

## Technical Information on LipoSan Ultra<sup>®</sup>

LipoSan Ultra<sup>®</sup>, a chitosan patented product (US Patent No. 6,130,321), is a unique, safe and effective weight loss supplement containing succinic acid, a GRAS food additive. It was developed to increase the density of chitosan. LipoSan Ultra<sup>®</sup> is produced by Primex ehf in Siglufjordur, Iceland, and has the following properties:

- more granular in texture than regular chitosan
- with much better flow properties
- with higher tap density allowing
  - ✓ easier and faster capsule filling
  - ✓ higher fill weights and
  - ✓ resulting in fewer capsules at meal time.

The proprietary technology used results in enhanced solubility of LipoSan Ultra<sup>®</sup> in acid, as shown in Figure 1. Chitosan must be completely dissolved in stomach acid to effectively bind

fat, something that usually takes up to an hour or more for regular chitosan products (Figure 2). The high rate of solubilization of LipoSan Ultra<sup>®</sup> in stomach acid significantly impacts its ability to bind fat compared to regular chitosan.

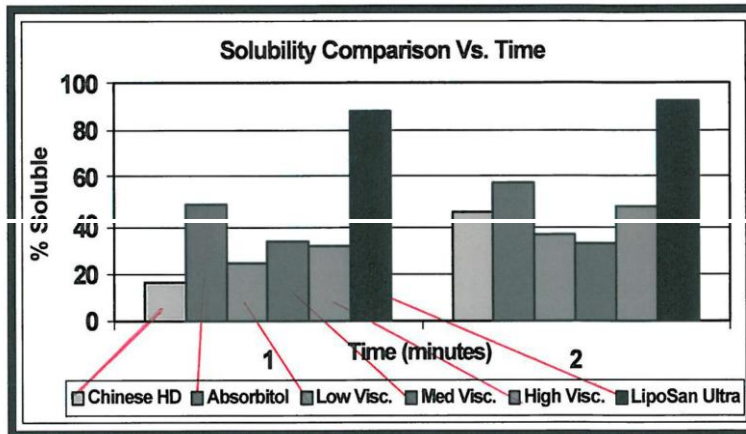
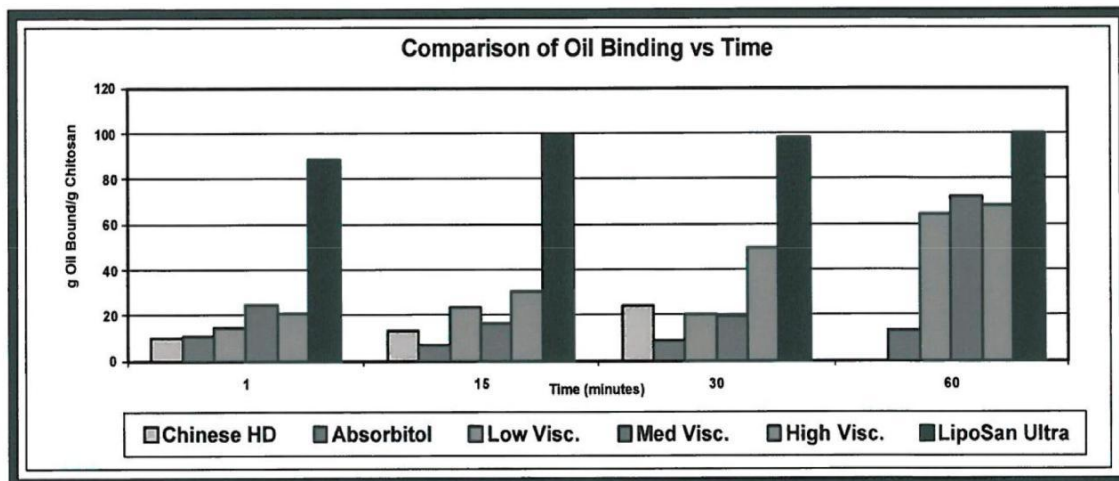


Figure 1. Effect of time in acid (0.16 N hydrochloric acid, equivalent to stomach acid) on solubility (%) of different chitosan products

