

Chitosan A Marine Medical Polymer And Its Lipid Lowering Capacity

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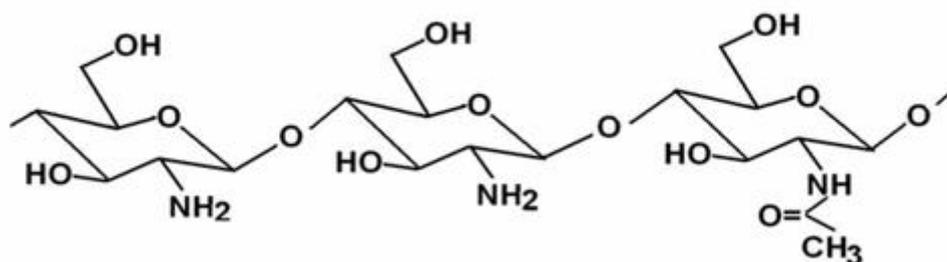
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Abstract

The present report is the collection of information on chitosan; a natural biodegradable copolymer; which is extensively researched the improvement of drug delivery like topical, ocular, implantation and injection (micro and Nanoparticles). However there are many other areas where chitosan is widely used like industrial work, nutrient supply and health care. The present review is focused on its fat binding and lipid lowering capacity as a nutrient or health care product.

Introduction

Chitin, the precursor to Chitosan, was first discovered in mushrooms by the French professor Henri Braconnot in 1811 (Braconnot H, 1811). In the 1820's chitin was also isolated from insects (Odier A, 1823). Chitin is an extremely long chain of N-acetyl-D-glucoseamineunits. Chitin is the most abundant natural fiber next to cellulose and is similar to cellulose in many respects. The most abundant source of chitin is in the shells of shellfish such as crab and shrimp.



Structure of chitosan

Chitin is made by cooking chitin in alkali, much like the process for making natural soaps. After it is cooked the links of the chitosan chain are made up of glucosamine units. Each glucosamine unit contains a free amino group. These groups can take on a positive charge which gives chitosan its amazing properties. The structure of chitosan is represented schematically in Figure 2. Research on the uses of chitin and Chitosan flourished in the 1930s and early 1940s but the rise of synthetic fibers, like the rise of synthetic medicines, overshadowed the interest in natural products. Interest in natural products, including chitin and chitosan, gained resurgence in the 1970s and has continued to expand ever since.

Chitosan is a copolymer of β -(1-4)-linked 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose. This polycationic biopolymer is generally obtained by alkaline deacetylation from chitin, which is the main component of the exoskeleton of crustaceans, such as shrimps (R. Muzzarelli, 1973). The main parameters influencing the characteristics of chitosan are its molecular weight and degree of deacetylation, representing the proportion of deacetylated units. These parameters are determined by the conditions set during preparation. Chitosan is currently receiving a great deal of interest for medical and pharmaceutical applications. The main reasons for this increasing attention are certainly its interesting intrinsic properties. Indeed, chitosan is known for being biocompatible allowing its use in various medical applications such as topical ocular application (P. Sorlier et al., 2001), implantation (Y.M. Dong, 2001) or injection (O. Felt, 1999). Moreover, chitosan is metabolised by certain human enzymes, especially lysozyme, and is considered as biodegradable (D. Koga, 1998). In addition, it has been reported that chitosan acts as a penetration enhancer by opening epithelial tight-junctions (H.E. Junginger, 1998). Due to its positive charges at physiological pH, chitosan is also bioadhesive, which increases retention at the site of application (P. He et al., 1998). Chitosan also promotes wound-healing (H. Ueno, 2001) and has bacteriostatic effects (X.F. Liu et al., 2001). Finally, chitosan is very abundant, and its production is of low cost and ecologically interesting (M.G. Peter, 1995).

