Clinical Studies on Flax (*Linum usitatissimum* L.)

Cardiovascular

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Jenkins *et al*., 1999	Effects on serum lipids, indicators of oxidation stress, and *ex vivo* sex hormone activities	R, SB, PC CO n=29 hyperlipidemic subjects (mean age 57 years)	3 periods: 1. 3 weeks treatment 2. 2 weeks wash-out 3. 3 weeks CO treatment	50 g/day	Partially defatted flaxseed meal baked in muffins	Significant reduction in total cholesterol (p=0.001), LDL serum cholesterol (p=0.001), and apolipoprotein (p=0.005) level with partially defatted flaxseed. No significant change in HDL cholesterol, serum protein carbonyl content, or *ex vivo* androgen or progestin activity with either treatment.
Arjmandi *et al*., 1998a	Effect on lipid profile	R, DB, CO n=38 severely hypercholesterolemic, post-menopausal women (mean age 56.3 years)	6 weeks treatment with flaxseed or sunflower seed; 2 weeks wash-out; 6 weeks CO to other seed	38 g/day	Flaxseed baked in bread and muffins or sunflower seed	Flaxseed significantly lowered LDL cholesterol (p<0.02) vs. sunflower seed. Serum Lp(a) decreased significantly with flaxseed (p<0.05). No effect on HDL cholesterol or triglycerides levels.
Nestel *et al*., 1997	Effect on arterial compliance	CC n=15 obese persons with markers of insulin resistance, mean BMI, 30.4 kg/m^2 (mean age 54 years)	16 weeks (4 periods of 4 weeks each) 1. Saturated/ high fat 2. Alpha-linolenic acid (ALA) /low fat 3. Oleic acid/low fat 4. High fat	2732 ± 533 kcal/3 days 20g ALA daily	Baked biscuits and muffins with purified deodorized flaxseed oil or Sunola oil (oleic acid-rich oil)	Significant increase in arterial compliance with flaxseed (p<0.0001) and with oleic acid (p<0.05). Significant decrease in mean arterial pressure with flaxseed (p<0.05) and with oleic acid (p<0.05). Significant decrease in HDL cholesterol with flaxseed (p<0.01) vs. oleic acid and control. Significant increase in insulin response with flaxseed vs. control (p=0.016).
Allman *et al*., 1995	Effect on platelet composition and function	R, P n=11 healthy non-smokers, mean BMI, < 30 kg/m^2 (mean age 22 years)	23 days	40 g/day flaxseed oil or sunflower oil	Flaxseed oil or sunflower oil	Improved platelet composition by 2x increase in platelet EPA (p<0.05) levels with ALA. Reduced platelet aggregation response (p<0.05) with alpha-linolenic acid.
De Lorgeril *et al*., 1994	Secondary prevention of myocardial infarction	R, MC, SB, P n=605 patients who had a myocardial infarction (MI) (n=302 treatment group; n=303 control group)	5 years	19 g/day	Flax-based spread substitution plus Mediterranean diet (rich in ALA)	Treatment group had 76% lower incidence of deaths due to MI and 70% lower mortality rate than control. 3x increase in omega-3 intake combined with decrease in saturated fat, cholesterol, and omega-6 intake reduces risk of second MI (adjusted risk rate=0.27; p=0.001).
Bierenbaum et al., 1993	Atherogenic risk	O n=15 subjects with hyperlipidemia on long-term vitamin E (800 IU/day) (mean age 52.2 years)	3 months	15 g/day plus 3 slices of 10% flaxseed bread	Ground flaxseed (flour) in diet	Significantly decreased both total cholesterol (p<0.01) and LDL cholesterol (p<0.01). Lack of effect on HDL cholesterol. ATP measurements suggest flax inhibits platelet aggregation.

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Breast Cancer

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Haggans *et al*., 1999	Estrogen excretion	R, CO n=28 healthy post-menopausal women, non-smokers, mean BMI, 23.9 kg/m^2 (mean age 68.3 years)	Three 7-week periods: 2 periods with flaxseed; 1 period as control	5–10 g/day (as single daily dose)	Raw, ground flaxseed vs. usual diet	Significant increase in urinary estrogen metabolites, 2-hydroxyestrogen ($p<0.05$) and 16-alpha-hydroxyestrone ($p<0.0005$). Suggests flaxseed may protect against breast cancer.
Ingram *et al*., 1997	Risk breast cancer	CC n=144 subjects with newly diagnosed breast cancer vs. matched women without breast cancer living in the same ZIP code area (ages 30–84 years)	23 months	Not applicable	Dietary intake of phyto-estrogens	Substantial reduction in breast cancer risk among women with high intake of phytoestrogens, as assessed by significant increase in excretion of equol ($p=0.009$) and enterolactone ($p=0.013$).
Phipps *et al*., 1993	Effect on menstrual cycle and serum hormone concentration	R, CO n=18 healthy women with regular menstrual cycle length (25-30 days) (ages 20–34 years)	7 consecutive menstrual cycles	10 g/day 2x 5 g or 3x 3.33 g	Raw flaxseed powder	Flaxseed associated with longer luteal phase ($p=0.002$), increased longer luteal phase estradiol ratios, and few anovulatory cycles. Overall, decreased tendency for ovarian dysfunction, which possibly decreases risk for breast cancer.
Bougnoux *et al*., 1994	Assessment of ALA content in adipose breast tissue and metastasis	E, P n=121 patients with initially localized breast cancer	Followed for 31 months	Not applicable	Dietary intake of fatty acids	Predictive factors for occurrence of metastasis are related to large tumor size and low levels of ALA in adipose breast tissue of breast cancer patients. Suggests low levels of ALA have a role in the metastatic process *in vivo*.
Willett *et al*., 1992	Breast cancer risk	E, P n=89,494 registered nurses (ages 34–59 years)	8 years	Not applicable	Dietary intake of alpha-linolenic acid	No evidence of association between total fat intake and dietary fiber intake in middle-aged women.

