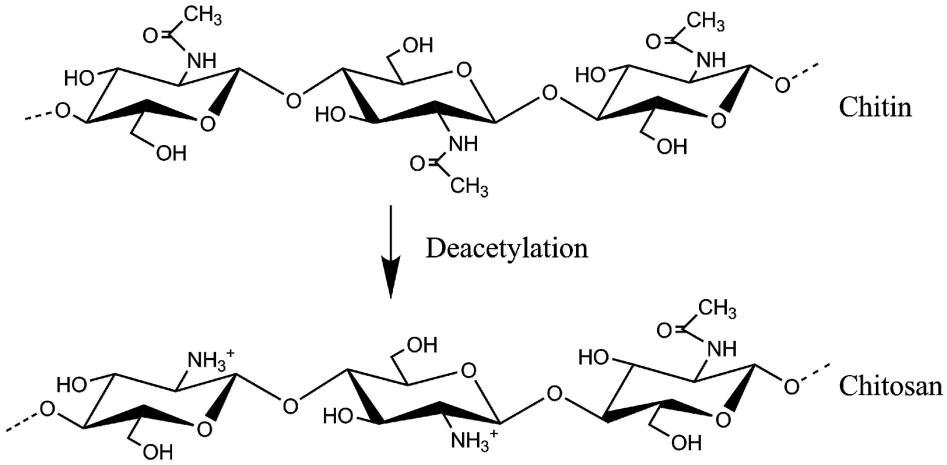
Important Facts about Chitosan and LipoSan Ultra®

Chitin or poly-*N*-acetyl glucosamine is widespread in nature as a structural material, particularly in marine arthropod shells. Chitosan, the deacetylated and acid-soluble form of chitin, possesses several biological properties [1]: biodegradable, biocompatible, antioxidative, emulsifying, flocculating, mucoadhesive, film-forming, permeation enhancing, fat-binding, hemostatic, antimicrobial, stimulating healing, analgesic, tissue-engineering scaffolds and drug-delivery.



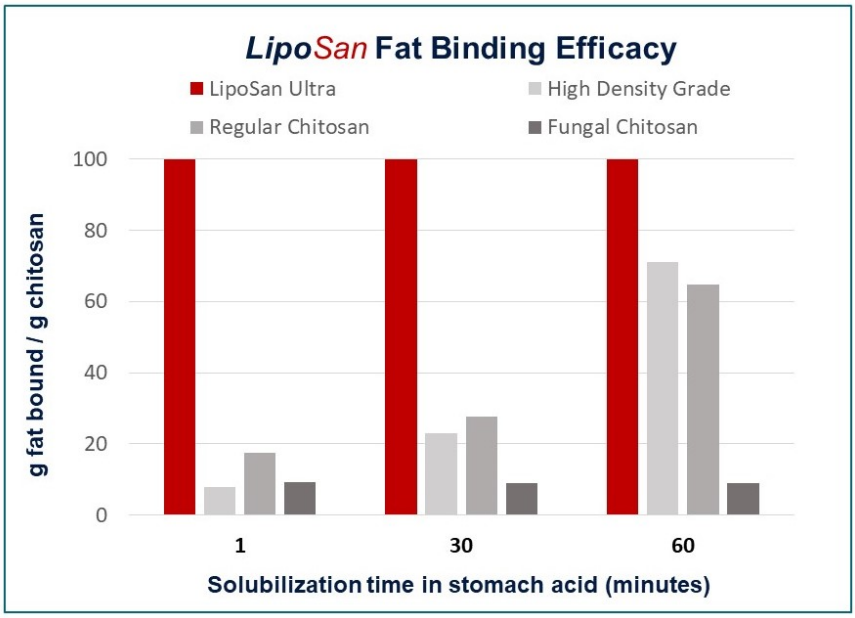
Primex Iceland, an Icelandic marine biotech company and a global leader in the manufacture and supply of chitosan, targets three main potential markets; dietary supplements, biomedical & wound healing, and cosmetics & personal care. Primex chitosan is made from fresh coldwater shrimp shell, *Pandalus borealis* wild caught in the North Atlantic Ocean. The combination of quality raw materials from untainted waters and a unique processing technology allows Primex Iceland to produce the purest chitosan possible and most effective chitosan on the market today.

Chitosan has been demonstrated to possess several biological properties. A meta-analysis involving 15 trials (1219 participants) indicated that chitosan-treated groups had a significantly greater weight loss than the placebo group, as well as a decrease in total cholesterol, systolic and diastolic blood pressure [2]. Due to its fat-binding properties, chitosan can contribute to weight management, and be hypolipidemic, hypocholesterolemic and antihypertensive. Indeed, chitosan can chelate fat and reduce cholesterol [3-4], but does not influence calcium, magnesium and iron status (based on 936 mg daily dose in a 8-week elderly study, [5]). According to EFSA, a daily consumption of 3-g chitosan will contribute to the maintenance of normal blood LDL cholesterol concentrations [6].

