Table 2: Details of human studies on effect of once-a-day intake of plant sterols/stanols on levels of serum lipoprotein cholesterols and triglycerides

Study	Design, Carrier, Treatment, Eating Occasion, and Feeding Duration	Subjects and Background Diet	Serum Lipid, Lipoprotein and Antioxidant Results	Quality of Science*
Plat J et al, EJCN 2000; 54:671-7	Design: randomized, double-blind, placebo-controlled, cross-over Carriers: margarine and shortening 4.2 g plant stanol (as esters)/100 g margarine; 12.5 g plant stanol (as esters)/100g margarine; 12.5 plant stanol (as esters)/100g shortening Treatments and Eating Occasion: 1: 0 g (placebo control); 2: 2.5g stanol at lunch; 3: 0.42 g at breakfast, 0.84 g at lunch and 1.25 g at dinner (total =2.51g/day). Feeding Duration: 4 weeks/period without washout	11 men, 28 women aged 31±14 years; BMI = 22.7±2.6; TC and TG = 4.74 and 0.99 for women, and 4.94 and 0.97 for men. Background diet: habitual diet : Fat: 38.2-38.9 en% Sat Fat:12.8 -13.5 en% Cholesterol: 231mg/day	2.5 g once/day: TC ↓ 6.3% LDLC ↓ 9.4% TC/HDLC ↓ 5.6%% 2.51g divided unevenly into 3 meals, in proportion to cholesterol intake intake: TC ↓ 6.6% LDLC ↓10.4% TC/HDLC ↓ 5.6% HDLC and TG unchanged LDLC standardized retinol and fat soluble antioxidant levels unchanged	High: Addressed all scientific quality issues
Volpe R et al, Br J Nutr 2001;86:233 -9	Design: Part 1: randomized, double-blind, placebo-controlled, cross-over Part 2: open labelled Carrier: 1g plant sterol (as esters not specified) in 100 ml low-fat yogurt drink Treatments: Part 1: 1: 0g (placebo control) ; 2: 1 serving/day Part 2: 2 servings/day Feeding Duration: Part 1: a 8 week run-in followed in sequence by a 4-week treatment period, a 2-week washout period and another 4-week treatment period. Part 2: 8-week open labeled period Eating occasion was unspecified. Whether the 2 servings of yogurt drink were consumed in one or two sitting was not reported.	Part 1: 21 men, 9 women aged 33-69 years Part 2: 7 men, 4 women aged 34 – 69 years TC: 6.2 -7.8 mmol/l, and unresponsive to low fat diet Background diet: low fat (≤ 30 en%), low saturated fat (≤10 en%), cholesterol < 300 mg/day	Part 1: Compared to baseline: TC ↓ 6.7% LDLC ↓ 11.1% LDLC/HDLC ↓ 15.1% Compared with placebo yogurt drink*: TC ↓4.4% LDLC ↓ 6.2% LDLC/HDLC ↓ 6.4% No change in HDLC and TG Part 2: Compared with baseline*: TC ↓11.2% LDLC ↓ 15.6% LDLC/HDLC ↓ 13.3% HDLC and TG unchanged in both Parts No changes in vitamins A and E, vitamin D decreased *estimated by reviewer	Part 1: Medium : Incorrect statistical model for data analysis Part 2: Low: no placebo control, eating occasion(s) not specified

