Newly published studies on satiety benefits of Korean pine nut oil (PinnoThin™)

**Abstract:** A Korean pine nut oil product, PinnoThin™, has been shown to trigger the release of the satiety gut hormone cholecystokinin (CCK) in vitro. Recently published randomized, placebo-controlled double-blind crossover clinical trials have investigated the effects of PinnoThin™ on satiety markers. A clinical trial in 18 overweight postmenopausal women, studied the effects of PinnoThin™ free fatty acid (FFA) and triglyceride (TG) versus placebo (olive oil) on CCK and glucagon peptide-1 (GLP-1) release and appetite sensations. PinnoThin™ FFA and TG were shown to have significant effects on CCK release, while PinnoThin™ FFA had significant effects on GLP-1. Prospective food intake assessed by visual analogue scale (VAS) was significantly reduced 30 minutes after PinnoThin™FFA intake. Another study on 42 overweight young women investigated the effects of PinnoThin™ FFA and different doses of PinnoThin™ TG versus placebo (olive oil) on food intake, feeding behaviour and appetite. PinnoThin™ FFA given 30 minutes prior to ad libitum buffet lunch significantly reduced food intake (grams) and tended to decrease energy intake (kcal) compared to placebo, while no compensation for the reduced intake was observed at ad libitum dinner. Since it was previously shown that PinnoThin™ TG is normally hydrolyzed to PinnoThin™ FFA, the differential results seen in the case of PinnoThin™ FFA and TG are consistent with a delay in TG conversion to FFA. These studies suggest that PinnoThin™ has satiating effects corresponding to increased release of satiety hormones CCK and GLP-1 and decrease in subsequent food intake.

**Key words:** satiety, satiation, fatty acids, triglyceride, CCK, cholecystokinin

Estimations of energy balance suggest that an increase in daily caloric intake of 50 kcal more than energy expenditure can result in a yearly increase in body weight of 1 to 2 kilos, contributing to the development of obesity [1]. One potential strategy in the fight against obesity is to reduce food intake by inducing satiety and thus suppressing appetite.

Food intake induces a complex feedback system regulating hunger and satiety. Intake, digestion and absorption of food are all regulated by the nervous and the hormonal system [2]. Cholecystokinin (CCK) and glucagon-like peptide 1 (GLP-1) are two key hormones in this system, which play an important role in appetite regulation and are seen as major biomarkers for satiety [3].

CCK release suppresses appetite and high concentrations of CCK produce larger appetite-suppressing effects [4]. CCK can be induced by fatty acids with a chain length of twelve carbons or longer [5, 6]. Long chain poly-unsaturated fatty acids (PUFA) have been shown to produce a large increase in CCK response [6-12]. After ingestion of long chain PUFA, free fatty acids (FFA) are hydrolyzed in the gut lumen and CCK is secreted [13]. The effect of CCK release is associated with a reduction in gastric motility and increase in gastric distension, resulting in feelings of fullness and inhibition of food intake [4]. TG hydrolysis is necessary for induction of CCK release, and inhibition of lipase action has been shown to markedly decrease CCK secretion [8, 13, 14]. Numerous studies have shown that exogenous CCK infusions reduce food intake and suppress appetite [11, 15-20]. CCK antagonists generally have the reverse effect on appetite and have been associated with weight gain in rodents [21, 22]. GLP-1 is also known to be a potent regulator of food intake. It has been shown that peripheral administration of GLP-1 reduces energy intake in a dose-dependent manner in both lean and overweight human subjects [23]. Much like CCK, GLP-1 is produced in response to the presence of fat in the gut lumen [24]. GLP-1 release leads to a delay in gastric emptying, early satiety and a decrease in food consumption, which serves as a negative feedback signal to limit the amount of food consumed [14, 23-26].

Korean pine nut oil consists mainly of long chain polyunsaturated fatty acids (PUFA) and has a uniquely high concentration of pinolenic acid. The fatty acid profile of Korean pine nut oil suggests a possible role on satiety hormone release. This role is in line with the available evidence showing an induction of satiety hormones and a consequent reduction of appetite after ingestion of long-chain PUFA [7, 13, 27].

This report summarizes data from previously published studies to support the role of Korean pine nut oil or PinnoThin™ on satiety. First, in vitro data are presented to demonstrate the stimulatory effect of PinnoThin™ on satiety hormones. Second, data from two human randomized double-blind placebo-controlled crossover trials are presented to show the effect of PinnoThin™ on satiety hormones in vivo, appetite sensations and food intake.

**Effects of PinnoThin™ FFA on CCK release in vitro**

Murine endocrine STC-1 cells were utilized in this study to investigate the capacity of Korean pine nut oil or PinnoThin™ to induce CCK compared to another type of pine nut (Italian pine nut) and common dietary fatty acids [28]. STC-1 cells secrete CCK in response to a number of stimuli and are a useful tool for examining the pathways involved in CCK secretion [29]. As a result to this exposure, the increase in...
CCK release was measured (figure 1). Capric acid and Italian stone pine nut FFA produced only a small amount of CCK release (46 pg/mL and 62 pg/mL respectively). Different dietary fatty acids, namely oleic, linoleic, and alpha-linolenic, produced an intermediate CCK release (145 pg/mL, 138 pg/mL and 124 pg/mL respectively). Korean pine nut oil FFA produced by far the largest CCK release (493 pg/mL). The strong stimulating effect of Korean pine nut FFA in vitro prompted further investigation. It was of great interest to confirm the induction of CCK release by PinnoThin™ in a human trial.

