Abstracts Flaxseed

J Clin Lipidol. 2018 Jan - Feb;12(1):70-77. doi: 10.1016/j.jacl.2017.11.004. Epub 2017 Nov 20.

Comparison of the effects of flaxseed oil and sunflower seed oil consumption on serum glucose, lipid profile, blood pressure, and lipid peroxidation in patients with metabolic syndrome.

Akrami A[1], Nikaein F[2], Babajafari S[3], Faghih S[1], Yarmohammadi H[2].

BACKGROUND:

Metabolic syndrome (MetSyn) increases the risk of type II diabetes and morbidity and mortality due to cardiovascular diseases. Flaxseed oil (FO), as a functional food, is one of the major vegetal sources of essential omega-3 fatty acids.

OBJECTIVE:

This study aimed to compare the effects of consumption of FO and sunflower seed oil (SO) on lipid peroxidation and other symptoms of MetSyn.

METHODS:

This randomized controlled interventional trial was conducted on 60 volunteers aged 30 to 60 years who were diagnosed with MetSyn in Shiraz, Iran. The participants who fulfilled the inclusion criteria were randomly assigned to SO (n = 30, receiving 25 mL/d SO) and FO (n = 30, receiving 25 ml/d FO) groups using block randomization. The diets were identical for all the participants. Blood pressure (BP), serum lipid, fasting blood sugar, and malondialdehyde were measured at baseline and at the end of week 7.

RESULT:

The results showed no significant difference between the 2 groups regarding blood lipid levels and fasting blood sugar at the end of the study. However, significant reductions in total cholesterol, low-density lipoprotein cholesterol (5.6% in FO and 10.8% in SO), and triglyceride levels were seen within each group after treatment with FO and SO (P < .05). Nonetheless, between-group changes were significant (<0.05) for systolic BP (mean [±standard deviation {SD}] changes were -14.0 ± 22.41 in the FO group [P = .004] and 0.92 ± 8.70 in the SO group [P = .594]) and diastolic BP (mean [±SD] changes were -4.26 ± 7.44 in the FO group [P = .007] and 1.30 ± 6.91 in the SO group [P = .344]), but marginally significant (P = .053) for malondialdehyde level (mean [±SD] changes were -1.29 ± 1.48 in the FO group [P < .001] and -0.52 ± 1.34 in the SO group [P = .52]). A significant decrease in weight was also found in both groups. However, waist circumference decreased significantly only in the FO group at the end of the study (P < .05).

CONCLUSION:

Our results indicated that dietary FO could be effective in amelioration of some symptoms of MetSyn and decrease BP and lipid peroxidation.

KEYWORDS: Blood pressure; Flaxseed oil; Lipid peroxidation; Metabolic syndrome; Sunflower seed oil

Nutr Rev. 2018 Feb 1;76(2):125-139. doi: 10.1093/nutrit/nux052.

Flaxseed supplementation on glucose control and insulin sensitivity: a systematic review and meta-analysis of 25 randomized, placebo-controlled trials.

Mohammadi-Sartang M[1], Sohrabi Z[2], Barati-Boldaji R[2], Raeisi-Dehkordi H[1], Mazloom Z[1].

CONTEXT:

The results of human clinical trials investigating the effects of flaxseed on glucose control and insulin sensitivity are inconsistent.

OBJECTIVE:

The present study aimed to systematically review and analyze randomized controlled trials assessing the effects of flaxseedconsumption on glycemic control.

DATA SOURCES:

PubMed, Medline via Ovid, SCOPUS, EMBASE, and ISI Web of Sciences databases were searched up to November 2016.

STUDY SELECTION:

Clinical trials in which flaxseed or its products were administered as an intervention were included.

DATA EXTRACTION:

The outcomes were fasting blood glucose, insulin concentration, insulin resistance (HOMA-IR), insulin sensitivity (QUIKI), and hemoglobin A1c (HbA1c).