Figure 2. Effect of solubilization time in acid on the fat binding capacity (g oil bound/g chitosan) of different chitosan products compared to LipoSan Ultra<sup>®</sup> (1 g chitosan solubilized in 100 ml of 0.16 N HCl; 100 g corn oil added, stirred for 30 s, and neutralized with bicarbonate solution to mimic pH in small intestine)



### Comparison of LipoSan Ultra® to Various Chitosan Products

The following table summarizes the characteristic properties of the different chitosan products evaluated. LipoSan Ultra® is almost completely solubilized after 1 min in acid while all other chitosans range in solubility from 17 to 48%. After 30 minutes, all but one of the other chitosans are still less than 50% soluble (data not shown). It is important to note that chitosan solubility is directly dependent on acid strength and not on the degree of deacetylation (DDA).

Chitosan Type	Viscosity (cP)	% Soluble (1 min)	g Oil/g Chitosan (bound in 1 min)	Tap Density (g/mL)	Flowability (mg/s)	DDA %
LipoSan Ultra®	170	88	88.5	0.53	602	80.0
Low Viscosity	110	25	14.5	0.37	9	81.8
Med Viscosity	435	34	24.8	0.26	95	81.3
High Viscosity	700	32	21.2	0.27	17	75.5
Absorbitol	12	48	10.8	0.55	287	nd
Chinese HD	60	17	10.0	0.97	405	93.0

nd, not determined

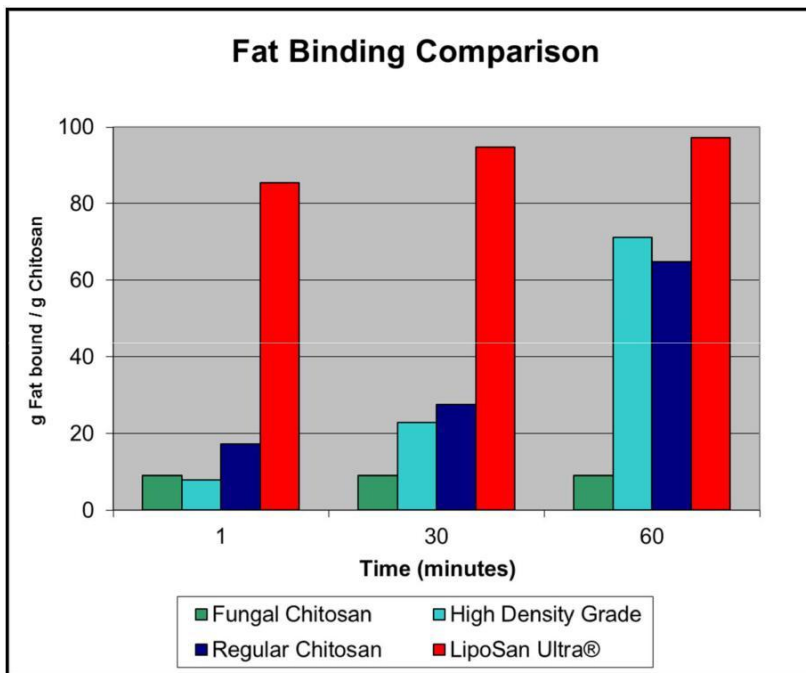


Figure 3. Fat binding comparison

Recent *in vitro* studies have confirmed that LipoSan Ultra® is more effective in binding triglycerides than other chitosans currently on the market, especially after a short solubilization time (1-30 min, see Figure 3) in acid. 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 capacity. This superior efficacy of LipoSan Ultra® implies that it can be taken just before a meal as a convenient weight management product.

### Oil Binding Comparison Data

The following oil binding results are reported as grams of oil bound per gram of LipoSan Ultra<sup>®</sup> or chitosan after mixing for one minute in 0.16 N hydrochloric acid, which is the equivalent of stomach acid according to the standard procedure of “Five -minute Triglyceride Binding Procedure STM-0161 -4/CP-011”. The tables below demonstrate that LipoSan Ultra<sup>®</sup> binds on average over 5 times more oil than regular dietary chitosan (Section 3) and almost 10 times more oil on average than the high density chitosans (Section 2).