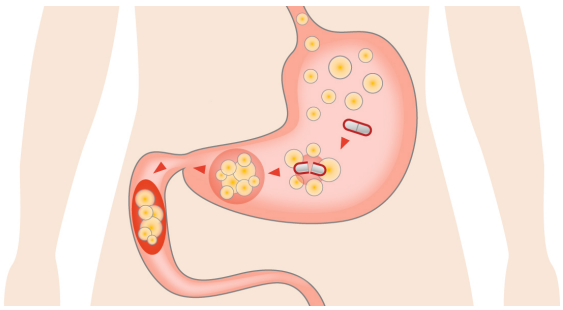
Chitosan is a natural fiber similar to cellulose, but it is a natural amino polysaccharide. Unlike cellulose, it is soluble in acidic environment following its protonation (with positive charge), resulting in its unique cationic (NH_3^+) and bioactive nature. This characteristic offers a great potential as a dietary fiber since chitosan will first dissolve in stomach acid and become soluble and viscous, behaving like a soluble fiber. Transiting from the stomach to the intestine, the higher pH will cause it to gel and become less soluble, contributing to faster

transit time and reduced putrefactive activity. This is advantageous because rapid intestinal transit is linked to higher energy recoveries by the host due to increased bacterial metabolite production in the colon [7].

LipoSan Ultra®, a **Primex** chitosan product prepared by an environment friendly patented process, is a unique, safe and effective weight management supplement. This process results in a more dense chitosan product with high fat-binding capacity. Chitosan must be completely dissolved in stomach acid in order to effectively bind and block fat, something that usually takes up to an hour or more for regular chitosan products. *In vitro* studies mimicking gastric and duodenal environment have shown **LipoSan Ultra®** to be more effective in binding triglycerides than other chitosan products, especially after a short solubilization time (1-30 min, see figure). The resulting enhanced performance of **LipoSan Ultra®** is characterized by its rapid solubility in stomach acid, high density and molecular weight, contributing to LipoSan Ultra's effective fat-binding activity. This superior efficacy of **LipoSan Ultra®** implies that it can be taken just before a meal as a convenient weight management product.



PRIMEX offers natural, effective and convenient solutions for weight management



Obesity has become a worldwide problem and the health burden of obesity-related complications is growing. This is because overweight and obesity lead to adverse metabolic effects on blood pressure, cholesterol, triglycerides and insulin resistance. If there was a simple explanation to this epidemic problem, there would be a simple solution. We all know though that obesity results from energy imbalance—too many calories in, too few calories burned. Further, coronary heart disease (CHD) is the leading cause of death in developed countries. Although its aetiology is multifactorial, high intakes of calories and fats, especially cholesterol-rich fats as well as saturated and trans fatty acids, are widely accepted as major contributing factors. Dietary interventions, such as reducing fat ingestion or its bioavailability, are therefore proposed as primary treatments to lower the risk of CHD.

The healthy keys to weight management include: monitoring calorie and fat intake, being active and following a healthy lifestyle. But why does this not work for everybody? Modernization, globalization and current life-style conditions contribute to the obesity problem. People eat differently nowadays and spend less energy. They become tempted by short-term weight loss solutions instead of following a long-term weight management program and choose a suitable lifestyle. A slow and steady weight loss plan is emphasized, being well supported by delicious, nutritive and well-balanced food choices. Improved eating habits, appropriate portion sizes and physical activity are important for a successful weight management plan which must be tailored to individuals' needs. Nevertheless, the most effective way to achieve weight loss is to reduce calories in our meal. This can be accomplished by the selection of appropriate food products, especially those that minimize hunger, fill the stomach and contribute to low caloric intake, such as dietary fiber.

A dietary fiber is a carbohydrate not digested in the small intestine, but that can be fermented by commensal bacteria once in the colon, resulting in the production of short chain fatty acids (SCFAs) and gases. SCFAs are an important source of energy for the gut and some are transported to other sites around the body for use. Further, the gut microbiota interacts with the host through its metabolites. Some metabolites can damage the gut mucosa, such as indoles, ammonia and amines, while others are beneficial, such as SCFAs [8]. Lin *et al.* [9] examined the effects of SCFAs on body weight, glucose metabolism, and gut hormones in mice and demonstrated that butyrate, propionate, and acetate all protected against diet-induced obesity and insulin resistance. Interestingly, butyrate and propionate, but not acetate, induced gut hormones and reduced food intake. Dietary fibers can therefore be used as prebiotics, i.e. non-digestible food ingredients selectively stimulating the growth and activity of bacterial species in the colon. Accumulating evidence indicates that prebiotics have a diverse range of health benefits, particularly by influencing microbial gut ecology, mineral absorption, laxation, potential anticancer properties, and lipid metabolism, together with anti-inflammatory and other immune effects, including atopic disease. Fermentation processes and SCFA production in the large intestine are believed to contribute to several of these phenomena [10].