RESULTS:

A total of 25 randomized clinical trials (30 treatment arms) were included. Meta-analysis suggested a significant association between flaxseed supplementation and a reduction in blood glucose (weighted mean difference [WMD], -2.94 mg/dL; 95%CI, -5.31 to - 0.56; P = 0.015), insulin levels (WMD, -7.32 pmol/L; 95%CI, -11.66 to -2.97; P = 0.001), and HOMA-IR index (WMD, -0.49; 95%CI,: -0.78 to - 0.20; P = 0.001) and an increase in QUIKI index (WMD, 0.019; 95%CI, 0.008-0.031; P = 0.001). No significant effect on HbA1c (WMD, -0.045%; 95%CI, -0.16 to - 0.07; P = 0.468) was found. In subgroup analysis, a significant reduction in blood glucose, insulin, and HOMA-IR and a significant increase in QUIKI were found only in studies using whole flaxseed but not flaxseed oil and lignan extract. Furthermore, a significant reduction was observed in insulin levels and insulin sensitivity indexes only in the subset of trials lasting ≥12 weeks.

CONCLUSIONS:

Whole flaxseed, but not flaxseed oil and lignan extract, has significant effects on improving glycemic control. Further studies are needed to determine the benefits of flaxseed on glycemic parameters.

KEYWORDS: flaxseed; glucose; insulin; insulin resistance; lignan

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Modulation of oxidative stress response by flaxseed oil: Role of lipid peroxidation and underlying mechanisms.

Yadav RK[1], Singh M[1], Roy S[1], Ansari MN[2], Saeedan AS[2], Kaithwas G[3].

Polyunsaturated fatty acids (PUFA's) are majorly classified as ω-3 and ω-6 fatty acids. The eicosapentaenoic acid (EPA, ω-3:20-5), docosahexaenoic acid (DHA, ω-3:22-6) and alpha-linolenic acid (ALA, ω-3:18-3) are known ω-3 fatty acids, extracted from animal (e.g fish oil) and plant sources (e.g flaxseed oil). Furthermore, linoleic acid (LA, ω-6:18-2) is recognized as ω-6 fatty acid and the most prominent biological fatty acid with a pro-inflammatory response. Flaxseed oil has variety of biological roles, due to a significant amount of ω-3/ω-6 fatty acids. Numerous studies have reported that ALA (ω-3:18-3) and LA (ω-6:18-2) has diverse pharmacological activities. The ALA (ω-3:18-3) and LA (ω-6:18-2) are recognised to be the pharmacological antagonist. For example, ALA (ω-3:18-3) is recognised as anti-inflammatory, whereas LA (ω-6:18-2) is considered to be pro-inflammatory. PUFA's get oxidized in three ways; firstly, free radical-mediated pathway, secondly non-free radical non-enzymatic metabolism, and lastly enzymatic degradation. The present report is an attempt to summarize various modes of PUFA's metabolism and elaborate biological effects of the associated metabolites concerning flaxseed oil.

KEYWORDS: Polyunsaturated fatty acids; enzymatic degradation; inflammation; lipid peroxidation

J Matern Fetal Neonatal Med. 2017 Dec 12:1-7. doi: 10.1080/14767058.2017.1407309. [Epub ahead of print]

The influence of a diet based on flaxseed, an omega-3 source, during different developmental periods, on the blood pressure of rats submitted to stress.

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OBJECTIVE:

This study aimed to investigate a flaxseed diet during different developmental periods, and its effect on the blood pressure of rats submitted to stress.

METHODS:

Fifty-six male rats (F_1), born from 14 rats (F_0), were divided into seven groups (n = 8): flaxseed group (FG); flaxseed group gestation and lactation (FG-GL); flaxseed group weaning (FG-W); flaxseed group weaning and stress (FG-WS); flaxseed group stress (FG-S); flaxseed group gestation lactation and weaning (FG-GLW), and control Group (CG). Stress protocol was undertaken for 1 month. Blood pressure was analysed before and after the stress protocol. The left adrenal glands and serum corticosterone levels were analysed.

RESULTS:

Systolic blood pressure before stress was lower in all groups with flaxseed diet compared with the CG ($p = .00001$). After stress, CG showed higher blood pressure compared with FG, FG-GL, and FG-GLW ($p = .004$). The levels of corticosterone were lower in the FG between all groups ($p < .000001$) and the CG showed higher compared with FG-W, FG-WS, FG-GL, and FG-GLW ($p < .0001$). The adrenal gland did not show differences.

CONCLUSIONS:

Results suggest a possible factor from a flaxseed diet against the effects of stress on a blood pressure in all periods of life but especially in the gestation and lactation periods.

