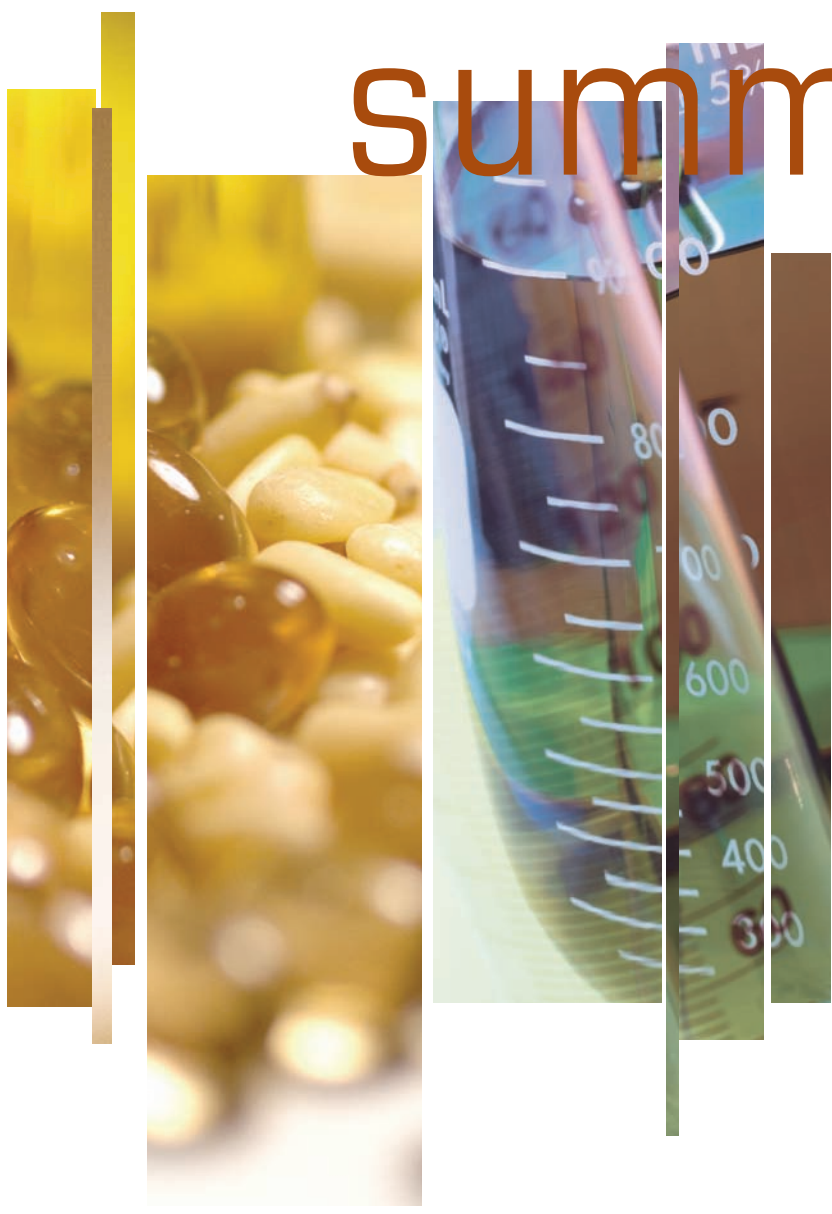


SCIENTIFIC BACKGROUND INFORMATION ON

PINNOOTHIN™

summary





PinnoThin™

PinnoThin™ is a product that comes from a natural plant source. It is based on pine nut oil derived from the nuts of the native Korean pine tree, *Pinus koraiensis*. This tree grows in Korea, Japan, Siberia and China (Manchuria). China is the world's largest producer and exporter of nuts of *Pinus koraiensis* to Europe and the U.S.A.