Availability of Chitosan

Chitin is the second most abundant polysaccharide in nature (cellulose being the most abundant). Chitin is found in the exoskeleton of crustacea, insects, and some fungi. Chitosan has a rigid crystalline structure through inter- and intra-molecular hydrogen bonding. The main commercial sources of chitin are the shell wastes of shrimp, lobster, krill, and crab. In the world, several million tons of chitin is harvested annually. (Roberts GAF. 1992, Rha CK. 1984)

Application of chitosan

Some of the Industrial uses of chitosan are enlisted as follow; (Int. Com. Nat. Health Products, 1995; Peniston QP and Johnson EL, 1970)

- Waste Water Purification
- Stabilizing Oil Spills
- Stabilizing Fats in Food Preparation
- Antibacterial Protection for Seeds
- Flavor Stabilizer
- Stabilizes Perishable Fruits/Vegetables

- Ion Exchange Media
- Bacterial Immobilizer
- Cosmetic and Shampoo Additive
- Tableting Excipient
- Absorbant for Heavy Metal Removal

Some of the Health and Nutrition application of chitosan enlist below (Kanauchi O. et al. 1994, Maezaki Y et al. 1993, Vahouny G. et al. 1983, Ikeda I. 1989, LeHoux JG and Grondin F. 1993, Fradet G. et al. 1986, Malette W. 1986, Okamoto Y. et al. 1995, Hiroshi S. et al. 1994, Nelson JL et al. 1994, Shibasaki K. et al. 1994, Kato H . et al. 1993, Ito F. 1995)

- Absorbs and Binds Fat
- Promotes Weight Loss
- Reduces LDL Cholesterol
- Boosts HDL Cholesterol
- Promotes Wound Healing
- Antibacterial/Anticandida/Antiviral
- Acts as Antacid
- Inhibits the Formation of Plaque/Tooth Decay
- Helps Control Blood Pressure
- Helps Dental Restoration/Recovery
- Helps to Speed Bone Repair
- Improves Calcium Absorption
- Reduces Levels of Uric Acid

Water purifying plants around the world uses chitosan to remove oils, grease, heavy metals, and fine particulate matter that cause turbidity in waste water streams. Chitosan has been used for about three decades in water purification processes (Patent by, Peniston QP and Johnson EL. 1970) due to its above characteristics. Chitosan has no caloric values as it is not digestible and that's why it is widely used in weight-loss products. Unlike plant fibers, chitosan's unique properties give it the ability to bind fat significantly, acting like a "fat sponge" in the digestive tract (table 1). Under optimal conditions, Chitosan can bind an average of 4 to 5 times its weight with all the lipid aggregates tested. Studies in Helsinki (Abelin J and Lassus A., 1994) have shown that individuals taking chitosan lost an average of 8 percent of their body weight in a 4-week period. Chitosan has increased oil-holding capacity over other fibers (Kanauchi O. et al., 1995). Among the abundant natural fibers, chitosan is unique. This uniqueness is a result of chitosan's amino groups which make it an acid absorbing (basic) fiber. Most natural fibers are neutral or acidic. It can be seen from the results listed, ingestion of chitosan resulted in 5-10 times more fat excretion than any other fiber tested (table 1). D-Glucosamine, the building block of chitosan, is not able to increase fecal fat excretion. This is due to the fact that glucosamine is about 97 percent absorbed while chitosan is nonabsorbable. Fats bound to glucosamine would likely be readily absorbed along with the glucosamine. Chitosan, on the other hand, is not absorbed and therefore fats bound to chitosan can not be absorbed.

