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Review Article

Role of Chitosan in Health and Weight Management

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Abstract: Researches from all over the world suggest that the rate of obesity is increasing rapidly. Also the frequency of obesity is rising in all the people of all age groups and regions of the world irrespective of whether it is developed or developing. This statistics, along with the population's need and desire for an easy "cure" of this problem, have led to a invention of a wide variety of dietary supplements regarded as weight-loss products. Chitosan is among one of these products emerged recently. Chitosan is a product that is known to binds to lipids in the gastrointestinal tract, in turn decreasing their absorption and aids in lowering body weight.
Keywords: Crustaceans, Biomedical, Obesity, Deacetylation, Haemostatic.

INTRODUCTION

Chitosan is a linear polysaccharide that is obtained from the hard outer skeleton of shellfish, including crab, lobster, and shrimp. It is obtained by treating shrimp and other crustacean shells with the alkali sodium hydroxide. Chemically it is composed of randomly distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit) [1, 2].

Chitosan finds a lot of commercial and possible biomedical uses. It can be used as biopesticide in agriculture, as a fining agent in wine making industry. In medicine, it can be useful in bandages to reduce bleeding and as an antibacterial agent and to assist dermal drug delivery. Its Role as a soluble dietary fiber has been investigated [1]. It has been reported to have anti-obesity properties [3]. As a nanocarrier it has been found to increase the intestinal transport [4]
Chitosan has been used in water purification has found application in used in the cosmetic and fabric industry [5.]

MANUFACTURE

Chitosan is obtained from the shells of shrimp and other sea crustaceans.

Commercially chitosan is produced by deacetylation of chitin that forms the outer structure in the exoskeleton of crustaceans (such as crabs and shrimp) and also the cell walls of fungi. The degree of deacetylation (%DD) can be determined by NMR spectroscopy, and the %DD in commercial chitosans ranges from 60 to 100%. The average molecular weight of chitosan produced commercially is between 3800 and 20,000 Daltons. A commonly employed method for chitosan production is the deacetylation of chitin by the use excess sodium hydroxide as the reagent and water as the solvent; on completion 98% yield is possible by this process [1].

BIOMEDICAL USES

Number of researches have been done using chitosan in various fields [6]. It has found wide-ranging applications in biomedical and other industrial areas [6-8].

Chitosan's has blood clotting properties. It gained approval in the United States and Europe for use in bandages and other hemostatic agents. Hemostatic products obtained from Chitosan reduce blood loss as comparison to gauze dressings and increase patient survival [1].

Chitosan hemostatic agents are produced from chitosan salts (mixing chitosan with an organic acid such as succinic or lactic acid) [9]. It works by an interaction between the cell membrane of erythrocytes (negative charge) and the protonated chitosan (positive charge) which involves platelets and accelerates thrombus formation [10].

The salts chitosan salts can be mixed with some other materials (such as alginate) to increase their absorbent property [11], or to change the rate of solubility and absorbancy of the chitosan salt [9]. The chitosan salts are biocompatible and biodegradable making them useful as absorbant haemostats [1].

Chitosan is hypoallergenic and has antibacterial properties. It further supports its use in field bandages [11].

Chitosan has also been found to be useful in transdermal drug delivery. It has mucoadhesive in nature, reactive (so it can be produced in many different forms). It has a positive charge under acidic conditions as the free amino groups gets protonated. Thus in an acid medium, protonation of the amino increases its solubility. Due to this property it has found application in biomedical field. The molecule maintains its structure in a neutral environment, but gets solubilized and degraded in an acidic environment. Thus, chitosancan be used in transporting a drug to an acidic environment, where the chitosan will degrade and will release the drug to the desired environment [13]. One example is the transport of insulin [1].

It has been found that chitosan as nano carrier increases the intestinal transport of drug e.g. Gemcitabine [4].

Chitosan as drug carriers have potential for a wider application [14]

PRELIMINARY RESEARCH

Chitosan is considered a cellulose-like dietary fiber; therefore, very little digestion occurs, and most of the ingested chitosan is excreted as such from the body [15]. Chitosan of suitable molecular weight can be cleared by the kidney in vivo. Those of excessive molecular weight can be degraded into fragments, that suitable for renal clearance [16].

Chitosan is believed to affect cholesterol levels and weight because it has positively charged amino groups at the same pH as the gastrointestinal tract [17]. The amino groups are supposed to bind to negatively charged molecules like lipids and bile and prevent their absorption and storage by the body. The ingested chitosan salts react with fatty acids and bind lipids by hydrophobic interactions. These bound lipids are extracted rather than absorbed [15, 18]. Animal studies have indicated that chitosan decreases VLDL-cholesterol levels while increases HDL-cholesterol levels [17].

Pittler MH *et al.* assessed chitosan for weight reduction in the absence of other dietary alterations. The age of the participants range was 18 -60 years with BMIs ranged from 23.9-29.9 kg/m^2. The participants received either four 250-mg chitosan capsules or four placebo capsules twice daily for 28 days. It was found that there were no significant differences except higher vitamin K concentration ($p<0.05$) in the serum in chitosan group [19].

