectin also acts as an antioxidant.<sup>57</sup>

### **Scientific Evidence:**

Apple pectin is a complex polysaccharide, it exhibits a high degree of esterification and a particularly high content of branched side chains.<sup>58,59</sup> Consumption of pectin is thought to form a viscous gel

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<sup>51</sup> Chen L, Liu J, Zhang Y, et al. The toxicity of silica nanoparticles to the immune system. *Nanomedicine (Lond)*. 2018 Aug 1;13(15):1939-1962.

<sup>52</sup> Preece KE, Glávits R, Murbach T, et al. A toxicological evaluation of monomethylsilanetriol (MMST) stabilized in acacia gum, a novel silicon preparation. *Regul Toxicol Pharmacol*. 2020 Nov;117:104782.

<sup>53</sup> Natural Medicines Comprehensive Database. Silicon Monograph. 2018; <http://naturaldatabase.therapeuticresearch.com>. Accessed 2018/08/22.

<sup>54</sup> Chung WSF, Meijerink M, Zeuner B, et al. Prebiotic potential of pectin and pectic oligosaccharides to promote anti-inflammatory commensal bacteria in the human colon. *FEMS Microbiol Ecol*. 2017 Nov 1;93(11).

<sup>55</sup> Wikiera A, Grabacka M, Byczyński Ł, et al. Enzymatically Extracted Apple Pectin Possesses Antioxidant and Antitumor Activity. *Molecules*. 2021 Mar 6;26(5):1434.

<sup>56</sup> Kumar M, Tomar M, Saurabh V, et al. Delineating the inherent functional descriptors and biofunctionalities of pectic polysaccharides. *Carbohydr Polym*. 2021 Oct 1;269:118319.

<sup>57</sup> Chaudhary DA, Chaudhary MR, Judal AL. Apple : Varieties and its Health Benefits. *Research journal of Animal Husbandry and Dairy Science* 2014;5(1):35-38.

<sup>58</sup> Ferretti G, Turco I, Bacchetti T. Apple as a Source of Dietary Phytonutrients: Bioavailability and Evidence of Protective Effects against Human Cardiovascular Disease *Food and Nutrition Sciences*. 2014;5:1234-1246.

<sup>59</sup> Thakur BR, Singh RK, Handa AK. Chemistry and uses of pectin--a review. *Crit Rev Food Sci Nutr*. 1997



which inhibits cholesterol absorption and improves bile acid excretion, likely responsible for the associated reduction in lipid levels in clinical trials.<sup>60</sup> At higher doses, apple pectin also has been shown to delay gastric emptying in diabetic study participants, with a reduction in postprandial hyperglycemia.<sup>61</sup> Pectin also exerts prebiotic effects and is fermented by the microflora in the large intestine resulting in the formation of short chain fatty acids, including acetate, propionate, and butyrate.<sup>62,63</sup> Apple pectin specifically appears to beneficially modulate the gut microbiome, increasing *Bifidobacterium* levels and reducing fecal ammonia and sulfide levels.<sup>64</sup> In animal studies, pectin has also demonstrated favorable effects on the intestinal barrier, mediated in part by induction of the mucous layer which protects epithelial cells.<sup>65</sup>

Pectin also acts as a natural prophylactic agent against poisoning with toxic cations.<sup>59</sup> It has been shown to be effective in removing lead and mercury from the gastrointestinal tract, and *in vitro* modeling suggests it also reduces the bioavailability of mercury.<sup>66,67</sup> Consumption of pectin is also reported to have an anti-inflammatory effect by modulating the composition and metabolism of the complex gut microbiota and promoting the production of interleukin-10.<sup>68</sup> Modulation of the gut microbiome by pectin also induces a shift in the ratio of *Firmicutes* to *Bacteroides*, a shift associated with a reduction in inflammation, as well as numerous metabolic benefits.<sup>63,69</sup>

### **Safety Summary:**

Pectin is considered safe and well tolerated in dietary amounts.<sup>70</sup> Pectin has Generally Recognized as Safe (GRAS) status. Consumption of 10 grams of apple pectin powder twice daily for 6 months has been safe and well tolerated without serious adverse reactions or significant hematological or

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Feb;37(1):47-73.

<sup>60</sup> Brouns F, Theuwissen E, Adam A, et al. Cholesterol-lowering properties of different pectin types in mildly hyper-cholesterolemic men and women. *Eur J Clin Nutr.* 2012 May;66(5):591-9.