The oil of these specific nuts contains more than 92% poly- and monounsaturated fatty acids. It is especially rich in very long chain fatty acids, such as pinolenic acid. Pinolenic acid is an omega-6 fatty acid (C18:3 - 5,9,12), which has double bonds in the cis configuration. Korean pine nuts contain about 40 times more pinolenic acid than, for example, Italian stone pine nuts.

Satiety

The global epidemic of obesity has led to an increasing number of studies investigating many different strategies for weight control. One potential strategy is appetite control through natural appetite suppressants. Appetite is the internal driving force for the search, choice and ingestion of food. This drive originates from the need for energy to be used for basal metabolism and physical activity. Three main factors are involved in appetite regulation: hunger, satiation and satiety. Hunger is the drive to consume, satiation is the drive to terminate a meal and satiety is the drive not to eat in between meals. Food intake induces a complex feedback system regulating these three main factors. Reasons for meal termination include feelings of fullness or loss of hunger and decline in pleasantness or reward value of the food being eaten. Intake, digestion and absorption of food are all regulated by the nervous and hormonal system.

Biomarkers for satiety

Meal termination is essentially determined by short-term signals, influenced by gut hormones. Two hormones playing a role in meal termination are cholecystokinin (CCK) and glucagon-like peptide1 (GLP1). CCK is released in the upper part of the small

intestines and is largely induced by protein and fat intake, especially long chain polyunsaturated fatty acids (LC-PUFAs). Several experiments have shown that lipid perfusion to the small intestines increases CCK release. This increase results in a delay in gastric emptying, early satiety and a decrease in food consumption. From these experiments it was concluded that fats act as a pre-absorptive signal to regulate food intake, mediated by an endogenous release of CCK.

GLP1 is released in the last part of the small intestines and is induced by fat and carbohydrate intake. It inhibits gastrointestinal motility, reduces gastrointestinal secretions and attenuates gastric emptying. GLP1 is known to be a potent regulator of food intake in humans. When GLP1 is administered peripherally it reduces energy intake in a dose-dependent manner in both lean and overweight human subjects.

CCK and GLP1 exert their effect by sending satiety signals to the brain and independently inducing a full stomach through delayed gastric emptying. These hormones have therefore an appetite-suppressing effect. Because of their close relation to food intake control, CCK and GLP1 are both scientifically valid biomarkers of satiety.

Satiety hormones like CCK and GLP1 help determine the moment you will stop eating.

PinnoThin™ as an appetite suppressant

Pine nuts have been consumed by humans for centuries. Since LC-PUFAs, present in pine nut oil, are known to induce satiety, research was performed to evaluate the appetite-suppressant effect of PinnoThin™. An in vitro experiment was carried out in which STC-1 enteroendocrine cells were used. These cells come from a mouse's intestinal tumor cell line and they express CCK. The cells were stimulated with 50 µM of different fatty acids and oils. CCK release was measured after stimulation. In comparison with Italian stone pine nut oil and linoleic acid, PinnoThin™ had by far the largest effect on CCK release in these cells (Figure 1).

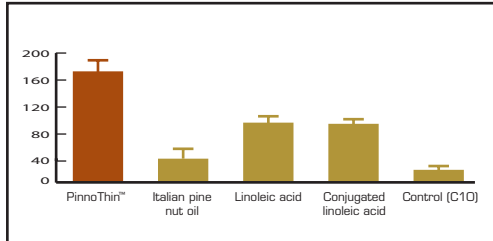


Figure 1
CCK release in STC-1 cells after stimulation with different oils and fatty acids (50 µM)