KEYWORDS: Blood pressure; flaxseed; omega-3; rat; stress

J Nutr Biochem. 2017 Oct 18;53:9-19. doi: 10.1016/j.jnutbio.2017.09.015. [Epub ahead of print]

Flaxseed oil rich in omega-3 protects aorta against inflammation and endoplasmic reticulum stress partially mediated by GPR120 receptor in obese, diabetic and dyslipidemic mice models.

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The "first hit" to atherogenesis is driven by toll-like receptor 4, endoplasmic reticulum stress and ultimately metabolic dysfunction. In this study, we hypothesized that a flaxseed oil-enriched diet (FS) abolishes these inflammatory signaling pathway and restore metabolic homeostasis by activating the fatty acid receptor GPR120 in aorta of obese mice. Glucose homeostasis was assessed by GTT and ITT; lipidomics was performed using a Hybrid Ion Trap-Orbitrap Mass Spectrometer; serum lipids were measured using colorimetric assays; GPR120 and infiltrating macrophages were analyzed by immunofluorescence; protein immunoprecipitation and gene expression were evaluated by Western blot and RT-PCR, respectively. There were no differences in body weight and food intake between the groups from both strains (Swiss and LDLr-KO mice). GTT and cholesterol levels were improved by FS in both mice models. Lipidomics showed an increase in ω3 (C18:3) content, meanwhile stearic acid (C18:0) was not detected in endothelial tissue in response to FS. Moreover, FS markedly decreased pro-inflammatory (IL-1β, TNF-α, pIκBα, pIKKβ) and unfolded protein response markers (ATF6 and GRP78) in aorta. In Swiss mice, GPR120 was partially involved in the ω3-mediated anti-inflammatory actions, disrupting TLR4 pathway, but not in LDLr-KO mice. Partial replacement of dietary saturated by unsaturated ω3 fatty acids contributes to inhibition of cardiovascular risk markers, pro-inflammatory cytokines and ER stress sensors and effectors in the aorta. However, downregulation of inflammation is not mediated by arterial GPR120 activation.

KEYWORDS: Atherogenesis; ER stress; GPR120; Inflammation; Nutrigenomics; Obesity; n-3 fatty acids

Obes Rev. 2017 Sep;18(9):1096-1107. doi: 10.1111/obr.12550. Epub 2017 Jun 21.

The effect of flaxseed supplementation on body weight and body composition: a systematic review and meta-analysis of 45 randomized placebo-controlled trials.

Mohammadi-Sartang M[1,2], Mazloom Z[1,2], Raeisi-Dehkordi H[1,2], Barati-Boldaji R[2,3], Bellissimo N[4], Totosy de Zepetnek JO[4].

Flaxseed consumption may be inversely associated with obesity; however, findings of available randomized controlled trials (RCTs) are conflicting. The present study aimed to systematically review and analyse RCTs assessing the effects of flaxseed consumption on body weight and body composition. PubMed, Medline via Ovid, SCOPUS, EMBASE and ISI Web of Sciences databases were searched up to November 2016. Mean changes in body composition indices including body weight, body mass index (BMI) and waist circumference were extracted. Effect sizes were expressed as weighted mean difference (WMD) and 95% confidence intervals (CI). Heterogeneity between studies was assessed with the I2 test. Publication bias and subgroup analyses were also performed. The quality of articles was assessed via the Jadad scale. A total of 45 RCTs were included. Meta-analyses suggested a significant reduction in body weight (WMD: -0.99 kg, 95% CI: -1.67, -0.31, p = 0.004), BMI (WMD: -0.30 kg m-2 , 95% CI: -0.53, -0.08, p = 0.008) and waist circumference (WMD: -0.80 cm, 95% CI: -1.40, -0.20, p = 0.008) following flaxseed supplementation. Subgroup analyses showed that using whole flaxseed in doses ≥30 g d-1 , longer-term interventions (≥12 weeks) and studies including participants with higher BMI (≥ 27 kg m-2) had positive effects on body composition. Whole flaxseed is a good choice for weight management particularly for weight reduction in overweight and obese participants.

KEYWORDS: Body mass index; body weight; flax; obesity

Nutr Rev. 2017 Dec 8. doi: 10.1093/nutrit/nux052. [Epub ahead of print]

Flaxseed supplementation on glucose control and insulin sensitivity: a systematic review and meta-analysis of 25 randomized, placebo-controlled trials.

