Selected Modified Citrus Pectin/Alginate Research*

Modified Citrus Pectin and Low Viscosity Alginates Combination Has Multiple Health Benefits

- Effectively and safely removes toxic heavy metals[2, 6-8]
- Binds to chemical toxins to prevent re-absorption, enhancing detoxification and removal[6-8,13,14]
- Does not deplete essential minerals when used long term for heavy metal removal[2]
- Binds and removes radioactive isotopes[9-12]
- Reduces pathogenic gut bacteria[15]
- Promotes growth of beneficial bacterial species[15, 17,18]
- Disrupts pathogenic bacterial biofilms[16]
- Reduces ulcer formation[1]
- Promotes healthy glucose regulation[19]

Functions Systemically and Within the Intestine

- Modified citrus pectin works primarily in the circulatory system after intestinal absorption.[1-3]
- Low viscosity alginates remain in the gastrointestinal tract to prevent absorption of toxins from diet and environment, also preventing reabsorption from bile production.[17,18]

Structural Characteristics

Pectin and alginates are naturally occurring complex polysaccharides classified structurally as polyuronides. Modified Citrus Pectin (MCP) is a modified form of pectin found in the white pith of citrus fruit peels. Citrus pectin is a soluble dietary fiber composed predominately of repeating galacturonic acid units.[1,2] Before modification it is a large complex molecule, 60-300 kilodaltons with approximately 70% esterification. Human digestion lacks the enzymatic capacity to degrade native pectin whose molecular structure too large to allow intestinal absorption.[1-3] Through an enzymatic process, citrus pectin is modified to smaller less complex molecules with a low molecular weight of <15 kilodaltons and a degree of esterification under 5%.[2] Modification enables absorption from the digestive tract into the circulation, where it produces a variety of health benefits.[1-3]

Alginate, found in the cell walls of seaweed, is made of linear chains of mannuronic (M) and guluronic (G) acid; the structure and charge of these compounds make them superior detoxifiers.[4]

- Promote removal of toxins without depleting essential minerals
- Function systemically and within the intestine
- Bind toxins to prevent their absorption

1. Niture SK, Refai L. Plant Pectin: A potential source for cancer suppression. *Am J Pharmacol Toxicol.* 2013;8(1);9-19.
2. Eliaz I, Hotchkiss AT, Fishman ML, *et al*. The effect of modified citrus pectin on urinary excretion of toxic elements. *Phytother Res.* 2006;20:859-864.
3. Georgiev Y, Ognyanov M, Yanakieva I, *et al.* Isolation, characterization and modification citrus pectin. *J BioSci Biotech*. 2012;1(3):223-233.
4. Pomin VH, Mourao PA. Structure, biology, evolution, and medical importance of sulfated fucans and galactans. *Glycobiology*. 2008 Dec;18(12):1016-27.

Toxic Metal Binding Mechanism

Pectins and alginates are classified as polyuronides which form stacks in solution in what is known as an "egg box" structure. Each pocket of the "egg carton" contains a positively charged ion to balance the negatively charged chains. Normally the positive ions are sodium and potassium.[5]

Toxic metals, especially lead, mercury, cadmium, arsenic, and radioactive compounds have a higher binding affinity for polyuronides than the essential ions like calcium, magnesium, and zinc. Toxic metal ions become trapped in the "egg box" structure and are eliminated from the body. USDA-ARS scientist attributed 10% rhamnogalacturonan II content found in the MCP to the selective binding to toxic metals.[2]

The toxin binding properties of polyuronides are also dependent on their degree of esterification and the type and pattern of the molecules that comprise the pectin or alginate chains. The highest binding affinities are found in pectins with a low degree of esterification and alginates that are rich in guluronic acid blocks.[5]

5. Grant GT, Morris ER, Rees DA, *et al*. Biological interactions between polysaccharides and divalent cations: the egg box model. *FEBS Lett*. 1973;32:195–198.