The physico-chemical properties of dietary fibers play other important roles in human physiology. Dietary fibers are differentiated based on their water solubility which is related to their structure. In the human body, soluble fibers increase viscosity and reduce the glycemic response and plasma cholesterol, while insoluble fibers are porous, contributing to fecal bulk and decreased intestinal transit time [11]. Recently, Kristensen and Jensen [12] reviewed several studies where most of them indicated that viscous dietary fiber enriched beverages increased the sensation of satiety or fullness. Indeed, dietary fibers have three primary mechanisms in the human digestive tract: bulking, viscosity and fermentation.

Chitosan, being a fiber, is also a valuable prebiotic which can promote optimal colonic conditions. Back in 1995, Terada *et al*. [13] showed that a 2-week intake of chitosan (3 g daily for 7 days and then 6 g) led to reduced occurrence of lecithinase-negative clostridia and

fecal concentrations of putrefactive products (ammonia, phenol, p-cresol and indole) which resulted in less offensive fecal odours. After 14-day intake, SCFA levels had significantly increased, especially propionic acid formation. Unfortunately, few studies have considered these beneficial effects of chitosan on human health but recent publications indicate its potential to modulate the colonic microbiota [14-15]. Mrazek *et al.* [16] observed changes in overall bacterial composition and *bifidobacteria* subpopulation in response to chitosan intake (3 g daily) after only 2-3 days. This was reflected by raised levels of fecal *Bacteroides*, slightly increased or unchanged levels of *Bifidobacterium* and a little increase in butyrate-producing bacteria. After termination of the 4-week chitosan treatment, it took only 2 days to reestablish the initial microbiota, emphasizing the importance of a regular intake of chitosan to maintain a healthy gut. In agreement to Lee *et al*. [17], the findings point to a prebiotic effect of chitosan on *Bifidobacterium*, beneficial for human health. **LipoSan Ultra®** chitosan is obviously a good candidate to stimulate a desirable gut microflora, enhancing gut health and well-being.

Dietary guidance universally recommends diets higher in fiber for health promotion and disease prevention, but there are inconsistencies in the literature on the relation of dietary fiber to body weight. This may be due to the fact that fibers represent a heterogeneous group. Also appropriate dosage is required to obtain health benefits, varying among types of fibers. The following table presents recommended dosage for different fiber products. It clearly shows that different dosage is required for different fiber types to achieve health benefits.

Consumption with a meal contributes to:	Pectin	Guar gum	HPMC	Glucomannan	Betaglucan	Chitosan
Reduction of blood glucose rise after that meal	10 g/day		4 g/serving			
Maintenance of normal blood cholesterol levels	6 g/day	10 g/day	5 g/day	4 g/day	3 g/day	3 g/day
Weight loss (with energy restricted diet)				3 g/day		

http://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public/?event=search

In the future, more studies will confirm the physiological effects some fibers may provide to enhance health with new findings demonstrating new uses. The ability of fibers to bind fat in the digestive tract differs among products found on the market, as shown on Figure 1 illustrating an *in vitro* fat-binding test (max 100 g oil bound/g product) simulating stomach acid solubilization (5 min) and pH changes in the intestine (duodenum).

Due to the cationic nature of chitosan, it is expected to bind more fat than regular fiber. Nevertheless a clear difference in product ability to bind fat is depicted in Figure 1 among chitosan products of crustacean and fungal origin. This is explained by the origin of the product (type and quality) as well as processing characteristics that are known to influence chitosan properties. **LipoSan Ultra®** has a superior efficacy compared to other products.