Mohammadi-Sartang M[1], Sohrabi Z[1], Barati-Boldaji R[1], Raeisi-Dehkordi H[1], Mazloom Z[1].

CONTEXT: The results of human clinical trials investigating the effects of flaxseed on glucose control and insulin sensitivity are inconsistent.

OBJECTIVE: The present study aimed to systematically review and analyze randomized controlled trials assessing the effects of flaxseedconsumption on glycemic control.

DATA SOURCES: PubMed, Medline via Ovid, SCOPUS, EMBASE, and ISI Web of Sciences databases were searched up to November 2016.

STUDY SELECTION: Clinical trials in which flaxseed or its products were administered as an intervention were included.

DATA EXTRACTION: The outcomes were fasting blood glucose, insulin concentration, insulin resistance (HOMA-IR), insulin sensitivity (QUIKI), and hemoglobin A1c (HbA1c).

RESULTS:

A total of 25 randomized clinical trials (30 treatment arms) were included. Meta-analysis suggested a significant association between flaxseed supplementation and a reduction in blood glucose (weighted mean difference [WMD], -2.94 mg/dL; 95%CI, -5.31 to - 0.56; P = 0.015), insulin levels (WMD, -7.32 pmol/L; 95%CI, -11.66 to -2.97; P = 0.001), and HOMA-IR index (WMD, -0.49; 95%CI,: -0.78 to - 0.20; P = 0.001) and an increase in QUIKI index (WMD, 0.019; 95%CI, 0.008-0.031; P = 0.001). No significant effect on HbA1c (WMD, -0.045%; 95%CI, -0.16 to - 0.07; P = 0.468) was found. In subgroup analysis, a significant reduction in blood glucose, insulin, and HOMA-IR and a significant increase in QUIKI were found only in studies using whole flaxseed but not flaxseed oil and lignan extract. Furthermore, a significant reduction was observed in insulin levels and insulin sensitivity indexes only in the subset of trials lasting ≥12 weeks.

CONCLUSIONS:

Whole flaxseed, but not flaxseed oil and lignan extract, has significant effects on improving glycemic control. Further studies are needed to determine the benefits of flaxseed on glycemic parameters. The protocol for this systematic review was registered in the international prospective register of systematic reviews (PROSPERO) database (http://www.crd.york.ac.uk/PROSPERO; registration no: CRD42016043500).

KEYWORDS: flaxseed; glucose; insulin; insulin resistance; lignin

Exp Clin Endocrinol Diabetes. 2017 Jun;125(6):353-359. doi: 10.1055/s-0042-117773. Epub 2017 Apr 13.

The Effects of Omega-3 Fatty Acids and Vitamin E Co-Supplementation on Indices of Insulin Resistance and Hormonal Parameters in Patients with Polycystic Ovary Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial.

Ebrahimi FA[1], Samimi M[1], Foroozanfard F[1], Jamilian M[2], Akbari H[3], Rahmani E[4], Ahmadi S[5], Taghizadeh M[6], Memarzadeh MR[7], Asemi Z[6].

This study was conducted to determine the effects of omega-3 fatty acids and vitamin E co-supplementation on indices of insulin resistance and hormonal parameters in women with polycystic ovary syndrome (PCOS). This randomized double-blind, placebo-controlled trial was done on 68 women diagnosed with PCOS according to the Rotterdam criteria aged 18-40 years old. Participants were randomly assigned into 2 groups to receive either 1 000 mg omega-3 fatty acids from flaxseed oil containing 400 mg α-Linolenic acid plus 400 IU vitamin E supplements (n=34) or placebo (n=34) for 12 weeks. Hormonal parameters were quantified at the beginning of the study and after 12-week intervention. After 12 weeks of intervention, compared to the placebo, omega-3 fatty acids and vitamin E co-supplementation resulted in a significant decrease in insulin (-1.0±3.5 vs. +2.7±6.6 μIU/mL, P=0.004), homeostasis model of assessment-estimated insulin resistance (-0.2±0.8 vs. +0.6±1.5, P=0.005), homeostasis model of assessment-estimated B cell function (-4.3±14.3 vs. +10.5±24.5, P=0.004) and a significant increase in quantitative insulin sensitivity check index (+0.006±0.02 vs. -0.01±0.04, P=0.008). Supplementation with omega-3 fatty acids plus vitamin E led to significant reductions in serum total testosterone (-0.5±0.7 vs. -0.1±0.5 ng/mL, P=0.008) and free testosterone (-1.2±2.1 vs. -0.2±1.7, P=0.04) compared to the placebo group. We did not observe any significant effect of omega-3 fatty acids and vitamin E co-supplementation on fasting plasma glucose and other hormonal profiles. Omega-3 fatty acids and vitamin E co-supplementation for 12 weeks in PCOS women significantly improved indices of insulin resistance, total and free testosterone.