Clinical Study on the Use of MCP and Alginates for Heavy Metal Removal

- A pilot study done in collaboration with the USDA (US Dept of Agriculture demonstrated that oral administration of MCP to healthy human subjects resulted in significant increases in the urinary excretion of lead, arsenic, cadmium, and mercury.[2]
- Essential minerals were unaffected and no adverse effects were noted.[2]

Safe and Effective Removal of Lead in Children

- Administration of MCP to hospitalized children with elevated serum lead levels who had not received any other form of therapy dramatically decreased serum levels of lead over the 28 day study period and significantly increased urinary excretion. No adverse effects were noted.[6]

Decrease in Toxic Metals Promotes Improved Clinical Outcomes

- A multiple case report study documented the progressive removal of lead and mercury with ongoing oral administration of MCP or MCP plus Alginates. Significant reduction of toxic metal body burden (average 74%) was accomplished safely over extended periods, with improvement in symptoms and enhanced response to concomitant therapies. No adverse effects were reported.[7]

Ongoing Use of MCP Significantly Reduced Heavy Metal Burden

- Subjects evaluated for mercury burden using DMPS (2,3-dimercapto-1-propanesulfonic acid) challenge, prior to and upon completion of administration of oral MCP. Study duration 4-10 months.[8]
- Significant reduction in mercury levels for all participants, increasing with duration of treatment. No side effects reported.[8]

6. Zhao ZY, Liang L, Fan X, *et al*. The role of modified citrus pectin as an effective chelator of lead in children hospitalized with toxic lead levels. *Altern Ther Health Med*. 2008;14:34-38.
7. Eliaz I, Weil E, Wilk B. Integrative medicine and the role of modified citrus pectin/aliginates in heavy metal chelation and detoxification-five case reports. *Forsch Komplementmed*. 2007;14:358-364.
8. Eliaz, I. Modified Citrus Pectin Decreases the Total Body Burden of Mercury: A Pilot Human Clinical Trial. Presented at the 228th ACS National Meeting, Philadelphia, PA, Aug 22-26 2004.

Pectins and Alginates Remove Radioactive Cesium

- A study evaluated a group of children exposed during the Chernobyl reactor accident with high body burden of radioactive cesium. Pectin administration resulted in a 33% reduction in levels compared to 14% with placebo.[9]
- Pectins bind to cations like cesium in the GI tract and increase fecal excretion.[9]
- A significant effect of the use of pectin in reduction of radioactive cesium was observed in a group of children after accounting for reductions based on ingestion of uncontaminated food.[10]
- Following the nuclear disaster in Fukushima a report found that a newly discovered green microalgae, *Parachlorella sp. binos* (Binos) accumulated iodine, and also exhibited highly efficient incorporation of the radioactive isotopes strontium and cesium.[11]

- The addition of alginate to the diet was found to have prophylactic properties under conditions of cesium-137 intake.[12]

9. Hill P, Schläger M, Vogel V, *et al*. Studies on the current 137Cs body burden of children in Belarus--can the dose be further reduced? *Radiat Prot Dosimetry.* 2007;125(1-4):523-6.
10. Nesterenko VB, Nesterenko AV, Babenko VI, *et al*. Reducing the 137Cs-load in the organism of "Chernobyl" children with apple-pectin. *Swiss Med Wkly*. 2004; Jan 10;134(1-2):24-7.
11. Shimura H, Itoh K, Sugiyama A, *et al*. Absorption of radionuclides from the Fukushima nuclear accident by a novel algal strain. *PLoS One*. 2012;7(9):e44200.
12. Sukhanov BP, Gorshkov AI, Korolev AA, *et al*. Medical and biological evaluation of new food products for children exposed to excessive radiation *Gig Sanit*. 1994 Sep-Oct;(8):24-6.

Pectins and Alginates Bind and Remove Dioxins and Other Toxic Chemical Compounds

- A preclinical study evaluated 16 dietary fibers for their ability to adsorb dioxins in exposed rats. Dioxin toxicity manifested as immune suppression, hepatic hypertrophy, splenic atrophy and enzyme induction. Pectins and alginates were effective in binding dioxins and enhancing fecal excretion.[13]
- The effect on survival of patients who ingested the herbicide paraquat was tested using a new treatment preparation which included alginates. The alginate component slowed the absorption of the toxin and allowed the other treatment components to have a better effect. Mortality was significantly reduced with use of the alginate-containing preparation.[14]

13. Aozasa O, Ohta S, Nakao T, et al. Enhancement in fecal excretion of dioxin isomer in mice by several dietary fibers. *Chemosphere.* 2001;Oct;45(2):195-200.
14. Wilks MF, Fernando R, Ariyananda PL, *et al*. Improvement in survival after paraquat ingestion following introduction of a new formulation in Sri Lanka. *PLoS Med*. 2008 Feb;5(2):e49.

