

CHITOSAN: A MARINE DIETARY FIBRE TO FIGHT LIFESTYLE- RELATED DISEASES

Chitosan can be used as a valuable and safe adjunct in the long-term dietary treatment of obesity, enhancing the reduction of blood pressure associated with weight reduction. Further, regular consumption will contribute to the maintenance of normal blood LDL-cholesterol concentrations.

Lifestyle-related diseases such as obesity, hyperlipidaemia, atherosclerosis, type 2 diabetes and hypertension are widespread in industrialized countries, threatening our cardiovascular health. As a result, our ageing population is facing major medical and socioeconomic problems. In recent years, consumers have become increasingly interested in the use of natural, alternative approaches to enhance their health and quality of life. Chitosan, a marine biomolecule and natural dietary fibre, is among those being considered, thanks to its proven multifunctionality.

Metabolic syndrome has emerged as a combination of metabolic disorders, including abdominal obesity, hypertriglyceridaemia, a low level of high-density lipoprotein (HDL) cholesterol, hypertension and a high fasting-glucose level, leading to an increase in cardiovascular morbidity and mortality.¹

There are many risk factors associated with cardiovascular disease: some cannot be altered whereas others can be modified by direct



action. Several of these modifiable risk factors are diet-related, which means that it's possible to voluntarily enhance an individual's health by making basic changes that lead to a healthier lifestyle. A diet that's high in saturated fat increases the risk of heart disease and stroke. It is estimated to cause about 31% of coronary heart disease and 11% of strokes worldwide.

Abnormal blood lipid levels, including high total cholesterol, high levels of triglycerides, high levels of low-density lipoprotein (LDL) or low levels of HDL-cholesterol, all increase the risk of heart disease and stroke. Hypertension is the single biggest risk factor for stroke, playing a significant role in heart attacks. Obesity is a major risk for cardiovascular disease and predisposes you to diabetes.² Ways and means to control these health-related parameters are being sought.

A MARINE DIETARY FIBRE FOR CARDIOVASCULAR HEALTH

An increased focus has been put on the use of natural, alternative approaches for disease prevention and therapeutic applications to enhance health and quality of life. Marine biomolecules are among those being considered. Chitosan is a natural dietary fibre and a deacetylated form of chitin that can be obtained from the shells of crustaceans as a by-product.

Chitin is one of the world's most abundant natural polymers. Chitosan is a copolymer of glucosamine and N-acetyl-glucosamine, which is soluble in acidic media following protonation, resulting in its unique cationic and bioactive nature. Chitosan has been demonstrated to possess several biological properties.³ Dietary fibres are differentiated according to their



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water solubility, which is related to their structure. Soluble fibres increase viscosity and reduce both plasma cholesterol and the glycaemic response, whereas insoluble fibres are porous, contributing to faecal bulk and decreased intestinal transit time.⁴ Chitosan is considered to be an insoluble fibre; but, it will dissolve in stomach acid and become soluble and viscous, behaving like a soluble fibre.

On transiting to the intestine, the higher pH will cause it to gel and become less soluble, contributing to faster transit times and reduced putrefactive activity. This is advantageous: rapid intestinal transit is linked to higher energy recoveries by the host owing to increased bacterial metabolite production in the colon.⁵ Chitosan chelates fat and reduces cholesterol.^{6,7} Xu, *et al.* suggest that chitosan improves lipid metabolism in rats by modifying total cholesterol and LDL-cholesterol levels by up-regulating hepatic LDL receptor mRNA expression, increasing the excretion of faecal bile acids.⁵ In fact, the European Commission Panel on Dietetic Products, Nutrition and Allergies has concluded that a cause and effect relationship has been established between the consumption of chitosan (3 g daily) and the maintenance of normal blood LDL-cholesterol concentrations.⁸

FAT-BINDING CAPACITY AND FAT SELECTIVITY OF CHITOSAN

In the dietary supplement industry, chitosan is used to prevent dietary fat absorption. Fat complexation or entrapment is a function of chitosan solubility in the acidic stomach environment and insolubility at basic intestinal pH levels.