#### 1. LipoSan Ultra<sup>®</sup> from Primex

Year	Lot Number	Type	Oil Bound g/g	Density g/cc
2004	LP143	LipoSan Ultra	99	0.50
2005	LP397	LipoSan Ultra	99	0.56
2006	LP684	LipoSan Ultra	99	0.52
2007	LP1053	LipoSan Ultra	99	0.54
2008	LP1270	LipoSan Ultra	99	0.50
2009	LP1709	LipoSan Ultra	99	0.58
2010	LP1859	LipoSan Ultra	99	0.60
2011	LP2080	LipoSan Ultra	99	0.58
2012	LP2349	LipoSan Ultra	99	0.57
2013	LP2531	LipoSan Ultra	99	0.60
			Avg = 99 g	Avg = 0.56 g/cc

#### 2. High Density Imported Chitosan

Source	Lot Number	Type	Oil Bound g/g	Density g/cc
Company A	MD-90305	High Density	14	0.88
Company B	CH-031099	High Density	10	0.60
Company C	CTS 990856	High Density	7	0.50
Company D	WA990856	High Density	13	0.42
Company E	1391	High Density	1	0.89
Company F	WA990607	High Density	6	0.56
Company G	99-AEMF	High Density	15	0.44
Company H	CT853G	High Density	5	1.58
Company I	990520	High Density	15	0.82
Company J	F090	High Density	10	0.97
Company K	WA990603	High Density	15	0.67
Company L	60154795	High Density	6	1.00
Company M	809503254	High Density	15	0.54
			Avg = 10 g	Avg = 0.75 g/cc

#### 3. Regular Dietary Chitosan

Source	Lot Number	Type	Oil Bound g/g	Density g/cc
Company A	CHI-820-25	Regular Dietary	14	0.34
Company B	PB-1402	Regular Dietary	17	0.37
Company C	PB-1420	Regular Dietary	16	0.38
Company D	1115	Regular Dietary	20	0.31
Company E	WA990315s	Regular Dietary	-	0.40
			Avg = 17 g	Avg = 0.36 g/cc



### *Summary of laboratory testing*

Although the laboratory results clearly show that LipoSan Ultra<sup>®</sup> is a superior fat binder when compared to a number of representative chitosans, the true benefit of Primex LipoSan Ultra<sup>®</sup> occurs in the digestive tract. When LipoSan Ultra<sup>®</sup> is taken at mealtime, its extremely fast solubility makes it available to complex with dietary fat for almost the entire time (1.5-2 h) that the ingested food is in the stomach. By the time the fat/chitosan emulsion reaches the small intestine and begins to gel, LipoSan Ultra<sup>®</sup> has had the opportunity to complex far more fat – up to 3 times more – than regular chitosan which may still not be fully dissolved. The complexed fat is trapped in the LipoSan Ultra<sup>®</sup> gel and protected from enzymatic (lipase) breakdown into absorbable free fatty acids. This trapped fat is now unavailable for absorption and is effectively removed from the body as waste.

The consumer will directly benefit from chitosan products containing LipoSan Ultra<sup>®</sup> in that they can take the product when they first sit down to eat, not 30 minutes or an hour beforehand. Most importantly, they will get up to three times more fat binding and, thus, as much as three times less fat absorption. And all of this can be accomplished by taking 1 to 2 grams of LipoSan Ultra<sup>®</sup> with lunch and dinner.

### *Clinical studies of Primex products*

In 2001, a randomized, double-blind, placebo- controlled study, involving 59 overweight, mildly obese women (21-55 yrs old), evaluated the efficacy of rapidly-soluble LipoSan Ultra<sup>®</sup> in facilitating weight loss and reducing body fat<sup>1</sup>. The dosage applied was 1.5 g chitosan as LipoSan Ultra<sup>®</sup> (3 capsules) taken prior to 2 main meals. After 8 weeks, they observed significant weight loss (1 kg) and a reduced body mass index (BMI) in LipoSan Ultra<sup>®</sup> treated subjects adhering to a non-restrictive diet compared to 1.5 kg weight gain and increased BMI in placebo group. Here, positive results were observed in treated subjects even though there was no modification of the diet, which is very exciting and indicates the beneficial use of LipoSan Ultra<sup>®</sup> to consumers who want to lose weight by simple routines and minimal changes of lifestyle. Moreover, no significant changes in functional gastrointestinal and elimination symptoms were reported in either group, but increased water consumption was recommended.

