

# A Prospective Randomized Trial for Reduction of Serum Low Density Lipoprotein (LDL) with Plant Stanol Ester Mixed in Coffee in a Hypercholesterolemic Thai Population.



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## Keywords:

plant stanol ester, coffee, LDL, hypercholesterolemia, Thai

**OBJECTIVE:** To determine whether replacing ordinary coffee with coffee mixed with the plant stanol ester decreases the serum low density lipoprotein (LDL) level in moderately hypercholesterolemic Thais.

**MATERIALS AND METHODS:** A randomized, double-blind, placebo-controlled trial of a common daily coffee was conducted on May 1, 2012 with continued treatment and follow-up through June 1, 2012. A total of 54 Thais whose serum LDL levels ranged from 130 to 239 mg/dL at randomization, were enrolled and randomized into two groups. The participants consumed a cup of plant stanol mixed coffee or a cup of placebo coffee once a day. The percentage of serum LDL reduction was measured at the end of the study.

**RESULTS:** Thirty-three subjects were randomized into each group. Forty-seven subjects completed the study, 30 in the group receiving coffee with added plant stanols as ester and 17 in the placebo coffee group. Statistical analysis was done by unpaired t-test using PASW (Predictive Analytics SoftWare) Statistics 18 (SPSS Inc., IL, USA). The results showed a significant difference in mean reduction of LDL levels ( $p < 0.001$ , 95% CI = 6.92 – 18.57). The means were 12.77% in the first group and 0.03% in the second group (SD = 9.33 and 9.88, respectively).

**CONCLUSION:** Among this population of hypercholesterolemic Thais, the daily replacement of an ordinary cup of coffee with a plant stanol mixed coffee reduced serum LDL levels by 12.77% demonstrating the efficacy of the cholesterol-lowering ingredient in the new food matrix.

Plant stanol is a compound of phytosterol (equivalent to cholesterol in mammals). It is found in natural foods particularly whole grains. Plant stanol ester (Beneco<sup>®</sup>) is an end result of esterifying stanol and fatty acid from vegetable oil. The obtained ester has high fat solubility sufficient to be incorporated into many processed foods. Laboratory evidence has shown that the plant stanol ester binds with diet cholesterol in the bowel lumen and limits cholesterol absorption. The plant stanol ester itself is also practically nonabsorbable. In 1995 an article published in the *New England Journal of Medicine*<sup>1</sup> showed that plant stanol ester significantly reduces serum low LDL and total cholesterol (TC). Since then more than 60 articles have been published with similar results. A study done in Greece<sup>2</sup> found that plant stanol ester spread reduced (by 1 month) TC 14%, LDL-Cholesterol (LDL-C) 16%, high-sensitivity C-reactive Protein (hsCRP) 17% and estimated cardiovascular disease (CVD) risk 30%. A study done in USA<sup>3</sup> showed that giving plant stanol containing spread to patients who had already been taking statin drugs

for 8 weeks, further reduced LDL-C by 14% compared with the placebo group. The effect of plant stanol is dose dependent. In one study<sup>4</sup> when patients were given 3 grams per day (gm/d) of plant stanol, the serum LDL-C decreased by 7.4%. When dose was increased to 6 gm/d, the serum LDL-C dropped a further 4.5%. When the dose was increased to 9 gm/d the serum LDL-C decreased by an additional 5.4% making a total reduction of 17.4% with a 9 gm/d dose. In one study,<sup>5</sup> increasing the dose to 8.8 gm/d reduced total serum and LDL-C concentrations by 12.0% and 17.1% from controls without changing liver enzymes, markers of hemolysis, serum vitamins A, D, and  $\gamma$ -tocopherol concentrations. The ratios of  $\alpha$ -tocopherol to cholesterol were also unchanged although the serum  $\beta$ -carotene concentrations dropped. This study implied that a high dose of plant stanol did not significantly interfere with the absorption of fat soluble vitamins. The addition of 1 gm of plant stanol to a 150 ml cup of low fat (0.7%) yogurt three times a day also reduced LDL-C by 13.7%.<sup>6</sup> One study done in metabolic syndrome patients found that plant stanol reduced not only LDL-C by 12.8% but also triglycerides by 27.5%.<sup>7</sup>

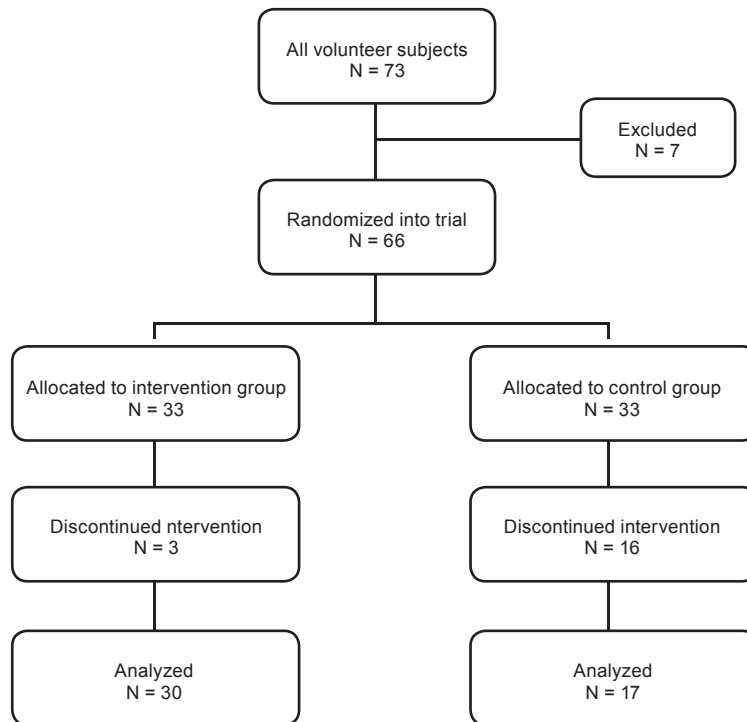
Plant stanol ester is used nowadays in the manufacture of several processed foods such as bread spreads, low fat dairy products, yogurt, soy-based or cereal-based products, pasta, and soft drinks etc. The idea of replacing coffee cream made of trans fat or carbohydrate is appealing for those who have hypercholesterolemia and still habitually

drink coffee with cream. So far there is no randomized controlled study to assess the LDL lowering effect of plant stanol ester in coffee. On the other hand, data concerning the efficacy of plant stanol ester among Thais is still very limited. This study will bridge both knowledge gaps.