Exp Clin Endocrinol Diabetes. 2017 Nov 8. doi: 10.1055/s-0043-119751. [Epub ahead of print]

The Effects of Flaxseed Oil Omega-3 Fatty Acids Supplementation on Metabolic Status of Patients with Polycystic Ovary Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial.

Mirmasoumi G[1], Fazilati M[1,2], Foroozanfard F[3], Vahedpoor Z[3], Mahmoodi S[3], Taghizadeh M[4], Esfeh NK[4], Mohseni M[4], Karbassizadeh H[5], Asemi Z[4].

OBJECTIVE

This study was conducted to evaluate the effects of flaxseed oil omega-3 fatty acids supplementation on metabolic status of patients with polycystic ovary syndrome (PCOS).

METHODS

This randomized double-blind, placebo-controlled trial was conducted on 60 women with PCOS according to the Rotterdam criteria aged 18-40 years old. Participants were randomly assigned into two groups to receive either 1,000 mg flaxseed oil omega-3 fatty acids (n=30) or placebo (n=30) twice a day for 12 weeks. Metabolic, endocrine, inflammatory factors were quantified at baseline and after the 12-week intervention.

RESULTS

After the 12-week intervention, compared to the placebo, flaxseed oil omega-3 supplementation significantly decreased insulin values (-2.6±7.7 vs.+1.3±3.9 μIU/mL, P=0.01), homeostasis model of assessment-estimated insulin resistance (-0.7±1.7 vs.+0.3±0.9, P=0.01), mF-G scores (-1.2±1.7 vs. -0.1±0.4, P=0.001), and increased quantitative insulin sensitivity check index (+0.01±0.02 vs. -0.01±0.02, P=0.01). In addition, supplementation with flaxseed oil omega-3 resulted in significant decreases in serum triglycerides (-5.1±20.9 vs.+9.7±26.1 mg/dL, P=0.01), VLDL-cholesterol (-1.0±4.2 vs.+1.9±5.2 mg/dL, P=0.01) and high-sensitivity C-reactive protein (hs-CRP) (-1.6±3.1 vs.+0.2±1.5 mg/L, P=0.004) compared to the placebo. We did not see any significant effect of flaxseed oil omega-3 supplementation on hormonal and other lipid profiles, and plasma nitric oxide levels.

CONCLUSIONS

Overall, flaxseed oil omega-3 supplementation for 12 weeks in women with PCOS had beneficial effects on insulin metabolism, mF-G scores, serum triglycerides, VLDL-cholesterol and hs-CRP levels, but did not affect hormonal and other lipid profiles, and plasma nitric oxide levels.

KEYWORDS flaxseed, lignan, suckling, mammary gland differentiation, breast cancer

Horm Metab Res. 2017 Jun;49(6):446-451. doi: 10.1055/s-0042-122782. Epub 2017 Feb 24.

The Effects of Omega-3 Fatty Acids Supplementation on Gene Expression Involved in the Insulin and Lipid Signaling Pathway in Patients with Polycystic Ovary Syndrome.