Solubilized chitosan mixes with fat and subsequently forms a semi-solid emulsion under basic pH conditions that is resistant to digestion and absorption. A useful *in vitro* test to evaluate the fat-binding capacity of chitosan under acidic condition should be based on well-defined quantity and time-dependent solubility parameters to allow a fair comparison between commercial products. Further, the type of fat/oil tested may influence the outcome owing to the varying fatty acid composition of oils and fat commonly used in the food industry.

Saturated fatty acids (SFAs) are known to have a hypercholesterolaemic effect on lipid metabolism, whereas polyunsaturated fatty acids (PUFAs) are hypocholesterolaemic and of major importance in normal physiological functions. Despite the fact that some PUFAs are not produced in our body and therefore considered to be essential, excessive amounts of omega-6 ($\omega 6$) PUFAs and very high $\omega 6/\omega 3$ ratios in our diet may promote the pathogenesis of many diseases associated with pro-inflammatory and prothrombotic mediators.⁹

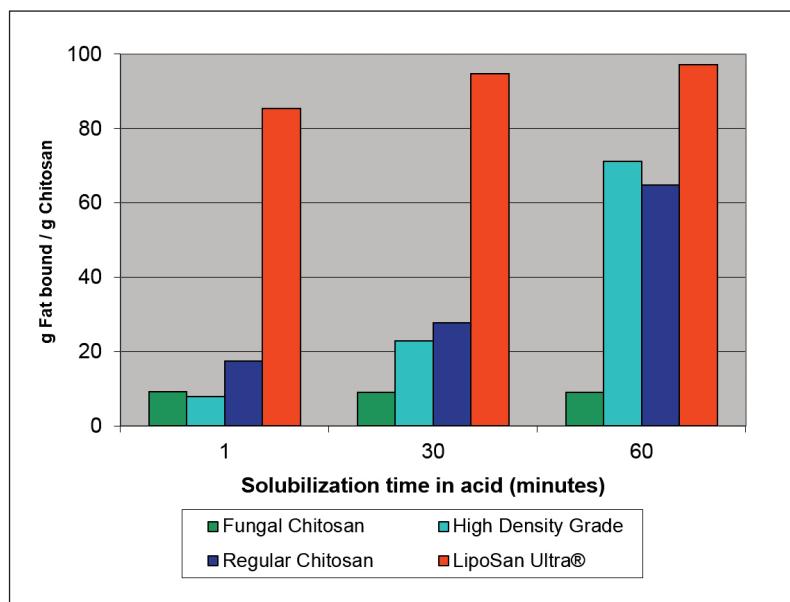
Therefore, the reduction of this ratio is important to approach more desirable levels. The common use of fat that is rich in $\omega 6$ PUFAs in our food production renders this task difficult. Linoleic acid (C18:2 $\omega 6$) as well as oleic acid (C18:1 $\omega 9$) are the major unsaturated fatty acids present in all oils.¹⁰ It is noteworthy that ChitoClear chitosan, produced by PRIMEX, has been shown to selectively bind to cholesterol and fats, specifically SFAs and $\omega 6$ PUFAs.¹¹

Intestinal bioconversion of cholesterol and bile acids is therefore inhibited by ChitoClear chitosan. Furthermore, the study reported that the ratio of $\omega 6/\omega 3$ fatty acids in faeces was significantly increased by ChitoClear chitosan, indicating that ChitoClear chitosan could contribute to balancing the ratio of $\omega 6/\omega 3$ essential fatty acids in our body.

EFFICACY OF LIPOSAN ULTRA AS A FAT BINDER

As the composition of dietary fat can influence our lipid metabolism, it is important to consider how chitosan will perform when binding different types of fats. This was recently investigated by PRIMEX, an Icelandic marine biotech company manufacturing high quality chitin and chitosan products.

