At the core of our food technology is the use of multiple cyclodextrins to lower digestion and improve the blood glucose response.

Cyclodextrins are the result of enzymatic degradation resulting from cyclomaltodextrin glucanotransferase (E.C. 2.4.1.19; CGTase) catalyzed reduction of starch formed during bacterial digestion of cellulose. The result are supramolecular cyclic oligosaccharide fibers with a (1→) linkage for glucose cyclic pyranose subunits. They have the unique ability to form a host/tenant inclusion complex giving allowing them to influence digestion of fats and carbohydrates and have been demonstrated to have marked anti-obesity, anti-diabetic properties on human metabolism.

Among some of the specific metabolic benefits demonstrated thus far include

Hypertension: a Cyclodextrins amelioration of hypertension via reduction in cholesterol crystals mediated by 2-hydroxypropyl-β-cyclodextrin which inhibits the signal proteins C1q (via IgM) and ficolin-2 leading to a reduction in phagocytosis and and oxidative stress via ROS production in monocytes and granulocytes thus leading to a reduction of inflammation in atherosclerosis.

Cholesterol and Inflammation: b Cyclodextrin has been shown to oxidative stress caused by cholesterol crystals in whole blood. Cholesterol crystals induce a proinflammatory cytokine response vial interleukin 1α, Tumor necrosis factor, interleukin 6 and 8. and induce gene activation of PBMC. BCD. Beta cyclodextrin inhibits the inflammasome response from cholesterol crystals. α-CD has been shown to lower micellar solubility of cholesterol in the lumen of the small intestine via the extraction of lecithin from bile salt micelles into the inclusion complex formation with α-CD. The lecithin extraction effect on the bile salt micelles by α-CD addition seems to be much more pronounced that other soluble fibers.

Serum Lipids: when given in the diet at a rate of 10% of the fat (w/w), significantly reduces plasma TC, PL, FC, and CE, primarily in the plasma LDL fraction, while maintaining blood HDL-cholesterol levels in LDLr-KO mice as compared to that of the controls. Milk fat, high in saturated fatty acids and cholesterol content, was used as a fat source in order to induce elevated plasma lipid levels. This goal was achieved as demonstrated by the early onset of significant increases in plasma.

Serum Glucose: α-CD has been demonstrated to reduce the glucose area under the curve in a meal.
with 50g carbohydrate without increasing insulin secretion. The lowered glycemic response along with the lipid binding properties of α-CD suggest that this soluble fiber may be useful in individuals with dyslipidemia, type 2 diabetes and metabolic syndrome. A 3 month double-blinded, placebo controlled study, α-CD was shown to reduce blood lipids and increase adiponectin levels in obese type 2 diabetic subjects when compared to a placebo. Since plasma adiponectin levels correlate with insulin sensitivity, α-CD potentially may be useful for treatment of type 2 diabetes.

Fat Binding: α-Cyclodextrin been shown to have the ability to bind into its inclusion complex at a ratio far beyond other fibers and allow as much as nine times its weight to be eliminated without digestion. Animal studies have shown α-CD can reduce saturate serum saturated fatty acids and trans fatty acids. Human studies have shown α-CD prevented weight gain in obese diabetic patients via exertion of dietary fat in a 1:9 ratio.

The mechanism of α-cyclodextrin interfering with fat absorption is via prevention of the free fatty acids and glycerol forming through inhibition of hydrolysis of bi- and triglycerides. α-cyclodextrin forms microemulsions with bi- and triglycerides when eaten with fat. While the each α-cyclodextrin conical structure can only contain 1 fatty acid tail per molecule, α-cyclodextrin can form aggregate microemulsions with interior hydrophobic cavities that can contain bi- and triglycerides. The α-cyclodextrin-fat complexes are digestion resistant and can reach the colon undigested. α-cyclodextrin is clearly fermented by the colon microbiota. Evidence from animal studies suggests fat complexes of α-cyclodextrin micro emulsions result in increase cecal loads of short-chain fatty acids acetate and propionate. Other papers have shown α- cyclodextrin increase fecal fat excretion suggesting that while these molecules can act as substrate for colonic bacteria, fat digestion is incomplete and passed from the body.

Clinical studies suggest α-cyclodextrin may yield vast benefits as a dietary component for weight control. A relevant human study with 66 subjects with diabetes mellitus and / obesity where subjects ingested 2 grams of α-cyclodextrin with fat meals at energy intakes > maintenance. α-cyclodextrin was successful in halting weight gain among all subjects. Vs placebo controls, subject weight stabilized where controls continued gaining an average of 2.2 lbs per month. When energy intake was adjusted for maintenance experimental subjects lost weight vs controls who did not. α-cyclodextrin was able to reduce total caloric yields, or rather correct digestion to an adjusted value of 237 calories per day vs controls. Further evidences seems to support the beneficial weight impact of α-cyclodextrin from a double-blind crossover of 41 overweight adults where α-cyclodextrin was able to reduce body weight. The study is of particular interest since all subjects did not engage in either
diet or exercise or calorie reduction. In addition to the fat binding mechanism elucidated above, α-cyclodextrin seems to lower elevated serum leptin levels. Leptin resistance and chronically elevated leptin has been demonstrated to concomitant with obesity in human subjects and α-cyclodextrin may be effective at renormalizing leptin in line with metabolically healthy status.