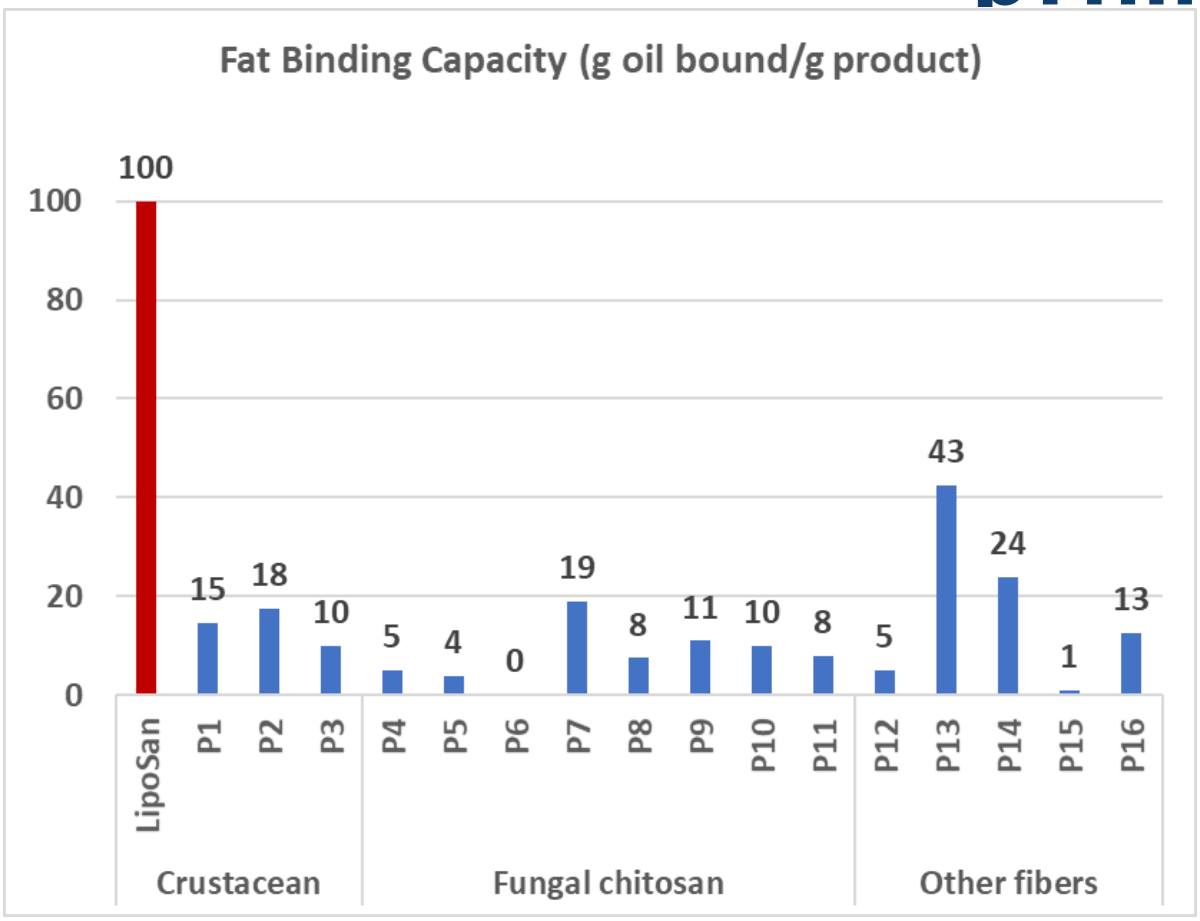


Figure 1. Comparison of fat-binding capacity of different chitosan and fiber products on the market

What happens after ingestion of LipoSan Ultra® with a fatty meal

Fat, like triglycerides, is generally digested and absorbed in the small intestine. Some fatty acids, called medium-chain triglycerides, only have 8 to 12 carbons. Such fat is digested like carbohydrates in the stomach, which means it is absorbed into the small intestine and enters the bloodstream. From there, they travel to the liver, where they are metabolized and used for energy.

When fat enters the digestive tract, various events may occur. First, some fat may be (partially) digested by lingual and gastric lipases but after exiting the stomach, it will be emulsified by bile acids. Emulsification helps the large fat globules to be broken down into smaller globules and made water soluble. This allows pancreatic lipases to hydrolyze (digest) triglycerides, liberating fatty acids and monoglycerides that will be absorbed into the gut epithelial cells and transformed back to triglycerides. They will be used for energy or stored in adipose tissues.

Ingestion of LipoSan Ultra® chitosan will lead to its rapid solubilization in stomach acid. Chitosan differs from other dietary fibers as it is positively charged (NH_3^+) in acid and has 2 hydroxyl groups. Consequently, adsorption has been proposed as the main mechanism responsible for its hypolipidemic properties, binding fatty acids, neutral sterols and bile acids

by electrostatic and hydrophobic forces. It has been shown *in vitro* that chitosan emulsifies lipids under acidic condition (pH 1-2, like stomach), resulting in a water in oil in water type (w/o/w) [18]. With increasing pH, approaching duodenal condition, the emulsion improves (increased number of droplets). At pH 6.2, chitosan precipitates and lipids become entrapped in the formed flocculus (gel-like type). Such interaction contributes to the inhibition of duodenal fat digestion and absorption, and enhanced lipid excretion from the digestive tract. Kanauchi *et al.* [19] studied *in vivo* the mechanism for the inhibition of fat digestion by chitosan in rats and based on observations of ileal contents they concluded that chitosan dissolves in the stomach and then changes to a gelled form, entrapping fat in the intestine.