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Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Demark-Wahnefried, 2001	Prostate cancer	PS n=25 men with prostate cancer (mean age 64 years)	Average 34 days (21–77 days)	30 g flaxseed meal (3 rounded Tblsp.)	Alena™	This study with and without a low-fat diet supplemented with flax showed significant decrease in total testosterone ($p<0.001$), lower cell proliferation rates, and higher apoptosis rates associated with short-term dietary intervention and flaxseed. PSA levels decreased among men who had biopsy Gleason sums of 6 or less and continued to rise among men with higher Gleason sums (despite evidence of lower rates of proliferation and higher rates of apoptosis).
Arjmandi *et al.*, 1998b	Osteoporosis	R, DB, CO n=38 healthy, non-smoking, post-menopausal women not receiving hormone replacement therapy (mean age 56.3 years)	6 weeks treatment followed by 2-week wash-out followed by 6 weeks of treatment	38 g/day	Flaxseed or sunflower seed (control) baked in muffins and bread	Flaxseed treatment significantly lowered tartrate resistant acid phosphatase activity in serum (a marker of bone resorption) ($p<0.05$). No effect on insulin-like growth factor and insulin-like growth factor protein-3 concentration (serum bone-specific). No effect on total alkaline phosphatase activity (marker of bone formation), and 17b estradiol levels. Tendency to decrease urinary excretions of both hydrooxyproline and calcium. Flaxseed may not enhance bone formation, but may slow down the rate of bone resorption.
Caughey *et al.*, 1996	Effect on cytokine production	Cm, PG n=15 healthy subjects (ages 24–44 years)	2 months	13.7 g/day ALA or 9 g/day fish oil (1.62 g EPA/day and 1.08 g DHA/day)	Flaxseed oil and flaxseed oil plus butter spread as dietary substitutions vs. sunflower oil	Vegetable oils rich in n-3 fatty acids inhibit TNF-alpha and IL-1-betasynthesis. This finding is significant, as these factors are implicated in inflammatory rheumatoid arthritis ($p<0.05$) and atherosclerosis ($p<0.05$).
McManus *et al.*, 1996	Non-insulin dependent diabetes	R, DB, CO n=11 (mean age 61.8 years)	3 months	35 mg/kg/day	Flaxseed oil capsules or olive oil (control)	Neither oil significantly affected glycemic control or insulin secretion.
Clark *et al.*, 1995	Lupus nephritis	O n=9 subjects with documented systemic lupus erythematosus, history of positive ANA, and with proteinuria >1 g/24 hours	17 weeks	Weeks 1–4: 15 g/day; Weeks 5–8: 15 g 2xday; Weeks 9–12: 15 g 3xday; Followed by 5-week wash-out period.	Crude flaxseed	Flaxseed was well-tolerated at 15 and 30 g/day, but not well-tolerated at 45 g/day. Total and LDL cholesterol levels and whole blood viscosity decreased significantly with 30 g/day. Reduction of serum creatine with 30 g and 45 g/day. Increase in creatinine clearance with 15 g and 30 g/day.
Nordstrom *et al.*, 1995	Rheumatoid arthritis	R, DB, PC n=22 (mean age treatment group, 51 years; mean age control group, 53 years)	3 months	30 g/day	Flaxseed oil or safflower oil (control)	No statistical alterations or effects were found. Concluded supplementation may have been for too short of a term, or low intake of zinc impaired EFA conversion.
Cunnane *et al.*, 1995	Nutritional status	R, CO n=10 healthy non-smokers (mean age 25 years)	1 month	50 g/day	Muffins with milled flaxseed or muffins without flaxseed	Significant reduction in total cholesterol ($p<0.05$) and LDL cholesterol ($p<0.05$) with flaxseed. No change in HDL cholesterol or triglycerides. Increased number of bowel movements ($p<0.05$) with flaxseed.

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