**Effects of PinnoThin™ FFA and TG on gut satiety hormones and appetite sensations**

The effect of pine nut oil on CCK in humans was evaluated in a randomized, double blind, placebo-controlled, cross-over trial [28]. In this study, eighteen overweight, but otherwise healthy, post-menopausal women participated in this study. They were given a simple breakfast, consisting of two slices of white bread and marmalade, along with 3G PinnoThin™ FFA, 3G PinnoThin™ TG or 3G placebo (olive oil). Both CCK and GLP-1 release in the blood was measured 30, 60, 90, 120, 180 and 240 minutes after the start of the breakfast. During the same time period, subjective measures of appetite sensations were quantified using a 100 mm visual analogue scale (VAS). Each volunteer completed all three interventions (PinnoThin™ FFA, PinnoThin™ TG and placebo) with 1 week wash-out in-between.

CCK release was significantly higher after PinnoThin™ TG and FFA intake compared to placebo and (figure 2; p < 0.05). The effect on CCK release became apparent after 60 minutes for the PinnoThin™ TG and after 30 minutes for the PinnoThin™ FFA. The total CCK release for PinnoThin™ TG was 22% higher compared to placebo and 60% higher for PinnoThin™ FFA (p < 0.05). GLP-1 release was significantly higher after PinnoThin™ FFA compared to placebo at 60 minutes (p < 0.05) (figure 3). The total GLP-1 release for PinnoThin™ FFA was 25% higher than placebo (p < 0.05).

When volunteers rated their prospective food consumption, which is a measure of how much food the volunteers believed they could consume, an effect of PinnoThin™ was observed. Prospective food consumption, calculated by VAS scores, tended to be lower after PinnoThin™ TG consumption (p = 0.06) and was significantly lower 30 minutes after PinnoThin™ FFA intake (p < 0.05).

In conclusion, this clinical trial showed that PinnoThin™ consumption is associated with increased release of the gut satiety hormones CCK and GLP-1 and may influence feelings of satiety by reducing prospective food intake.

**Effects of PinnoThin™ FFA and TG on food intake, feeding behaviour and appetite**

The effect of PinnoThin™ TG and FFA was evaluated in a randomized double-blind placebo-controlled cross-over trial [30]. This trial included 42 overweight, but otherwise healthy women. The volunteers received a standard breakfast in the morning. Half an hour before lunch time, they were given 2, 4, 6 g of PinnoThin™ TG, 2 g of PinnoThin™ FFA or
2 g placebo (olive oil) in the form of capsules with water. At lunch time, the volunteers received an ad libitum buffet meal (containing high- and low-fat foods, both sweet and savoury). The amount of food consumed was noted by the difference in weight of the food plate pre- and post-lunch to the nearest 0.1 g. In the evening, they received an ad libitum supper, consisting of a pasta meal with ice cream dessert, which was subsequently weighed. During the entire study day, subjective measures of appetite and feeding behaviour were quantified using VAS scores. Each volunteer completed all three interventions (PinnoThin™ FFA, PinnoThin™ TG and placebo) with 1 week wash-out in-between.

The study results found a statistically significant lower food intake (9%) during lunch after PinnoThin™ FFA intake compared to the placebo (p < 0.05). There was also a trend for reduction in energy intake with PinnoThin™ FFA, 7% (p < 0.1). There was no difference in food and energy intake between the groups for the supper, indicating that the volunteers in the PinnoThin™ FFA group did not overcompensate for the reduced lunch food and caloric intake at supper. These differences found for PinnoThin™ FFA were not observed for PinnoThin™ TG. No effects were seen on subjective measures of appetite and feeding behaviour after PinnoThin™ FFA or TG intake.

Previous studies have shown that PinnoThin™ TG is digested to FFA, like similar dietary TG [31]. Furthermore, in the previous PinnoThin™ trial [28], the effects of CCK response took longer to develop for TG (60 minutes) compared to the FFA (30 minutes). Consequently, insufficient time had passed between the intake of the TG capsules and the ad libitum lunch for lipase action to convert sufficient TG to FFA. Adequate TG hydrolysis is necessary for induction of CCK release [8, 13, 14]. In addition, uptake of fat from capsules could have been further delayed since there was no simultaneous food ingestion [32]. Therefore, the differential results seen in the case of PinnoThin™ FFA and TG are anticipated. In conclusion, this study showed that PinnoThin™ FFA directly reduces food intake, without compensation during the subsequent meal. The reduction in daily food intake observed with PinnoThin™ FFA, which corresponded to about 50 kcal, is biologically relevant. This type of reduction on a daily basis could counteract a yearly increase in body weight of 1 to 2 kg, which in the end leads to overweight and obesity [1].

Conclusion

PinnoThin™ TG and FFA have been shown to increase satiety hormones, CCK and GLP-1 and affect subjective appetite sensation scores. Since CCK and GLP-1 are valid biomarkers of satiety and increased levels of these hormones have been associated with reduced food intake, PinnoThin™ TG and FFA may be effective in suppressing appetite and a useful tool for weight management.

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