**Materials and Methods**

The study was a randomized, double-blind and placebo-controlled trial of a parallel design with an intervention and a control group. The time frame of the trial was from May 1 to June 1, 2012. The plant stanol ester and a placebo coffee sample were prepared and analyzed. The plant stanol coffee sample contained a total plant stanol value of 11.22 gm/100 gm (expected value 11.76 gm/100 gm) or 1.91 gm/17 gm in each bag (expected value 2 gm/17 gm in each bag). The placebo coffee sample contained total plant stanol 0.02 gm/100 gm (expected value 0 gm/100gm). A 1/1 randomization was performed using a computer generated randomization list.

The intervention group consumed one cup a day of coffee enriched with 2 gm of plant stanol ester Benecol<sup>®</sup> per cup, for 30 days. The control group consumed the same coffee products with no added plant stanols. The products were received blind, and labelled with computer generated different codes. The codes were only revealed after the analysis was concluded. Table 1 showed the subjects' baseline characteristics. Routine laboratory measurements were made to ensure each subject was in good health



*Figure 1: Subject eligibility and adherence*

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**Table 1:** Basic characteristics and initial measurements of analyzed subjects

	Intervention Group	Control Group	Total
n	30	17	47
Age (years)	45 (9)	44 (8)	45 (9)
Males (n (%))	8 (17%)	5 (11%)	13 (28%)
Body weight (kg)	64.7 (7.2)	63.1 (9.1)	64.1 (8.2)
Height (cm)	161.4 (4.5)	162.1 (4.5)	161.6 (4.6)
BMI (kg/cm <sup>2</sup> )	24.8 (2.7)	24 (3.3)	24.5 (3)
Abdominal circumference (cm)	77.9 (9.7)	76.2 (9.6)	77.3 (9.9)
Pulse	77 (8)	74 (6)	76 (7)
Blood pressure	131/81 (14, 10)	126/78 (8,5)	129/79 (12, 9)
Triglycerides (mg/dL)	145 (91)	95 (35)	127 (79)
Total cholesterol (mg/dL)	250 (33)	237 (31)	245 (33)
HDL (mg/dL)	56.1 (13.4)	61.4 (10.7)	58.0 (12.9)
LDL (mg/dL)	178 (33)	165 (25)	173 (31)

Values are given as means (SD) BMI = Body Mass Index, LDL = Low Density Lipoprotein HDL = High Density Lipoprotein

before commencing the study. Subjects were asked to list any medications, vitamins or nutritional supplements they were currently taking via a structured questionnaire handed out at the start and end of the process. Blood samples after a 12 hour fast were taken, at the beginning and at the end of the intervention.

Subjects were then compared for changes in serum LDL-C levels. The primary endpoint was the relative reduction of directly measured LDL compared to each subjects' pre-intervention values. Statistical analysis was done with an unpaired t-test using PASW Statistics 18 (SPSS Inc., IL, USA).

### Results

A total of 73 Thais whose serum LDL levels ranged from 130 to 239 mg/dL were enrolled and assessed for eligibility. Seven of them did not meet the inclusion criteria and were excluded, leaving 66 of them for randomization. Thirty-three subjects were allocated to the intervention group and 33 were allocated to the control group. Forty-seven subjects completed the study: 30 in the first group and 17 in the second group. (Figure 1)

The results showed a significant difference in mean reduction of LDL levels ( $p < 0.001$ , 95% CI = 6.92 - 18.57). The means were 12.77% in the first group and 0.03% in the second group (SD = 9.33 and 9.88, respectively).

### Discussion

The drop-out rate in the control group was higher than the intervention group. The taste of the placebo coffee is probably one of the causes. The 12.77% mean LDL reduction difference implies that plant stanol ester in a form of coffee mix reduced LDL-C in a similar percentage to other forms such as yogurt, or bread spread. The findings are encouraging for patients with hypercholesterolemia, and habitual coffee with cream drinkers. Replacing ordinary coffee cream or trans-fat coffee cream with a plant stanol ester will help both the reduction of LDL and maintain a creamy coffee taste. Since there have been so few publications about plant stanol ester in Asian populations, this study is a contribution to show that plant stanol ester reduces LDL in Thai population in a similar way to Caucasian populations.

### Conclusion

Among this group of Thai population with hypercholesterolemia, the daily replacement of an ordinary cup of coffee with a plant stanol-mixed coffee reduced serum LDL levels by 12.77%.

### Conflict of interest statement

The authors claim no conflict of interest associated with the manuscript.

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### Statement of authorship

Dr. Sant Chaiyodsilp had the primary responsibility for the research design, supervised the execution of the

study, and wrote the manuscript except for the statistical analysis section. Miss. Yuwaret Khunaphakdipong prepared the experimental and control coffee samples. Miss. Rungsiya Srisawas and Mrs. Thanavee Pureekul carried out the studies and were responsible for the organization of data collection. Dr. Paul Chaiyodsilp performed the statistical analyses and outcome assessments. All authors read and approved the final manuscript.

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