Chitosan has the very unique ability to lower LDL cholesterol (the bad kind) while boosting HDL cholesterol (the good kind) (Maezaki Y. et al. 1993). Laboratory tests performed on rats showed that "chitosan depresses serum and liver cholesterol levels in cholesterol- fed rats without affecting performance, organ weight or the nature of the feces." (Kobayashi T. et al. 1979) Japanese researchers have concluded that Chitosan "appears to be an effective

hypocholesterolemic agent.” (Sugano M. et al. 1978) In other words, it can effectively lower blood serum cholesterol levels with no apparent side effects. It effectively lowered cholesterol absorption more than guar gum or cellulose. (Ikeda I. et al. 1989)

Dietary Fiber	% Fat Excreted	Dietary Fiber	%Fat Excreted
Chitosan	50.8 + 21.6	Carrageen	9.6 + 1.9
Kapok	8.3 + 1.1	Sodium Alginate	8.1 + 2.2
Pectin	7.4 + 1.9	Locust Bean	6.0 + 1.8
Guar	6.0 + 1.7	Konjak	5.2 + 0.6
Cellulose	5.1 + 2.1	Karaya	4.9 + 1.5
Acacia	4.6 + 0.9	Furcellaran	4.4 + 0.9
Chitin	4.3 + 1.0	Agar	2.8 + 0.4

Table 1. Effects of Dietary Fibers on Fecal Lipid Excretion (McCausland CW. 1995, Deuchi K. 1994)

Mechanisms Of Fat Binding And Fat Lowering

The different no one fully understood mechanism is there but two basic mechanisms based on experiments are explained. In the first mechanism the attraction of opposite charges which can be compared to the attraction of opposite magnetic poles due to that positive charge on chitosan attract the negatively charged fatty acids and bile acids binding them to the indigestible chitosan fiber. In the second mechanism entrapment can be compared to the effect of a net. This mechanism can explain why chitosan reduces LDL cholesterol levels. Our bodies make bile acids in the liver using the cholesterol from LDL. When chitosan binds bile acids and increases the rate of LDL loss thus improving the LDL to HDL ratio. If enough bile acids are bound, the fats are not solublized, which prevents their digestion and absorption. The second mechanism describes a netting effect of chitosan fiber; wraps around fat droplets and prevents their being attacked and digested by lipid enzymes, “netting” mechanism has been seen to operate in vivo. Fats unprotected by chitosan are digested and absorbed. (Kanauchi O. et al., 1995)

Compounds Trigger the Action of Chitosan

Citric Acid: The experiments with animals, adding citric acid to a chitosan enriched diet resulted in a decreased feed consumption. (Kanauchi O. et al., 1994) The mechanism behind this may be the citric acid can enhancing the swelling action of chitosan leading to a sense of fullness, producing satiety and appetite suppression.

Chelated Minerals: Chelated minerals act to bolster, support and protect the organ systems of the body; (Ashmead HD. Et al.1985, Bodwell CE. Et al. 1988) e.g. when fat is burned, heat and energy are released; if in such condition lack of certain minerals exists, energy levels will

dropdown. Minerals help to transport needed nutrients to depleted areas of the body, thereby stemming off the fatigue we so often experience after eating a fatty meal. Even more importantly, free radicals are released whenever fat is consumed and burned and the presence of chelated minerals helps to expedite the removal of these metabolites and facilitate the availability of fuel for energy.

Essential Fatty Acids: The dietary building blocks for making prostaglandins (control and balance many body functions) are the essential fatty acids (EFAs). The role of prostaglandins in weight loss has been extensively discussed in a review by Heleniak EP. et al. (1989). EFAs exert profound lipid-lowering effects by reducing the synthesis of triglycerides and very low density lipoproteins (bad cholesterol) in the liver. EFA supplementation coupled with a low-cholesterol, low-saturated fat in diet produces a complementary effect in lowering serum lipid levels. (Connor WE. et al. 1993)

Vitamine C: D-Ascorbic acid (erythorbic acid) and L-ascorbic acid can enhance chitosan's ability to bind lipids. Combining chitosan with ascorbic acid results in even less fat absorption and greater fecal fat losses. (Kanauchi O. et al., 1995) Cholesterol oxides cause lesions in artery walls which predispose blood vessels to collect plaque. These dietary cholesterol oxides profoundly influence the initiation of heart disease. Free radicals can also contribute to the formation of cholesterol oxides which are even more likely to damage the heart.