LipoSan Ultra chitosan, a safe and effective dietary supplement for weight management and cholesterol control, is a unique, patented product (US Patent No. 6,130,321) produced by PRIMEX. LipoSan Ultra rapidly dissolves in the stomach, complexes and traps fats and oils, thereby reducing the digestion of dietary fat and limiting the calorie intake. The superior efficacy of LipoSan Ultra compared with other products implies that it can be taken just before or during a meal as a convenient weight management product.



This is demonstrated in Figure 1, in which an *in vitro* fat-binding test performed at room temperature and based on 0.1g of chitosan product and 10 g of oil is used to assess fat binding, with a maximum binding efficacy of 100 g of oil by 1 g of chitosan product. As shown, the solubilization time (1–60 min) can be varied to mimic the time in the stomach acid before oil or fat addition and to demonstrate different fat-binding capacities among different products, reflecting the time needed before intake for maximal activity during a meal.

Using this test, LipoSan Ultra fat-binding capacity is found to be 99–100 g(oil)/g(product). Any higher (>100 g[oil]/g[chitosan]) fat-binding capacity cannot be evidenced unless a slightly lower (<0.1 g) chitosan weight is tested against 10 g of oil. Doing so, one can evaluate the maximal fat-binding capacity of a chitosan product if it is expected to exceed 100 g(oil)/g(product).

FAT-BINDING CAPACITY AND SELECTIVITY OF LIPOSAN ULTRA

Primex recently compared the fat-binding capacity of LipoSan Ultra for different oils and fats commonly used by the food industry. The temperature of the test was varied (22 °C in Figure 2 and 37 °C in Figure 3) to allow for the evaluation of saturated fats in a simulated stomach environment.

Figure 2 shows that fat-binding was lowest for extra virgin olive oil and highest for rapeseed oil, reaching up to 144 g(oil)/g(product) when tested at 22 °C. At 37 °C (Figure 3), the fat-binding capacity of LipoSan Ultra was greater, with the highest values reaching 154–164 g(oil)/g(product).

It is observed that sunflower, peanut and rapeseed oil, which bound similarly well to LipoSan Ultra, are high in linoleic acid (C18:2ω6) or compensated with higher levels

Figure 1: Fat-binding capacity of different chitosan products as influenced by solubilization time in acid

of oleic acid (C18:1ω9). By contrast, olive oil, which is rich in oleic acid, was not as well captured by LipoSan Ultra. Corn oil and butter were bound at similar levels, despite having different fatty acid and saturation patterns. This may be explained by the higher levels of saturated fatty acids (palmitic, stearic and myristic) of butter in comparison with the high levels of linoleic and oleic acids in corn oil. Further, based on the result for coconut oil, it can be concluded that the binding capacity of LipoSan Ultra for lauric acid (C12:0) is less than expected.

In fact, these findings correlate well with the results presented by Santas, *et al.* who evaluated the recovery of fatty acids in the faeces of guinea pigs fed a fibre-rich diet.¹¹ They observed that ChitoClear chitosan, used in the preparation of LipoSan Ultra, selectively reduced fat absorption and had a greater