Further, an *in vitro* study comparing the interaction of chitosan of different molecular sizes with milk fat and protein (casein) confirmed that proteases can attack (digest) casein-chitosan micelles (aggregates), while hydrolysis of chitosan-fat micelles by pancreatic lipases is reduced, especially with increasing molecular size [20]. This indicates that optimal chitosan-fat aggregates (with chitosan of sufficient molecular size) will protect the fat in the small intestine and be brought to the colon without being digested. This may lead to higher energy recoveries by the host due to increased bacterial metabolite production in the colon [7].

LipoSan Ultra rapidly dissolves in gastric acid and emulsifies oil, before forming a flocculus under the higher duodenal pH value. The flocculus formed entraps dietary oil and prevents lipid absorption through the intestinal wall, so the oil is excreted with the faeces.

Maintenance or lowering of cholesterol level

Large amounts of bile acids are secreted into the intestine every day, but only relatively small quantities are lost from the body. This is because approximately 95% of the bile acids delivered to the duodenum are absorbed back into blood within the ileum. Bile acids are derivatives of cholesterol synthesized in the hepatocyte. Cholesterol, ingested as part of the diet or derived from hepatic synthesis is converted into the bile acids. Chitosan can reduce fat absorption and interrupt enterohepatic bile acid circulation [1]. Chitosan differs from other dietary fibers as it has cationic characteristics. Consequently, adsorption has been proposed as the main mechanism responsible for its hypolipidemic properties, binding fatty acids, neutral sterols and bile acids by electrostatic and hydrophobic forces [21]. Therefore, chitosan can increase fecal elimination of steroids. As the absorption of cholesterol from diet and from bile acids decreases, the hepatic bile acid pool is depleted, and more cholesterol is diverted to produce bile acids, thus reducing blood lipid levels.

Liao *et al.* [5] showed that chitosan (936 mg daily for 8 weeks) reduced total cholesterol and LDL-C levels in older-aged patients with hypercholesterolemia. Chitosan reduced the serum cholesterol level by 8.9% and LDL-C by 6%. It is reported that for every 1% reduction in cholesterol, an estimated 2.5% reduction in coronary heart disease incidence is indicated, but cholesterol reduction must be at least 8% to 9% to be effective in lowering total mortality [22]. Dietary chitosan has been shown to improve blood lipid profiles in diabetic and renal disease patients [23-24].

Synergism between vitamin C and chitosan

It has been reported that the presence of ascorbic acid may substantially modify the ability of chitosan to bind water and lipids. Compared to lactic and citric acid or none, ascorbic acid added to chitosan caused a larger increase in fecal fat excretion in rats during a 2-week trial [25]. Kanauchi *et al.* [19] further investigated the synergistic effect of ascorbic acid (AsA, vitamin C) on the inhibition of fat digestion by chitosan in rats. They concluded that it is not acid-dependent but due to the specificity of AsA itself. The following mechanism for the synergistic effect is proposed: 1) viscosity reduction in the stomach, which implies that chitosan mixing with a lipid is better than chitosan alone, 2) an increase in the oil-holding capacity of the chitosan gel, and 3) the chitosan-fat gel being more flexible and less likely to leak entrapped fat in the intestinal tract.

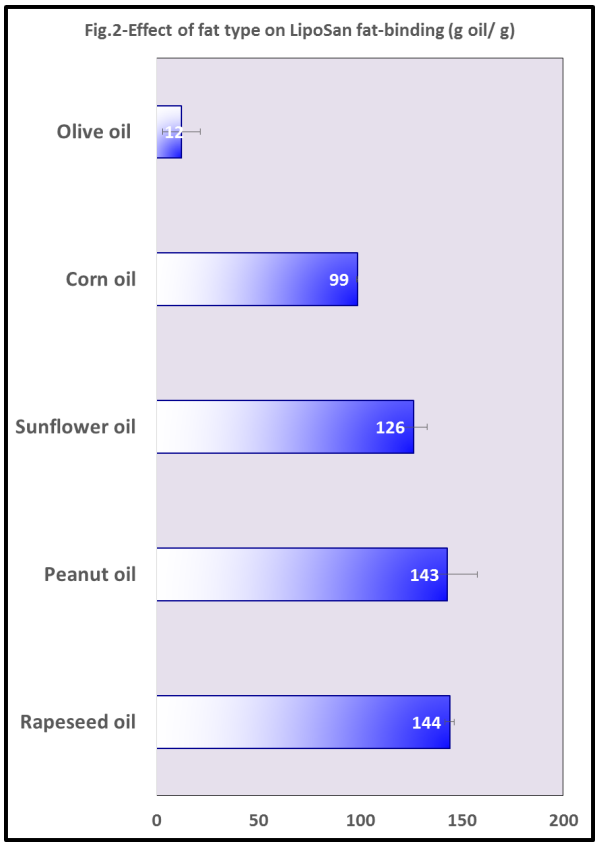
Selectivity of LipoSan Ultra® towards different oils and fat