Indoles: Indoles are remarkable phytochemicals which have the ability to selectively activate certain Mixed Function Oxidases (MFOs). (Chen Y-H. et al. 1995) These MFO's helps to balance estrogen metabolism and prepare dietary toxins for elimination before they get absorbed.

Garcinia Cambogia: Garcinia Cambogia contains hydroxycitric acid (HCA) which is a form of citric acid inhibits the liver's ability to make fats out of carbohydrates. (Conte AA. 1963) Carbohydrates are converted to glycogen stores, not fat stores, thus giving the body a better energy reserve and an increase in stamina.

Ephedra and Methylxanthines in Thermogenesis: Thermogenesis means "creating heat." It is one of the way by which our body burn off excess calories and maintain a constant weight. (Bray GA. 1991). When we repeatedly take diet or abuse ourselves by eating too much, our thermogenic ability may be reduced. Numerous animal and humans studies have confirmed the benefits of ephedra and methylxanthines in inducing weight loss and restoring thermogenic responsiveness. (Arai K. et al. 1968)

Method of Taking

The best way to take Chitosan is prior to eat a high-fat meal, which is usually lunch or dinner. Do not take with essential fatty acids, fat soluble vitamins, minerals or medications with Chitosan as their bioavailability may be inhibited. In order to avoid any type of nutrient deficiency, take your other supplements in the morning, when Chitosan is normally not used. Taking of one to two grams of chitosan is adequate for most meals.

Safety

Chitosan has been used extensively in numerous industrial, health, and food applications and proven to be safe. To determine the relative safety of various foods, scientists run experiments to determine the food's toxic level or LD50. Chitosan has been found to have an LD50 of over 16 grams/day/kg body weight in mice. Chitosan is a fiber which expands to form a gel in the acidic environment of the stomach. The problem encountered with extremely high doses of chitosan was caused by gastric dehydration and impaction due to the expansion of the fiber. Arai K. et al. (1968) compared chitosan to common sugars and concluded that chitosan is less toxic than these substances. For safety purposes data gathered in mice is divided by 12 to get the human equivalent. (Freidrich EJ. et al. 1966) The relative LD50 in humans then would be 1.33 grams/day/kg. Given that an average person weighs 150 pounds or 70 kg, this means that the toxic amount for a person would be greater than 90 grams per day. Conservatively, one could feel very confident below the 10% level, or 9 grams per day. Clinical studies have used amounts in the 3-6 grams per day range with no adverse effects. As with any fiber, a person is well advised to drink plenty of water. Changing our diets affects our colon function. Constipation or diarrhea may occur in some persons depending on their individual constitutions and on how well the Chitosan supplement was originally formulated. Even though Chitosan is not digestible by our enzymes, it can and is degraded by soil and water microorganisms. This makes Chitosan environmentally friendly. This was recently acknowledged by the US Environmental Protection Agency when it exempted chitosan from tolerance level testing. (Environmental Protection Agency 40 CFR Part 180. April, 19, 1995.) Any breakdown of chitosan by our colon microflora would release D-glucoseamine which is itself a wonderfully beneficial nutrient for osteoarthritis sufferers.(A Drovanti et al. 1980) Because chitosan can bind lipids and certain minerals, it is best to take essential fatty acid supplements, fat soluble vitamins and mineral supplements separate from chitosan. Taking chitosan with D- or L-ascorbic acid helps increase the amount of fat bound and decrease the loss of minerals. (K Deuchi et al. 1995). Avoid taking chitosan in the following conditions like in person with shellfish allergy or pregnant or breast-feeding.

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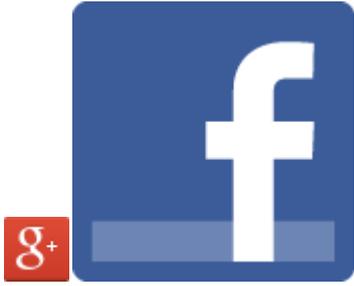
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