Pectins and Alginates Enhance Digestive Health

- Pectins have been shown to have anti-ulcer effects, stimulate the growth of beneficial colonic bacteria and inhibit pathogenic strains.[1]
- A clinical study investigated the effect of alginates on stool microbial populations. During alginate consumption, the levels of *Bifidobacteria* increased significantly *(P<0.05),* while the levels of *Enterobacteriaceae* and the frequency of occurrence of lecithinase-negative clostridia decreased.[15]
- A preclinical study showed that low molecular weight alginates acted as an anti-biofilm therapy; disrupting biofilms formed by the opportunistic pathogens *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.[16]
- Low molecular weight polysaccharides derived from alginate bearing seaweeds are being extensively investigated for their potential as prebiotics, with studies demonstrating that these compounds are fermented by gut bacteria [17,18]

15. Terada A, Hara H, Mitsuoka T. Effect of dietary alginate on the faecal microbiota and faecal metabolic activity in humans. *Microbial Ecology in Health and Disease*. 1995;8:259-266.
16. Powell LC, Sowedan A, Khan S, *et al*. The effect of alginate oligosaccharides on the mechanical properties of Gram-negative biofilms. *Biofouling*. 2013;29(4):413-21.
17. Ramnani P, Chitarrari R, Tuohy K, *et al*. *In vitro* fermentation and prebiotic potential of novel low molecular weight polysaccharides derived from agar and alginate seaweeds. *Anaerobe*. 2012 Feb;18(1):1-6.
18. Gupta S, Abu-Ghannam N. Bioactive potential and possible health effects of edible brown seaweeds.*Trends Food Sci Technol.* 2011;22:315–326.

Alginates Favorably Modulate Blood Glucose

- Forty healthy males participated in a study to determine the glycemic response to a controlled test-lunch of mixed composition following an ionic-gelling alginate preload drink. Individual baseline area under the curve was 52% lower and peak glycaemia was 14% lower with a significant reduction in peak and total glycaemia, effectively modulating the glycemic index.[19]

19. Harden CJ, Richardson JC, Dettmar PW, *et al*. An ionic-gelling alginate drink attenuates postprandial glycaemia in males. *J of Function Foods*. 2012;4(1):122–128.

Role of Toxins in Acute and Chronic Disease

- Toxins impose a large burden on the digestive system leading to compromised detoxification.[20]
- Environmental toxins act as potent carcinogens via a number of mechanisms.[20]
- A review paper describes the cancer initiation process as related to toxin and heavy metal exposure:[20]
  - Metals (iron, copper, chromium, cobalt, vanadium, cadmium, arsenic, nickel) generate the formation of free radicals (*e.g.* Fenton chemistry).
  - Oxidative damage to DNA (both mitochondrial and nuclear), and damage to lipids and proteins contribute to the mechanisms of carcinogenesis.
  - Reactive Oxygen Species (ROS) stimulate AP-1 (activator protein) and NF-*k*β signal transduction pathways, which in turn lead to the transcription and up regulation of genes involved in cell growth regulatory pathways.
  - DNA mutation is a critical step in carcinogenesis; elevated levels of oxidative DNA lesions (8-OH-G) have been noted in various tumors, strongly implicating such damage in the etiology of cancer.
- Acute/short term exposure to toxins in cells and tissues produce free radicals which damage organ function over time.[21]
- Long term toxin exposure to toxins may result in metabolic and genetic alterations that can affect cell growth and immune response due to interaction of toxins with molecules such as DNA and proteins.[21]
- Toxins are implicated in promotion of cancer, metabolic syndrome, lung disease, infertility, neurodegenerative disease, diseases of mitochondrial dysfunction, cardiovascular disease, accelerated telomere shortening and other chronic degenerative diseases.[21]
- A study of 3,348 adults, 45-74 years of age, found increased urine cadmium levels, a biomarker of long-term exposure, associated with increased incidence of cardiovascular disease and mortality.[22]
- Cadmium is nephrotoxic causing kidney tubular damage, and can also damage bone. Primary sources are food via contaminated soil, smoking and shellfish consumption. Women with low iron (a high prevalence in pregnant women), are particularly susceptible to toxic effects.[23]
- Lead concentrations in subjects with metabolic syndrome were significantly higher than those in healthy subjects. The prevalence of metabolic syndrome and risk of cardiovascular disease also increased with increasing lead levelsy.[24]
- A review article describes the potential mechanisms of heavy metal toxicity, as well as the deleterious effects of specific metals on organs or systems:[25]
  - Heavy metals may have cumulative deleterious effects that can cause chronic degenerative changes, especially to the nervous system, liver, and kidneys, and in some cases, teratogenic and carcinogenic effects.
  - Heavy metals generate many of their adverse health effects through the formation of free radicals, resulting in DNA damage, lipid peroxidation, and depletion of glutathione.
  - Heavy metals have a slow excretion rate from the body, as indicated by their long half-life. For example, the half-life of lead is 27 years in cortical bone; cadmium is 10–30 years.