Saturated fatty acids (SFAs) are known to have a hypercholesterolemic effect on lipid metabolism, whereas polyunsaturated fatty acids (PUFAs) are hypocholesterolemic 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 (ω6) PUFAs and very high ω6/ω3 ratio in our diet may promote the pathogenesis of many diseases associated with pro-inflammatory and prothrombic mediators, such as asthma, cancer and autoimmune diseases [26]. Consequently, it has been suggested that reduction of the $n-6/n-3$ ratio in the diets may reduce the risk of many chronic diseases [27]. Therefore, the reduction of this ratio is important to approach more desirable levels. The common use of fat that is rich in ω6 PUFAs in our food production renders this task difficult. Linoleic acid (C18:2ω6) as well as oleic acid (C18:1ω9) are the major unsaturated fatty acids present in all oils [28].

It is noteworthy that ChitoClear® chitosan, produced by Primex Iceland, has been shown to selectively bind to cholesterol and fats, specifically SFAs and ω6 PUFAs [29]. This was demonstrated during a 4-week trial of guinea pigs fed with a high-fat isocaloric diet including chitosan compared to a water-soluble fiber or placebo. Intestinal bioconversion of cholesterol and bile acids was inhibited by ChitoClear® chitosan. Furthermore, the study reported that the ratio of ω6/ω3 fatty acids in faeces was significantly increased by ChitoClear® chitosan, indicating that ChitoClear® chitosan could contribute to balancing the ratio of ω6/ω3 essential fatty acids in our body.

As the composition of dietary fat can influence our lipid metabolism, it is important to consider how **LipoSan Ultra® chitosan will perform in binding different types of fats**. Primex Iceland 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 gastric and duodenal environment. Figure 2 shows that fat-binding was lowest for extra virgin olive oil and highest for rapeseed oil, reaching up to 144g (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 154–164g (oil)/g(product). To better understand the varying fat binding seen among different fats and oils, a general fatty acid composition of oils and fats is presented in Tables 1 and 2.



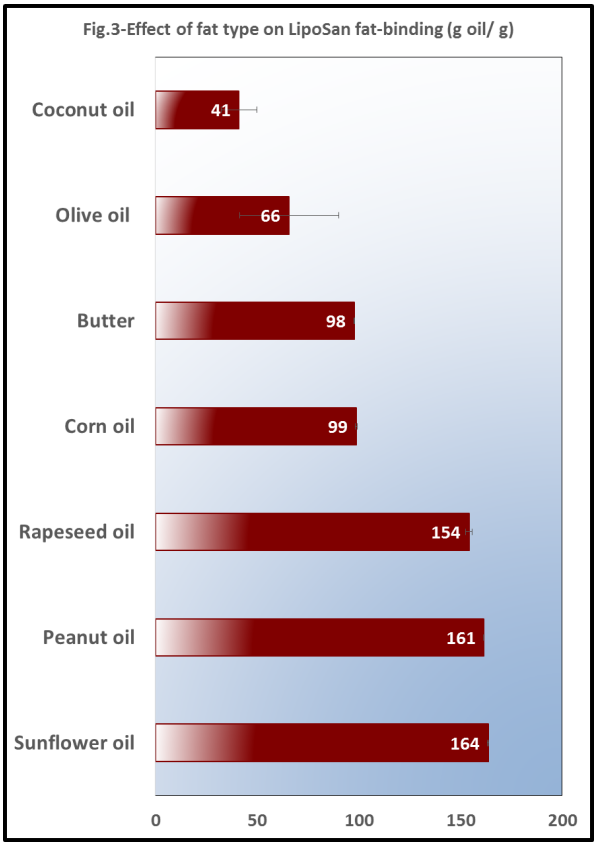


Table 1. Comparison of saturated fatty acid (SFA, %) profile among different oils and fats