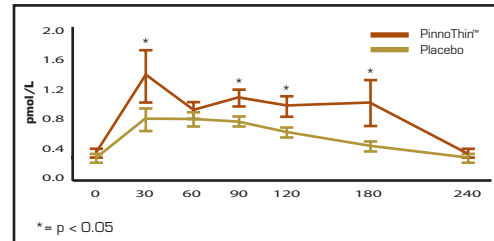


Figure 2
CCK release after PinnoThin™ or placebo consumption

This appetite-suppressing effect of pine nut oil was further evaluated in a randomized, double blind, placebo-controlled, cross-over human trial. The trial was performed by a renowned research institute, TNO, in the Netherlands. Eighteen overweight but otherwise healthy, middle-aged women participated in this study. They were given a simple breakfast consisting of two slices of white bread and marmalade, along with three grams of PinnoThin™ or three grams of placebo (olive oil). The women were monitored up to four hours after the breakfast. Both CCK and GLP1 release in the blood was measured 30, 60, 90, 120, 180 and 240 minutes after the start of the breakfast. Each subject completed both interventions (PinnoThin™ and placebo) with a 1 week wash-out between them.

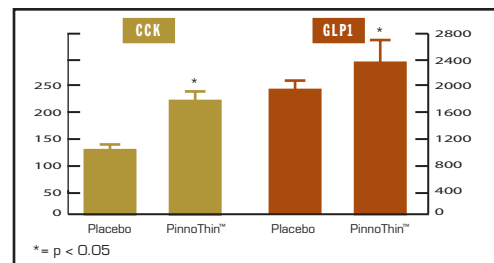


Figure 3
Total CCK and GLP1 release in plasma during the 4 hours after PinnoThin™ or placebo consumption

The study showed a clear increase in CCK release after PinnoThin™ consumption when compared to the placebo. The effect on CCK release became apparent after 30 minutes and lasted for three hours (Figure 2). GLP1 release was also increased after PinnoThin™ consumption as compared to the placebo. An effect on GLP1 release was observed after 60 minutes and lasted again for three hours. In summary, the total amount of plasma CCK and GLP1 in response to PinnoThin™ over a period of four hours was respectively 60% and 25% higher than in response to placebo (Figure 3). The differences between PinnoThin™ and the placebo were all statistically significant.

The results of this research are consistent with the biological release of intestinal hormones. CCK is released in the upper part and GLP1 is released in the lower part of the small intestines. The difference in time shown between the effects on CCK and GLP1 represents the transit time of PinnoThin™ through the small intestines. An overview of the effect of PinnoThin™ is given in Figure 4.

PinnoThin™ quickly increases the feeling of fullness and the effect lasts for at least three hours.

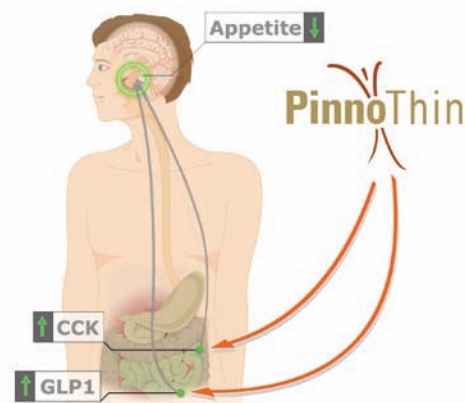


Figure 4
PinnoThin™ increases the satiety hormones CCK and GLP1. These hormones send signals to the brain leading to a reduced appetite.



Mechanism of action

The effect of PinnoThin™ on intestinal hormone release is most likely mediated through chylomicron formation. Fatty acids with a chain length of less than 12 carbon atoms are transported from the enterocyte directly into the circulation via the portal vein. Fatty acids with a chain length of more than 12 carbon atoms are absorbed into the circulation as chylomicrons. A study in rats has shown that suppression of food intake by long chain fatty acids is inhibited by blocking chylomicron transport through specific inhibitors. CCK signaling pathways are closely related to the transport of chylomicrons. This suggests that the fatty acids from PinnoThin™ may particularly affect chylomicron formation or transport and thereby influence release of CCK.