In 2008, Tapola and coworkers<sup>2</sup> evaluated the effect of two different doses of Primex ChitoClear<sup>®</sup> chitosan, the main component of LipoSan Ultra<sup>®</sup>, on serum fat-soluble vitamin concentrations, cholesterol concentrations, and other safety parameters. A total of 65 men and women consumed 0, 4.5, 6.75 g per day of chitosan or 6.75 g per day glucomannan for eight weeks in a parallel, placebo-controlled, single-blind study. Altogether, 56 participants completed the study. No differences were detected among the treatments in serum vitamins (vitamin A, vitamin E, 25-hydroxyvitamin D), carotenes, clinical chemistry or hematology measurements. The changes in the total and LDL-cholesterol concentrations among the study groups were not statistically significant. Finally, the consumption of chitosan tablets was found to be safe, but there was no significant effect on cholesterol concentration.

A long-term study assessed the supplementation of a low calorie diet (1000 kcal/day during 6 months) with ChitoClear<sup>®</sup> chitosan (1.5 g, 3 times a day) in a randomized, placebo-controlled, double-blind study<sup>3</sup>. Significantly higher body weight loss and decrease of systolic and diastolic



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blood pressure were noted in the chitosan-supplemented group. After six months of treatment, the body weight and body fat decrease in the chitosan group was 15.9 kg and 12.3 kg, respectively, in contrast to 10.9 kg and 7.4 kg in the placebo group. In the chitosan group, systolic blood pressure decreased by 13 mm Hg after 3 months and by 19 mm Hg after 6 months of treatment compared to 4 and 9 mm Hg, respectively, in the placebo group. Therefore, ChitoClear<sup>®</sup> chitosan can be used as a valuable and safe adjunct in the long-term dietary treatment of obesity and seems also to enhance the reduction of blood pressure associated with weight reduction.

Finally, a more recent study assessed the selective fat-binding capacity of ChitoClear<sup>®</sup> chitosan to different fat types, monitoring fatty acid absorption, neutral sterol and bile acid excretion in guinea pigs<sup>4</sup>, a suitable animal model due to its similarities with human lipid metabolism. This is quite important as different fat types have different metabolism in animals and humans. The results show that ChitoClear<sup>®</sup> chitosan selectively reduces fat absorption and has higher affinity to bind fatty acids with higher polarity. ChitoClear<sup>®</sup> chitosan significantly increases the excretion of lauric (C12:0) and myristic (C14:0) acids, highly atherogenic saturated fatty acids, compared to other fibres. Intestinal bioconversion of cholesterol and bile acids is therefore inhibited by ChitoClear<sup>®</sup> chitosan. Furthermore, the ratio of  $n-6/n-3$  fatty acids in faeces is significantly increased by ChitoClear<sup>®</sup> chitosan, indicating that ChitoClear<sup>®</sup> chitosan could be of relevant interest for balancing the ratio of  $n-6$  and  $n-3$  essential fatty acids. It is an interesting findings since excessive amounts of  $n-6$  polyunsaturated fatty acids and very high  $n-6/n-3$  ratios may promote the pathogenesis of many diseases associated to pro-inflammatory and prothrombotic mediators, such as asthma, cancer and autoimmune diseases<sup>5</sup>. Consequently, it has been suggested that reduction of the  $n-6/n-3$  ratio in the diet may reduce the risk of many chronic diseases<sup>6</sup>.

### Conclusion

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<sup>7</sup>. 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<sup>8-9</sup>. Considering current scientific knowledge and population needs, it is necessary to provide weight management solutions to tackle the obesity epidemic while promoting calorie restriction to enhance overall wellness.

### Main highlights of LipoSan Ultra<sup>®</sup>

- A safe and natural dietary fiber
- Rapidly soluble and fast-acting in the stomach
- Superior fat binding as shown by *in vitro* tests
- Proven effective in a clinical human study
- Convenient weight management supplement– can be taken at mealtime

## References

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