FATTY ACID	butyric-caproic	caprylic	capric	lauric	myristic	palmitic	margaric	stearic	arachidic-behenic-lignoceric	Total
OIL TYPE[7]	C4:0-C6:0	C8:0	C10:0	C12:0	C14:0	C16:0	C17:0	C18:0	C20:0-C24:0	SFA
Coconut oil		6,38	5,56	**45,46**	**18,8**	10,1		4,3	0,1	90,7
Olive oil						8,7	0,2	3,5	0,6	13,0
Butter*	5,2	1,2	2,5	**2,6**	**7,4**	**21,7**		10		50,6
Corn oil						10,3	0,1	2	1,0	13,4
Rapeseed oil					0,1	3,7		1,9	1,26	7,0
Peanut oil						9,4	0,1	2,7	6,2	18,4
Sunflower oil					0,1	5,7		4,8	1,3	11,9

*USDA average: http://www.eatwisconsincheese.com/dairy/butter/butter-basics/composition-of-butter

Table 2. Comparison of mono- and polyunsaturated fatty acid profile among different oils and fats

FATTY ACID	palmitoleic	myristoleic	oleic	gadoleic	erucic-nervonic	Total	linoleic	linolenic	eicosadienoic	docosodienoic	Total
OIL TYPE[7]	C16:1ω7	C17:1ω5	C18:1ω9	C20:1ω9	C22:1-C24:1ω9	MUFA	C18:2ω6	C18:3ω3	C20:2ω6	C22:2ω6	PUFA
Coconut oil			7,45	0,06		7,5	1,8				1,8
Olive oil	0,5	0,3	76,3	0,3		77,4	8,6	0,8		0,2	9,6
Butter*	1		**20**			21,0	2,7	0,3			3,0
Corn oil			**25,5**	0,4	0,2	26,1	**59,3**	1,1	0,1		60,5
Rapeseed oil	0,2		**62,4**	1,5	0,3	64,4	**20,1**	8,4	0,1		28,6
Peanut oil	0,1		**48,7**	1,4	0,1	50,3	**31,1**	0,2			31,3
Sunflower oil	0,1		**16,8**	0,2		17,1	**70,7**	0,3			71,0

*USDA average: http://www.eatwisconsincheese.com/dairy/butter/butter-basics/composition-of-butter

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 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.

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 [29]. They observed that ChitoClear® chitosan, used in the preparation of **LipoSan Ultra®**, selectively reduced fat absorption and had a greater binding affinity to fatty acids with higher polarities. 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 [28]. 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 MCFA 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 [30].

Clinical studies have already demonstrated the advantages of Primex products to human health. LipoSan Ultra® (3 g daily for 8 weeks) has been shown to be efficacious in facilitating weight loss and reducing body fat in overweight and mildy obese individuals (BMI 31-32) despite simple routines and minimal changes of lifestyle [31]. Similarly, **ChitoClear®** chitosan (4.5 g daily for 6 months) supplemented to a low calorie diet (1000 kcal/day) contributed to significantly higher body weight loss and decrease of systolic and diastolic blood pressure in fifty obese women [32]. Another study revealed that daily consumption of **ChitoClear®** chitosan (4.5 and 6.75 g) for 8 weeks did not affect serum-fat soluble vitamins or other safety parameters in 56 mildy hypercholesterolemic Finnish subjects (BMI ≤ 26) eating a typical diet. A modest reduction in plasma cholesterol concentrations was observed [33].

Chitosan in antioxidant and anti-aging strategies

Chitosan research indicates that it may contribute to anti-ageing and endurance. Recent studies in rodents reported that chitosan supplementation significantly reduced the age-associated dyslipidemic abnormalities noted in the levels of total cholesterol, HDL-

cholesterol, and LDL-cholesterol in plasma and heart tissue. Its administration significantly attenuated the oxidative stress in the heart tissue of aged rats through the counteraction of free radical formation by maintaining the enzymatic and non status at levels comparable to that of normal young rats [34]. It is suggested that dietary intake of chitosan restores the depleted myocardial antioxidant status and could be an effective therapeutic agent in treatment of age-associated disorders where hypercholesterolemia and oxidative stress are the major causative factors. In rodents, chitosan oligosaccharides increase the mitochondrial content in skeletal muscle and enhanced exercise endurance. *In vitro* cell studies further demonstrated that COS-mediated induction of mitochondrial biogenesis was achieved in part by the activation of silent information regulator Sirt1 and AMP-activated protein kinase (AMPK) [35]. Recent findings indicate other beneficial properties: prebiotic, antidiabetic, antioxidant and renoprotective. Anraku *et al.* [36] reported the antioxidative potential of chitosan in the systemic circulation in human volunteers. The results suggest that chitosan reduces lipid hydroperoxides and other uremic toxins that induce reactive oxygen species (ROS) production in the intestinal tract, thereby inhibiting the subsequent occurrence of oxidative stress in the systemic circulation in human volunteers. The antioxidative effect of chitosan is unique and differs from that of typical, conventional antioxidants**,** such as antioxidant vitamins and N-acetyl cysteine. This fact suggests that chitosan can be co-administered with such agents and represents a new strategy for antioxidative treatment for various health problems. Further, Liu *et al.* [37] findings suggest that chitosan may provide a strategy for diabetes therapy.