- Arsenic's known effects include cancers, central nervous system damage, peripheral vascular disease, lung damage, skin lesions, hearing loss, digestive and circulatory damage, reproductive toxicity, kidney damage, neurological disease, hematological disorders, developmental abnormalities and neurobehavioral disorders.
- Lead effects include central nervous system damage, cancer, kidney damage, neurological disease, liver damage, detrimental effects on erythropoiesis, impaired intellectual ability and behavioral problems in children.
- Cadmium effects include kidney damage, cancer, liver and lung damage including bronchiolitis, COPD, fibrosis, and emphysema, skeletal damage including osteomalacia and osteoporosis.
- Mercury effects include central nervous system damage, kidney, liver, and lung damage, neurological disease, contact eczema, impaired intellectual ability and behavioral problems in children.

20. Valko M, Rhodes CJ, Moncol J, *et al*. Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chem Biol Interact*. 2006;160:1–40.
21. Jackson SP, Bartek J. The DNA-damage response in human biology and disease. *Nature*. 2009;461:1071-1078.
22. Tellez-Plaza M, Guallar E, Howard BV, *et al*. Cadmium exposure and incident cardiovascular disease. *Epidemiology*. 2013 May;24(3):421-9.
23. Järup L, Akesson A. Current status of cadmium as an environmental health problem. *Toxicol Appl Pharmacol*. 2009 Aug;238(3):201-8.
24. Rhee SY, Hwang YC, Woo J, *et al*. Blood lead is significantly associated with metabolic syndrome in Korean adults: an analysis based on the Korea National Health and Nutrition Examination Survey (KNHANES). *Cardiovascular Diabetology*. 2013 Jan;12(1):9.
25. Alissa EM, Ferns GA. Heavy metal poisoning and cardiovascular disease. *J Toxicol.* 2011:870125.

Heavy Metals Act As Xenoestrogens, Disrupting Normal Hormone Levels

- Preclinical studies demonstrated that cadmium mimics the effects of estrogen on estrogen-responsive breast cancer cell lines, activating estrogen receptor-α.[26]
- Cadmium has features of an estrogen mimetic that may promote the development of estrogen-dependent malignancies, such as breast cancer.[27]
- In a large study involving 55,987 postmenopausal women, the risk of breast cancer increased with increasing cadmium exposure, suggesting a role for dietary cadmium in postmenopausal breast cancer development.[27]
- The role of exogenous estrogen exposure in perturbing normal male spermatogenesis and fertility has been conclusively established in a comprehensive literature review.[28]

26. Stoica A, Katzenellenbogen BS, Martin MB. Activation of estrogen receptor-alpha by the heavy metal cadmium. *Mol Endocrinol.* 2000 Apr;14(4):545-53.
27. Julin B, Wolk A, Bergkvist L, *et al*. Dietary cadmium exposure and risk of postmenopausal breast cancer: a population-based prospective cohort study. *Cancer Res.* 2012;72(6);1459–66.
28. O'Donnell L, Robertson KM, Jones ME *et al.* Estrogen and spermatogenesis. *Endocrine Reviews*. 2001;22(3):289–318.