Schiller RN *et al*. had done a study in 69 mildly obese women with BMI range of 27-40 kg/m^2. They had compared chitosan with placebo for a period of 8 weeks for weight loss in the absence of other lifestyle modifications Participants were given either three 500-mg capsules of rapidly dissolving chitosan or placebo daily for two times. The study revealed decreased mean weight (1 kg) in the treatment group while it was found to be increased (1.5 kg) in the placebo group significantly. Also BMI was found to be significantly decreased in the treatment group while fecal fat elimination had found to be increased non significantly in the treatment group. The treatment group had adverse effects such as gastrointestinal discomfort, flatulence, and stool bulkiness [20].

Gades MD and Stern JS had performed a trial study of chitosan in seven healthy males. The study assessed the fat absorption by fecal fat excretion. Participants received diet containing more than 120 g of fat/ day for 12 days along with 5.25 g of chitosan daily on days 6-9. Fecal samples had been collected daily on days 2 through 12. The results revealed no significant difference in fecal fat content between the placebo and treatment periods. Moreover there were no significant differences in fecal mass. Chitosan supplement did not increase fecal fat content and therefore did not block fat absorption [21].

Giustina A and Ventura P had performed a study with 100 mildly obese adults. The participants were given hypo-caloric diet (1000 kcal/day) in order to evaluate the effect of chitosan on body weight and blood pressure. The participants received two tablets of chitosan or placebo twice daily for four weeks. The study revealed significant decrease in all measures in both of the groups. Chitosan group had shown greater reduction in mean body weight (from 83.6 kg to 76.3 kg) than the placebo group (from 82.3 kg to 79.3 kg). Two participants both groups had shown adverse effect of occasional mild nausea [23].

Guerciolini R *et al*. had done a study with 12 healthy volunteers. They had compared the effect of chitosan and orlistat on fat absorption. The study consisted of 14-day (1-week run-in period, week of treatment with orlistat (120 mg 3 times daily)/ 1 week with chitosan ()445 mg 3times daily. Throughout the participants had received diets of 2500 kcal/day throughout the trial. The fecal samples were collected during the run-in and treatment periods. It had been observed that orlistat produced a significant increase in fat excretion from baseline. However, chitosan had found to have no significant effect on fat excretion. However, the chitosan receving participants had fewer gastrointestinal adverse effects than the orlistat group. It was reported that orlistat has inhibitory effect on dietary fat absorption, while chitosan has no effect on fecal fat excretion [22].

Ho SC *et al*. had performed a study on 88 participants. They had evaluated the effect of chitosan

on both weight loss and cholesterol management. The participants were obese and hyper cholesterolemic. After 4-week placebo run-in period, the subjects were randomly given placebo or 250 mg of chitosan capsules (3 times daily). Weight, body mass index, lean body mass, waist, hip, blood pressure, fasting lipids and insulin levels were taken at baseline, 4^{th} and 16^{th} week of the study. The results revealed that there were no significant changes from baseline in any outcome measures in the chitosan group when compared to placebo, with exception of HDL-cholesterol. It was found to increase in the = chitosan group and decreased in the placebo group. Side effects of both groups were comparable [24].

In general, people use chitosan in a dose between 1000 and 1200 mg two times daily to reduce cholesterol level. Some studies reported dosages as high as 6 g/day. Chitosan for the management of weight has been used in dosages that ranges from 1-5 g/day, in different divided doses [25].

The most commonl adverse effects of chitosan are gastrointestinal problems, such as nausea, diarrhea, and constipation [25-27]. Patients having allergy from shellfish should take extreme caution in using shellfish chitosan supplements. Chitosan products may be adulterated with heavy metals and they should be given to children, pregnant ladies and nursing mothers. [27]

The reported drug interactions due to chitosan are very limited, though care may be taken during the administration of chitosan along with highly lipophilic drugs [27]. There may be some possibilities exists regarding the inhibition of the absorption of fat-soluble vitamins that chitosan [25].

Chitosan is often supposed to limit fat absorption and often sold in tablet form as a "fat binder". Study has reported that body weight, blood pressure and parameters related to cholesterol were found to be changed only in some low-quality trials, indicating a very little effect on body weight. In some higher quality trials no significant effect of chitosan was reported to be observed and no clinical justification was given for advising overweight patients to receive chitosan supplements as a remedy [28]

Chitosan has been shown to interact with fat inhibiting the absorption in the duodenum and enhancing excretion of lipid [29]. However, interaction mechanism between chitosan and fat is not been fully understood [30]. The U.S. FDA has given warning letters to supplement retailers for making inappropriate claims about the supposed health benefits of using chitosan [1].

Several researchers are being done on chitosan for its biomedical and other uses [1]:

1. As it is a soluble dietary fiber, it may increase gastrointestinal lumen viscosity, prolonging gastric emptying rate.
2. Chitosan alters bile acid composition, increasing the excretion of sterols and reducing the digestion of fats in the small intestines.
3. Chitosan might stop the uptake of dietary lipids by increasing the thickness of the intestinal lumen wall.

CONCLUSION

More long-term researches are necessary to assess the proper utility of this substance in weight management. The effect of chitosan on the cholesterol and total lipid levels in blood, needs to be validated by large and scrupulous clinical trials.

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