Study	Design, Carrier, Treatment, Eating Occasion, and Feeding Duration	Subjects and Background Diet	Serum Lipid, Lipoprotein and Antioxidant Results	Quality of Science*
Matvienko OA et al, AJCN 2002;76:57-64	Design: triple blind, placebo-controlled, parallel arms without run-in period Carriers: 7 ground beef based food items rotating through the week (hamburger, sloppy joy, spaghetti, tacos, cheeseburger, chili, ground beef and rice casserole) Treatments: 1; 0g (placebo control); 2: 2.7 g plant sterols (2/3 as esters, 1/3 in free form) Feeding Duration: 2 4-week parallel arms Eating Occasion: lunch, supervised on weekdays unsupervised on weekends	34 men with at least 3 CVD risk factors Average group ages: 22.2-23.6 years Average group BMI: 25.7 – 27.0 Average group TC: 5.8 – 5.9 mmol/l Average group LDLC: 3.95 – 4.10 mmol/l Background diet: habitual diet; Fat:35.6en% Sat Fat: not reported Cholestreol: 328 mg/day	Compared with individual placebo-control baseline: TC LDLC TC/HDLC control ↓ 0.9% (ns) ↓ 1.3% (ns) ↓ 0%(ns) 2.7g/d ↓ 9.3% ↓ 14.6 % ↓ 9.1 % this is from baseline comparison! Compared with placebo* TC LDLC TC/HDLC ↓ 8,4% ↓ 13.4% ↓ 9.1% *estimated by reviewer HDLC and TG unchanged No change in LDL and HDL particle size	High: Addressed all scientific quality issues associated with a parallel design despite no controlled run-in period
Salo P & Wester I AJC 2005:96(S): 51D-4D Note: this is a review article and not the original publication of the studies	Design: double blind, placebo-controlled, parallel arms with run-in period Carriers: meat products (meat balls, frankfurters), mayonnaise, wheat pasta, low-fat yogurt drink. Treatments: 1: 0 g (placebo-control); 2: 2 g plant stanols (as esters) Feeding Duration: Low Fat Meal and Pasta studies: 1-week run-in followed by 2 2-week parallel arms Yogurt Drink study: 2-week run-in followed by 2 6-week parallel arms Eating Occasion: lunch or main meal	60 subjects in the meat-based meal study, 40 subjects in pasta and yogurt studies. Age: 20-65 TC:174 – 270 mg/dl TG <265 mg/dl Background diet: habitual diet	Compared with placebo-control group: TC LDLC Low Fat Meals ↓ 6.8% ↓ 10.1% Pasta ↓ 8.0% ↓ 10.9% Yogurt Drink ↓ 10.4% ↓ 12.6 % Note: Based on the original German publication (Emmi Studie Benecol, 2004) the 12.6% is the baseline-end comparison, Placebo-controlled effect on LDL lowering is 11.3%	Low: Insufficient description of subjects, food carriers, run-in period No disclosure of actual data and no description of derivation of reported data

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Emmi Studie Benecol, Ernährungs-Umschau 2004; 51 (12): 521	Design: randomized, placebo-controlled, double-blind parallel arms without a run-in Carriers: Yogurt: 150 g tubs with 2 g plant stanols in the form of stanol esters Yogurt drink: 65 ml with 2 plant stanols in the form of stanol esters Treatments: 1. Once-a-day Placebo 0 g stanols 2. Once-a-day 2 g stanols in the form of stanol esters Feeding: 6 weeks duration parallel arms Eating occasion: with a meal (meal not further specified)	40 subjects Age range 40-65 years Mildly hypercholesterolemic with TC in the range of 220-330 mg/dl No further specifications made Background diet: habitual diet habits No data on nutrient intakes provided although subjects were apparently asked to write food diaries	Yogurt study As compared to baseline: Placebo group TC: ↓ 0.7% (ns); LDLC: ↓ 2.8% (ns) Stanol group TC: ↓ 6.0%; LDLC: ↓ 10.5% Compared with placebo yogurt drink*: TC: ↓5.3%; LDLC: ↓ 7.7% ($p<0.01$) * estimated by reviewer Yogurt drink study As compared to baseline: Placebo group TC: not reported; LDLC: ↓ 1.3% (ns) Stanol group TC: ↓ 10.4%; LDLC: ↓12.6% Compared with placebo yogurt drink*: LDLC: ↓ 11.3% *estimated by reviewer	Medium-Low:
AbuMweis SS et al, Abstract presented at EB 2005 Manuscript to be submitted for publication J Nutr 2006; 136: 1012-1016 (in press)	Design: randomized, placebo controlled, single-blind, crossover Carriers: margarines Treatments: 1: 0 (placebo control) 2:free sterols - at 22 mg/kg body weight (BW); 3:sterols (as esters of sunflower oil esters) – at 22 mg/kg BW; 4:sterols (as fish oil esters) at 35.2 mg/kg BW; 5: 2 + 4 at 13.2 mg/kg BW Treatments 2-5 received ≈ 1.7g/day (range 1.0-1.8 g/day) Feeding Duration: 4 weeks per treatment with a 2-4 week washout period in between Eating Occasion: breakfast (supervised)	15 men: age: 60 ±11 years, BMI:29±4, TC & LDLC: 5.8±0.6 & 3.9±0.6 15 women age: 59 ±10 years, BMI:26±5, TC & LDLC: 5.9±1.0 & 3.7±1.0 Background diet: all foods and beverages provided	No significant treatment effect found for TC, LDLC, TG , ApoB, Apo A1, and Lp(a) HLDC were comparable among all sterol forms and higher than control TC/HDLC was highest in control, lowest in free sterols Results may suggest a time-of-day variation coincident with a possible circadian rhythm of cholesterol absorption	High: Study design, and data analysis appear to be appropriate Subject compliance to study protocol not reported but appears to be acceptable based on BW data Sterol intake dose was based per kg BW and not as typically done a fixed dose was applied