Gut microbiota modulation

The gut microbiota interacts with the host through its metabolites [38]. Dietary fiber is the main energy source of colonic bacteria, which ferment certain types of fibers, produce SCFAs and influence the diversity of the gut microbiota [39-41]. In the human gut, SCFAs (such as butyrate, acetate, and propionate) are an important source of energy and some are transported to other sites around the body for use. Propionate and acetate are carried in the bloodstream to different organs where they are used as substrates for energy metabolism, particularly by the hepatocyte cells which use propionate for gluconeogenesis [42]. The gut microbiota also plays a fundamental role in the induction and function of the host immune system [43], protection from pathogens, and stimulation and maturation of epithelial cell [44]. Endurance athletes present a high prevalence of upper respiratory tract infections and gastrointestinal troubles, including increased permeability of the gastrointestinal epithelial wall, disruption of mucous thickness and higher rates of bacterial translocation [45]. Understanding the effect of exercise on gut microbiota composition and structure is still in its infancy and the function of microbiota on exercise adaptation remains unknown, but few studies have shown the impact exercise has on gut microbiota composition [46].

Dietary fibers can contribute to gut microbiota modulation. Dietary guidance universally recommends diets high in fiber for health promotion and disease prevention. However, fibers represent a heterogeneous group of dietary components with mixed physiological effects on human health and gut microbial diversity. Chitosan or „**LipoSan**“, the “natural fiber of the sea”, has been used as a fat-binder and weight management supplement. Chitosan traps fats

and oils in the stomach, thereby reducing the digestion and uptake of dietary fats and limiting the caloric intake. A recent *in vitro* study mimicking the human gut demonstrated that **LipoSan Ultra®** (i) reduces detrimental putrefactive fermentation in colon; (ii) stimulates good bacteria, having a positive effect on colonic health by producing higher levels of acetate and propionate; promoting colonic health [47].

Exercise damaging effects and repair solutions

The physiological and biochemical demands of intense exercise elicit both muscle-based and systemic responses. The main adaptations to endurance exercise include the correction of electrolyte imbalance, a decrease in glycogen storage and the increase of oxidative stress, intestinal permeability, muscle damage, and systemic inflammatory response. The gut microbiota may influence adaptations to exercise since microbes play an important role in the production, storage, and expenditure of energy obtained from the diet as well as in inflammation, redox reactions and hydration status. Therefore, modifying the microbiota through the use of dietary supplements like prebiotics could be an important therapeutic tool to improve athletes' overall general health, performance, and energy availability while controlling inflammation and redox levels. The literature supports the hypothesis that intestinal microbiota might be able to provide a measurable, effective marker of an athlete's immune function and that microbial composition analysis might also be sensitive enough to detect exercise-induced stress and metabolic disorders. Unlike probiotics, the effects of prebiotics have not been tested in athletes [46].

Gut microbiota ferment complex dietary polysaccharides into SCFAs, which may be used as sources of energy in liver and muscle cells and improve endurance performance by maintaining glycemia over time. In addition, the resulting SCFAs seem to regulate neutrophil function and migration, reduce colonic mucosal permeability, inhibit inflammatory cytokines and control the redox environment in the cell, which might help delay fatigue symptoms in endurance athlete. However, the fermentation of amino acids produces a range of potentially harmful compounds. Many endurance dietary plans are based on high protein and carbohydrate levels. A key challenge is to design diets that limit the production of toxic metabolites from protein degradation while supporting a beneficial gut microbiota to maintain body hemostasis and improve performance. **LipoSan Ultra®** could be a wise strategy in the development of sport nutrition.

In conclusion - Obesity is a well-established risk factor for cardiovascular disease, diabetes, hyperlipidemia, hypertension, osteoarthritis, and stroke. *In vivo* antioxidative properties of chitosan have also been reported [34,36]. Over the last 20 years, nutrition research has looked into the role of some nutrients and non-nutritive compounds in disease prevention and risk reduction [48]. **Recent advances in calorie restriction research on aging have revealed that reduced calorie intake contributes to the extension of both median and maximum lifespan as well as the suppression of age-related diseases in laboratory animals.** These effects are mostly explained by the ability of calorie restriction to suppress oxidative related alterations and oxidatively induced age-related diseases [49-50]. Considering current

scientific knowledge and population needs, it appears tactical to provide weight management solutions to tackle the obesity epidemic while promoting calorie restriction to enhance overall wellness. **LipoSan Ultra®** is a promising supplement to support our health.

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