Finally, α-cyclodextrin seems to have a normalizing effect on dislipidemia. Clinical trials have shown hypertriglycemic subjects experience substantial reductions in total cholesterol effected by reductions in low density lipoproteins. α-cyclodextrin was also shown to reduce serum Apo B, a key marker for disease of the endothelium and heart disease. Perhaps the most compelling evidence for α-cyclodextrin comes from a study in which 34 metabolically normal subjects ingesting 2 grams of α-cyclodextrin per day with meals were able to effect significant reductions in post prandial circulating triglycerides. Individuals with higher fasting triglyceride levels showed the strongest effect suggesting the unique ability of α-cyclodextrin to effect key markers of metabolic health. The remarkable cholesterol lowering ability of α-cyclodextrin is most likely due to its ability to sequester lecithin into bile salt micelles effecting reductions in the solubility of cholesterol and thus lowering cholesterol absorption. α-cyclodextrin also seems able to improve glucose tolerance via inhibition of alpha amylase, thus lowering postprandial glucose peak. Studies on overweight subjects have demonstrated reductions in serum insulin reaching almost 10% over control subjects.
STUDY: On the binding ratio of α-cyclodextrin to dietary fat in humans
“These data support the earlier observation in both in vitro and animal studies that α- CD binds with dietary fat in a 1:9 ratio and further demonstrate the efficacy of α-CD in binding to and eliminating dietary fat, especially saturated fats.”

STUDY: The Beneficial Effects α-Cyclodextrin on Blood Lipids and Weight Loss in Healthy Humans
“In 28 compliant participants (8 males and 20 females), when the active phase was compared to the control phase, there were significant decreases in body weight (-0.4 ± 0.2 kg, P < 0.05), serum total cholesterol (mean ± s.e.m., -0.295 ± 0.10 mmol/l, 5.3%, P < 0.02) and low-density lipoprotein (LDL) cholesterol (-0.23 ± 0.11 mmol/l, -6.7%, P < 0.05). Apolipoprotein B (Apo B) (-0.0404 ± 0.02 g/l, -5.6%, P = 0.06) and insulin levels also decreased by 9.5% (-0.16 ± 0.08 pmol/l, P = 0.06) while blood glucose and leptin levels did not change. These results suggest that α-CD exerts its beneficial health effects on body weight and blood lipid profile in healthy nonobese individuals, as previously reported in obese individuals with type 2 diabetes.’

STUDY: The Beneficial Effects α-Cyclodextrin on Blood Lipids and Weight Loss in Healthy Humans
“We observed a 10 % reduction in small LDL-particle number when subjects were on α- CD versus placebo, with no other changes in the lipid and lipoprotein profile...Overall, these results suggest that α-CD may be more effective in lipid lowering in a more dyslipidemic and obese population, but this will have to be more definitively established in larger clinical trials.”

A study on the inhibitory mechanism for cholesterol absorption by α- cyclodextrin administration
“α-CD decreases the micellar solubility of cholesterol in the lumen of the small intestine via the precipitation of lecithin from bile salt micelles by complex formation with α-CD. It further indicates that the lecithin precipitation effect on the bile salt micelles by α-CD addition clearly differs from addition of other water-soluble dietary fibers. The decrease in micellar cholesterol solubility in the FeSSIF was the strongest with α-CD addition.”

Lipid Lowering of Cyclodextrin In Comparison to Other Fibers
The remarkable lipid lowering effects of Cyclodextrin were demonstrated when compared to other fibers such as resistant maltodextrin, inulin, Partially Hydrolyzed Guar Gum, polydextrose and Cholestyramine. A Cyclodextrin was able to bind far more cholesterol than other fibers. Results with other fibers were in line with previously reported studies.
REFERENCES

Alpha-cyclodextrin: Enzymatic production and food applications

Zhaofeng Lia,b, Sheng Chena,c, Zhengbiao Gua,b, Jian Chena,c and Jing Wua,c, * a State Key Laboratory of Food Science and Technology, Jiangnan University


Relating to ‘The Science Of Professor Nutz’


1. The Effect Of Alpha-Cyclodextrin On Acute Blood Lipid And Glycemic Responses To A Fat Containing Meal
2. The beneficial effects of α-cyclodextrin on blood lipids and weight loss in healthy humans.
3. Randomized double blind clinical trial on the effect of oral α-cyclodextrin on serum lipids
4. Cyclodextrins in Food Technology and Human Nutrition: Benefits and Limitations
5. Dose-Dependent Inhibition of the Post-Prandial Glycaemic Response to a Standard Carbohydrate Meal following Incorporation of Alpha-Cyclodextrin
6. On the binding ratio of α-cyclodextrin to dietary fat in humans.
7. Dietary alpha-cyclodextrin lowers LDL-C and alters plasma fatty acid profile in LDLr-KO mice on a high-fat diet
8. Lipid Lowering with Soluble Dietary Fiber