<sup>61</sup> Müller M, Canfora EE, Blaak EE. Gastrointestinal Transit Time, Glucose Homeostasis and Metabolic Health: Modulation by Dietary Fibers. *Nutrients.* 2018 Feb 28;10(3):275.

<sup>62</sup> Larsen N, Bussolo de Souza C, Krych L, et al. Potential of Pectins to Beneficially Modulate the Gut Microbiota Depends on Their Structural Properties. *Front Microbiol.* 2019 Feb 15;10:223.

<sup>63</sup> Blanco-Pérez F, Steigerwald H, Schülke S, et al. The Dietary Fiber Pectin: Health Benefits and Potential for the Treatment of Allergies by Modulation of Gut Microbiota. *Curr Allergy Asthma Rep.* 2021 Sep 10;21(10):43.

<sup>64</sup> Shinohara K, Ohashi Y, Kawasumi K, Terada A, Fujisawa T. Effect of apple intake on fecal microbiota and metabolites in humans. *Anaerobe.* 2010 Oct;16(5):510-5.

<sup>65</sup> Xie J, Yu R, Qi J, et al. Pectin and inulin stimulated the mucus formation at a similar level: An omics-based comparative analysis. *J Food Sci.* 2020 Jun;85(6):1939-1947.

<sup>66</sup> Kohn R. Binding of toxic cations to pectin, its oligomeric fragments and plant tissues. *Carbohydrate polymers.* 1982;2(4):273-275.

<sup>67</sup> Jadán-Piedra C, Vélez D, Devesa V. In vitro evaluation of dietary compounds to reduce mercury bioavailability. *Food Chem.* 2018 May 15;248:353-359.

<sup>68</sup> Chung WSF, Meijerink M, Zeuner B, et al. Prebiotic potential of pectin and pectic oligosaccharides to promote anti-inflammatory commensal bacteria in the human colon. *FEMS Microbiol Ecol.* 2017 Nov 1;93(11).

<sup>69</sup> Amabebe E, Robert FO, Agbalalah T, et al. Microbial dysbiosis-induced obesity: role of gut microbiota in homeostasis of energy metabolism. *Br J Nutr.* 2020 May 28;123(10):1127-1137.

<sup>70</sup> Natural Medicines Comprehensive Database. Professional Monograph: Pectin. 2018; <http://naturaldatabase.therapeuticresearch.com>. Accessed 30/08/2018.

biochemical changes in individuals with duodenal ulcers.<sup>71</sup> Considered safe during pregnancy and breastfeeding.<sup>70</sup>

## Humic Acid

### Biological Actions:

Anti-inflammatory, antioxidant,<sup>72</sup> anti-viral,<sup>73</sup> chelating agent.<sup>74</sup>

### Traditional Use:

Humic substances occur naturally as biogenic, heterogeneous organic substances. They can be subdivided into humic acid, fulvic acid, and humin. Humic substances can be found in soils, waters, sewage, compost heaps, marine and lake sediments, peat bogs, carbonaceous shales, lignites, and brown coals. Humic substances, such as Shilajit, have a long history of use in Ayurvedic medicine, with alleged immune and anti-viral effects, as well as modulators of the intestinal microbiome.<sup>73</sup>

### Scientific Evidence:

Humic acid is soluble in water under alkaline conditions and has a molecular weight of 5–10 kDa, and is not absorbable in the intestinal tract.<sup>75</sup> It plays an important role in buffering the pH, cleansing the colon, and detoxifying the body by blocking the absorption of toxins. Animal studies suggest that humic acid may act as a chelator for heavy metals such as lead, reducing plasma lead levels in animals chronically exposed.<sup>76,77</sup> Long suspected to influence the microbiome, the first small, human clinical trial found humic acids supported increased microbial growth without substantially altering microbial diversity.<sup>78</sup> Fulvic acid is soluble in water under diverse pH conditions and because of its low molecular weight (around 2 kDa), it is well absorbed in the intestinal tract and eliminated within hours from the body.<sup>79</sup> Fulvic acid is thought to be a strong antioxidant, anti-

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<sup>71</sup> Kang JY, Tay HH, Guan R, et al. Dietary supplementation with pectin in the maintenance treatment of duodenal ulcer. A controlled study. *Scand J Gastroenterol.* 1988 Jan;23(1):95-9.