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Doornbos AME et al EJCN 2006; 60: 325-333. Abstract presented at EB 2005	Design: randomized, placebo controlled, double blind, parallel with run-in control period Carriers: single shot yoghurt drink (100 ml) drink A: 3.2 g plant sterols (as esters), 0.1% dairy fat, 2.2% total fat drink B: 2.8 3g plant sterols (as esters), 1.5% dairy fat, 3.3% total fat Treatments: 1: 0g (placebo control) with a meal 2: drink A with meal 3: drink A without a meal 4: drink B with meal 5: drink B without meal Treatments 2-5 received about 3 g /day Feeding Duration: 4 weeks run-in for all and 4 weeks intervention Eating Occasion: without meal=>0.5 hour before breakfast; with meal = with or immediately after lunch	81 men age: 59.4±2.5 years BMI: 25.5±0.6 TC & LDLC: 5.96± 0.2 & 4.03±0.19 103 women age: 55.5±2.7 years BMI: 25.0±0.6 TC & LDLC: 6.25± 0.18& 4.01±0. 20 Background diet: habitual diets	Compared with run-in period: TC LDLC placebo control ↑2.6%(ns) ↑3.5%ns) Compared with placebo-control drinkA+ meal ↓ 7% ↓ 9.5% drinkB + meal ↓ 6.5% ↓ 9.3% drinkA - meal ↓ 4.1% ↓ 5.1% drinkB - meal ↓ 4.7% ↓ 6.9% HDLC and TG unchanged	High: Study design, and data analysis appear to be appropriate Subject compliance to treatment assessed
Pineda J.A. et al Rev Clin Esp, 2005; 205 (2): 63-66	Design: double bind, randomized, placebo-controlled, parallel arms without run-in period Carrier: 2 g plant stanols (as esters) in 1 low-fat yogurt drink (70 g)	32 subjects 19 men and 13 women Mean age 42 years (24-57 years) Mean BMI: 26 (21-37)	Compared with baseline TC LDLC Placebo group ↓ 2.4% (ns) ↓ 1.5% (ns) Test group ↓ 6.7% ↓ 10.3%	Medium-High:
	Treatmernts: 1: 0 g Placebo yogurt drink 2: 2 g plant sterols (as esters) enriched yogurt drink Feeding Duration: 2 times 3-weeks parallel arms Eating occasion: after main meal	Background diet: habitual diet No nutrient intakes reported	Compared with placebo-control group*: TC LDLC ↓ 4.3% ↓ 8.8% p<0.01 p<0.01 *estimated by reviewer	

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Hyun Y.J.et al, Nutrition Research 2005; 25: 743-753	Design: double bind, randomized, placebo-controlled, parallel arms with 2 week run-in (maintenance) period Carrier: 2 g plant stanols (as esters) in 1 cup (150 ml) low-fat strawberry yogurt Treatments: 1: 0 g Placebo yogurt 2: 2 g plant sterols (as esters) Feeding Duration: 2-week run-in (maintenance period to establish usual dietary pattern) followed by 2 4-weeks parallel arms Eating occasion: at breakfast	51 subjects completed study 26 men and 25 women Mean age: 28.7 years (21-39 years) Mean BMI: 22.6 (17-30.5) Mean TC: 192±2.6 mg/dl Mean TG: 103±7.2 mg/dl Background diet: habitual diet, placebo or test yogurt was substituted for another food with same caloric content. Nutrient intakes reported	Compared with baseline TC LDLC Placebo group ↓ 1.3% (ns) ↓ 1.9% (ns) Test group ↓ 5.8% ↓ 9.8% Compared with placebo-control group*: TC LDLC ↓ 4.5% ↓ 7.8% *estimated by reviewer Plasma levels of oxidized LDL were significantly lower in the test group. Serum concentrations of beta-carotene and retinol were not changed. Lipid-corrected alpha-tocopherol concentrations were significantly increased in the test group.	High: Addressed relevant scientific aspects addressed