Conclusions

Current data indicate that three grams of PinnoThin™ increase the release of CCK and GLP1 for over a period of at least three hours. Through this effect PinnoThin™ may influence meal termination and meal size. Since the effect lasts for a longer period, it may also effect satiety and reduce snacking in between meals. PinnoThin™ is therefore a scientifically proven appetite suppressant that can help people to get and maintain a healthy body weight and can help in the fight against obesity.

PinnoThin™ helps to:

- Promote a feeling of satiety
- Suppress appetite
- Reduce meal size
- Reduce snacking
- Control food intake
- Increase satiety value of PinnoThin™ fortified foods

Suggested Reading

Blundell JE, Goodson S, Halford JCG. Regulation of appetite: role of leptin in signaling systems for drive and satiety. Intern J Obesity 2001;25(Suppl 1):s29-s34.

Degen L, Matzinger D, Drewe J, Beglinger C. The effect of cholecystokinin in controlling appetite and food intake in humans. Peptides 2001;22:1265-1269.

De Graaf C, Blom WAM, Smeets PAM, Stafleu A, Hendriks HFJ. Biomarkers of satiation and satiety. Am J Clin Nutr 2004;79:946-961.

Einerhand AW, Pasman W, Rubingh C, van den Berg R, O'Shea M, Gambelli L, Hendriks H. Korean pine nut fatty acids affect appetite sensations, plasma CCK and GLP1 in overweight subjects. FASEB J. 2006;20:A829-c.

Lawton CL, Delargy HJ, Brockman J, Smith FC, Blundell JE. The degree of saturation of fatty acids influences post-ingestive satiety. Br J Nutr 2000;83:473-482.

Matzinger D, Degen L, Drewe J, Meuli J, Duebendorfer R, Ruckstuhl N, D'Amato M, Rovati L, Beglinger C. The role of long chain fatty acids in regulating food intake and cholecystokinin release in humans. Gut 2000;46:689-694.

Moran TH. Gut peptides in the control of food intake: 30 years of ideas. Physiol Behavior 2004;82:175-180.

Strader AD, Woods SC. Gastrointestinal hormones and food intake. Gastroenterology 2005;128:175-191.

Verdich C, Flint A, Gutzwiller JP, Naslund E, Beglinger C, Hellstrom PM, Long SJ, Morgan LM, Holst JJ, Astrup A. A meta-analysis of the effect of glucagons-like peptide-1 (7-36) amide on ad libitum energy intake in humans. J Clin Endocrinol Metab 2001;86:4382-4389.

Wynne K, Stanley S, McGowan B, Bloom S. Appetite control. J Endocrinol 2005;184:291-318.



LIPID NUTRITION HEAD OFFICE
Hogeweg 1, P.O. Box 4
1520 AA Wormerveer
The Netherlands
Phone: +31 (0)75 629 29 11
Fax: +31 (0)75 629 28 17

LIPID NUTRITION NORTH AMERICA
24708 W. Durkee Road
Channahon, Illinois 60410-5249
U.S.A.
Phone: +1 815 730 5200
Fax: +1 815 730 5202

LIPID NUTRITION SOUTH AMERICA
P.O. Box 18912
UZ N° 9
11500 Montevideo
Uruguay
Phone: +598 99 289453

LIPID NUTRITION ASIA PACIFIC
Level 10, Two IOI Square
IOI Resort
62502 Putrajaya
Malaysia
Phone: +603 8947 8888
Fax: +603 8947 8889

LIPID NUTRITION CHINA
Room 302A, Capital Group Plaza
6 Chaoyangmen Beidajie
Dongchengqu, 100027 Beijing
China
Phone: +86 (0)10 8528 3359
Fax: +86 (0)10 8528 3359

LIPID NUTRITION 中国
中国北京市东城区朝阳门北大街6号
首创大厦302A 邮编 100027
电话: +86 (0) 10 8528 3359
传真: +86 (0) 10 8528 3359

www.lipidnutrition.com
Email: info@lipidnutrition.com