<sup>72</sup> Cárdenas Rodríguez N., Coballase Urrutia E., Huerta Gertrudis B., et al. Antioxidant activity of fulvic acid: A living matter-derived bioactive compound. *J. Food, Agric. Environ.* 2011;9:123–127.

<sup>73</sup> Cagno V, Donalisio M, Civra A, Cagliero C, et al. In vitro evaluation of the antiviral properties of Shilajit and investigation of its mechanisms of action. *J Ethnopharmacol.* 2015 May 26;166:129-34.

<sup>74</sup> Krempaská K, Vaško L, Vašková J. Humic Acids as Therapeutic Compounds in Lead Intoxication. *Curr Clin Pharmacol.* 2016;11(3):159-167.

<sup>75</sup> Winkler J, Ghosh S. Therapeutic Potential of Fulvic Acid in Chronic Inflammatory Diseases and Diabetes. *J Diabetes Res.* 2018 Sep 10;2018:5391014.

<sup>76</sup> Vašková J, Krempaská K, Žatko D, et al. Effects of Humic Acids in Chronic Lead Poisoning. *Biol Trace Elem Res.* 2019 Jan;187(1):230-242.

<sup>77</sup> Vašková J, Vaško L, Mudroň P, et al. Effect of humic acids on lead poisoning in bones and on a subcellular level in mitochondria. *Environ Sci Pollut Res Int.* 2020 Nov;27(32):40679-40689.

<sup>78</sup> Swidsinski A, Dörffel Y, Loening-Baucke V, et al. Impact of humic acids on the colonic microbiome in healthy volunteers. *World J Gastroenterol.* 2017 Feb 7;23(5):885-890.

<sup>79</sup> Carrasco-Gallardo C, Guzmán L, Maccioni RB. Shilajit: a natural phytocomplex with potential procognitive activity. *Int J Alzheimers Dis.* 2012;2012:674142.

inflammatory agent, and animal studies suggest it has an anti-diarrheal effect.<sup>80,72,81</sup>

### **Safety Summary:**

Despite its long-standing safe use in Ayurvedic medicine, presently there is limited scientific information regarding the safety of humic substances in humans, though animal data strongly suggests they are quite safe.<sup>82,83,84</sup> 1.8g per day potassium humate has been administered to humans with allergic rhinitis with no adverse effects.<sup>85</sup> Supplementation with fulvic acid (3.8% 5-40 mL twice daily) for 3-7 days has been safely used without any serious adverse effects in individuals with predetermined atopy.<sup>86</sup> Exercise caution during pregnancy and lactation as safety has not been established during these times.<sup>84,87</sup>

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<sup>80</sup> Winkler J, Ghosh S. Therapeutic Potential of Fulvic Acid in Chronic Inflammatory Diseases and Diabetes. *J Diabetes Res.* 2018 Sep 10;2018:5391014.

<sup>81</sup> Qin Y, Zhang M, Dai W, et al. Antidiarrhoeal mechanism study of fulvic acids based on molecular weight fractionation. *Fitoterapia.* 2019 Sep;137:104270.

<sup>82</sup> Murbach TS, Glávits R, Endres JR, et al. A toxicological evaluation of a fulvic and humic acids preparation. *Toxicol Rep.* 2020 Sep 14;7:1242-1254.

<sup>83</sup> Dai C, Xiao X, Yuan Y, et al. A Comprehensive Toxicological Assessment of Fulvic Acid. *Evid Based Complement Alternat Med.* 2020 Dec 16;2020:8899244.

<sup>84</sup> Natural Medicines Comprehensive Database. Professional Monograph: Humic Acid. 2018; <http://naturaldatabase.therapeuticresearch.com>. Accessed 30/08/2018.

<sup>85</sup> Gandy JJ, Meeding JP, Snyman JR, et al. 2010. The clinical efficacy of potassium humate in the treatment of allergic rhinitis: a double blind placebo controlled trial. *Drug Dev Res* 71: 358–363.

<sup>86</sup> Gandy JJ, Meeding JP, Snyman JR, et al. Phase 1 clinical study of the acute and subacute safety and proof-of-concept efficacy of carbohydrate-derived fulvic acid. *Clin Pharmacol.* 2012;4:7-11.

<sup>87</sup> Natural Medicines Comprehensive Database. Professional Monograph: Fulvic Acid. 2018; <http://naturaldatabase.therapeuticresearch.com>. Accessed 30/08/2018.