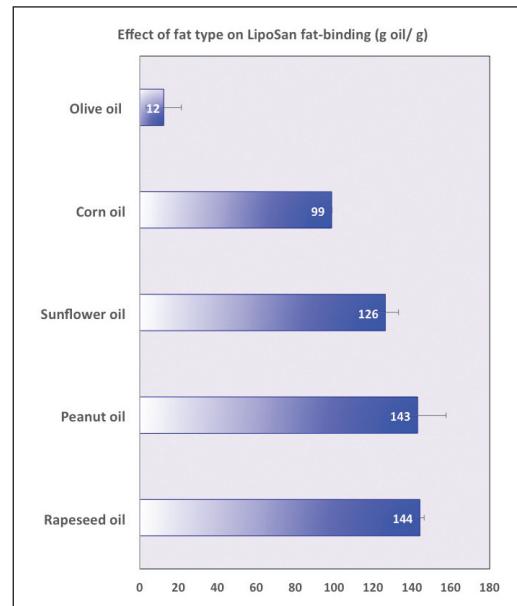


Figure 2: Effect of fat type on LipoSan Ultra fat binding at 22 °C

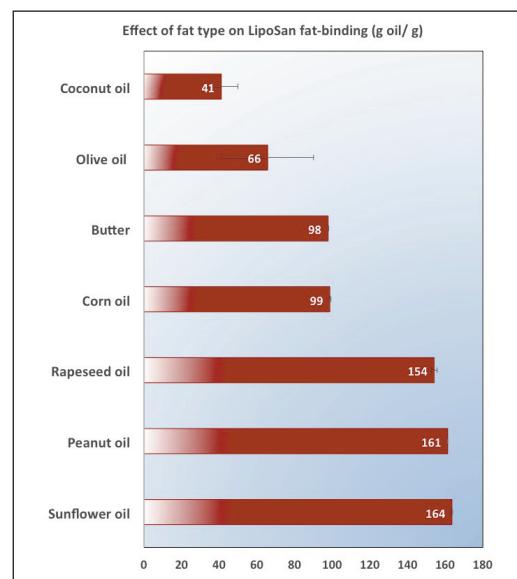


Figure 3: Effect of fat type on LipoSan Ultra fat binding at 37 °C



binding affinity to fatty acids with higher polarities. ChitoClear chitosan significantly increased the excretion of lauric (C12:0) and myristic (C14:0) acids, highly atherogenic saturated fatty acids, compared with other dietary fibres (cellulose and digestion-resistant maltodextrin). It also bound well to palmitic (C16:0), stearic (C18:0) and linoleic (C18:2 ω 6) acids based on the fatty acid profile given for the diet and that recovered from faeces.

The fact that a fat or oil that is rich in oleic acid (olive oil) or medium-chain fatty acids (coconut oil) is less well captured by LipoSan Ultra is noteworthy, considering their health promoting effects. A higher intake of oleic acid decreases LDL-cholesterol but does not affect HDL-cholesterol levels.¹⁰ Coconut oil contains caprylic and capric acids, which are referred to as medium-chain fatty acids (MCFAs) and found in medium-chain triglycerides (MCTs) as MCFAs esters of glycerol. MCTs are hydrolysed rapidly and the resulting MCFAs are absorbed directly into the liver and used as an energy source. A recent review indicated that experimental studies in animal and human subjects have shown that dietary MCFAs/MCTs suppress fat deposition through enhanced thermogenesis and fat oxidation. Furthermore, several reports suggest that MCFAs/MCTs offer the therapeutic advantage of preserving insulin sensitivity in animal models and patients with type 2 diabetes.¹²

HEALTH BENEFITS OF CHITOCLEAR CHITOSAN AND LIPOSAN ULTRA

Both the *in vitro* fat-binding test and the Santas, *et al.* study provide additional information regarding the usefulness of chitosan in preventive and therapeutic treatments. Earlier studies have shown that a daily dose (3 g) of

A higher intake of oleic acid decreases LDL-cholesterol but does not affect HDL-cholesterol levels

LipoSan Ultra led to a significant weight loss (1 kg) and reduced body mass index (BMI) in treated subjects (overweight, mildly obese women, 21–55 years old) adhering to a non-restrictive diet for 8 weeks compared with a 1.5 kg weight gain and increased BMI in the placebo group.¹³

A 6-month study assessed the supplementation of a low calorie diet (1000 kcal/day) with ChitoClear chitosan (1.5 g, three times a day).¹⁴ Significantly higher body weight loss and a decrease in systolic and diastolic blood pressure were noted in the chitosan group. Therefore, chitosan can be used as a valuable and safe adjunct in the long-term dietary treatment of obesity, enhancing the reduction of blood pressure associated with weight reduction. Further, regular consumption will contribute to the maintenance of normal blood LDL-cholesterol concentrations.⁸ Considering these benefits, supplementing our diet with chitosan can contribute to cardiovascular health.

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FOR MORE INFORMATION

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