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Limited data are available evaluating the effects of omega-3 fatty acids supplementation on gene expression involved in the insulin and lipid-signaling pathway in women with polycystic ovary syndrome (PCOS). This study was conducted to evaluate the effects of omega-3 fatty acids supplementation on gene

expression involved in the insulin and lipid signaling pathway in women with PCOS. This randomized double blind, placebo-controlled trial was done among 60 women aged 18-40 years old and diagnosed with PCOS according to the Rotterdam criteria. Participants were randomly assigned into 2 groups to receive either 1 000 mg omega-3 fatty acids from flaxseed oil containing 400 mg α-linolenic acid (n=30) or placebo (n=30) twice a day for 12 weeks. Gene expressions involved in the insulin and lipid-signaling pathway were quantified in blood samples of PCOS women with RT-PCR method. Quantitative results of RT-PCR demonstrated that compared with the placebo, omega-3 fatty acids supplementation upregulated peroxisome proliferator-activated receptor gamma (PPAR-γ) mRNA (p=0.005) in peripheral blood mononuclear cells of women with PCOS. In addition, compared to the placebo, omega-3 fatty acids supplementation downregulated expressed levels of oxidized low-density lipoprotein receptor (LDLR) mRNA (p=0.002) in peripheral blood mononuclear cells of women with PCOS. We did not observe any significant effect of omega-3 fatty acids supplementation on expressed levels of glucose transporter 1 (GLUT-1) and lipoprotein(a) [Lp(a)] genes in peripheral blood mononuclear cells. Overall, omega-3 fatty acids supplementation for 12 weeks in PCOS women significantly improved gene expression of PPAR-γ and LDLR.

Mol Cell Endocrinol. 2017 Jan 5;439:247-255. doi: 10.1016/j.mce.2016.09.008. Epub 2016 Sep 9.

The effects of omega-3 fatty acids and vitamin E co-supplementation on gene expression of lipoprotein(a) and oxidized low-density lipoprotein, lipid profiles and biomarkers of oxidative stress in patients with polycystic ovary syndrome.

Rahmani E[1], Samimi M[2], Ebrahimi FA[2], Foroozanfard F[2], Ahmadi S[3], Rahimi M[4], Jamilian M[5], Aghadavod E[6], Bahmani F[6], Taghizadeh M[6], Memarzadeh MR[7], Asemi Z[8].

This study was conducted to determine the effects of omega-3 fatty acids and vitamin E co-supplementation on gene expression of lipoprotein(a) (Lp[a]) and oxidized low-density lipoprotein (Ox-LDL), lipid profiles and biomarkers of oxidative stress in women with polycystic ovary syndrome (PCOS). This randomized double-blind, placebo-controlled trial was done on 68 women diagnosed with PCOS according to the Rotterdam criteria aged 18-40 years old. Participants were randomly assigned into two groups to receive either 1000 mg omega-3 fatty acids from flaxseed oil containing 400 mg α-Linolenic acid plus 400 IU vitamin E supplements (n = 34) or placebo (n = 34) for 12 weeks. Lp(a) and Ox-LDL mRNA levels were quantified in peripheral blood mononuclear cells of PCOS women with RT-PCR method. Lipid profiles and biomarkers of oxidative stress were quantified at the beginning of the study and after 12-week intervention. Quantitative results of RT-PCR demonstrated that compared with the placebo, omega-3 fatty acids and vitamin E co-supplementation downregulated expressed levels of Lp(a) mRNA ($P < 0.001$) and Ox-LDL mRNA ($P < 0.001$) in peripheral blood mononuclear cells of women with PCOS. In addition, compared to the placebo group, omega-3 fatty acids and vitamin E co-supplementation resulted in a significant decrease in serum triglycerides (-22.1 ± 22.3 vs. +7.7 ± 23.6 mg/dL, $P < 0.001$), VLDL- (-4.4 ± 4.5 vs. +1.5 ± 4.7 mg/dL, $P < 0.001$), total- (-20.3 ± 16.6 vs. +12.2 ± 26.1 mg/dL, $P < 0.001$), LDL- (-16.7 ± 15.3 vs. +11.9 ± 26.1 mg/dL, $P < 0.001$) and total-/HDL-cholesterol (-0.5 ± 0.6 vs. +0.4 ± 0.8, $P < 0.001$). There were a significant increase in plasma total antioxidant capacity (+89.4 ± 108.9 vs. +5.9 ± 116.2 mmol/L, $P = 0.003$) and a significant decrease in malondialdehyde levels (-0.3 ± 0.4 vs. -0.008 ± 0.6 μmol/L, $P = 0.01$) by combined omega-3 fatty acids and vitamin E intake compared with the placebo group. Overall, omega-3 fatty acids and vitamin E co-supplementation for 12 weeks in PCOS women significantly improved gene expression of Lp(a) and Ox-LDL, lipid profiles and biomarkers of oxidative stress.

KEYWORDS: Gene expression; Lipid profiles; Omega fatty acids and vitamin E; Oxidative stress; Polycystic ovary syndrome

Can J Diabetes. 2017 Apr;41(2):143-149. doi: 10.1016/j.jcjd.2016.09.004. Epub 2016 Nov 21.

A Randomized Controlled Clinical Trial Investigating the Effects of Omega-3 Fatty Acids and Vitamin E Co-Supplementation on Biomarkers of Oxidative Stress, Inflammation and Pregnancy Outcomes in Gestational Diabetes.

Jamilian M[1], Hashemi Dizaji S[2], Bahmani F[3], Taghizadeh M[3], Memarzadeh MR[4], Karamali M[2], Akbari M[5], Asemi Z[6].

OBJECTIVES:
Limited data are available for assessing the effects of omega-3 fatty acids and vitamin E co-supplementation on metabolic profiles and pregnancy outcomes in gestational diabetes (GDM). This study was designed to determine the effects of omega-3 fatty acids and vitamin E co-supplementation on biomarkers of oxidative stress, inflammation and pregnancy outcomes in women with GDM.

METHODS:
This randomized, double-blind, placebo-controlled clinical trial was conducted in 60 patients with GDM who were not taking oral hypoglycemic agents. Patients were randomly allocated to intake either 1000 mg omega-3 fatty acids from flaxseed oil plus 400 IU vitamin E supplements (n=30) or placebo (n=30) for 6 weeks. Fasting blood samples were obtained from the women at the beginning of the study and after the 6-week intervention to quantify related markers.

RESULTS:
After 6 weeks of intervention, omega-3 fatty acids and vitamin E co-supplementation, compared with the placebo, resulted in a significant rise in total antioxidant capacity (TAC) (+187.5±224.9 vs. -32.5±136.1 mmol/L; p<0.001); nitric oxide (NO) (+5.0±7.7 vs. -12.0±28.0 μmol/L; p=0.002) and a significant decrease in plasma malondialdehyde (MDA) concentrations (-0.1±0.9 vs. +0.6±1.4 μmol/L; p=0.03). Co-supplementation with omega-3 fatty acids and vitamin E showed no detectable changes in plasma glutathione and serum high-sensitivity C-reactive protein levels. Joint omega-3 fatty acids and vitamin E supplementation resulted in lower incidences of hyperbilirubinemia in newborns (10.3% vs. 33.3%; p=0.03).

CONCLUSIONS:
Overall, omega-3 fatty acids and vitamin E co-supplementation for 6 weeks in women with GDM had beneficial effects on plasma TAC, MDA and NO and on the incidence of the newborns' hyperbilirubinemia.

KEYWORDS: acides gras oméga-3; diabète gestationnel; femmes enceintes; gestational diabetes; omega-3 fatty acids; pregnant women; supplementation; supplémentation; vitamin E; vitamine E

Neurochem Int. 2017 Sep;108:183-189. doi: 10.1016/j.neuint.2017.03.014. Epub 2017 Mar 22.

The effects of omega-3 fatty acids and vitamin E co-supplementation on clinical and metabolic status in patients with Parkinson's disease: A randomized, double-blind, placebo-controlled trial.

Taghizadeh M[1], Tamtaji OR[2], Dadgostar E[3], Daneshvar Kakhaki R[4], Bahmani F[1], Abolhassani J[4], Aarabi MH[1], Kouchaki E[5], Memarzadeh MR[6], Asemi Z[7].

The current research was performed to evaluate the effects of omega-3 fatty acids and vitamin E co-supplementation on clinical signs and metabolic status in people with Parkinson's disease (PD). This randomized double-blind placebo-controlled clinical trial was conducted in 60 patients with PD. Participants were randomly assigned into two groups to receive either 1000 mg omega-3 fatty acids from flaxseed oil plus 400 IU vitamin E supplements (n = 30) or placebo (n = 30) for 12 weeks. Unified Parkinson's disease rating stage (UPDRS) were recorded at baseline and the after 3-month intervention. After 12 weeks' intervention, compared with the placebo, omega-3 fatty acids and vitamin E co-supplementation led to a significant improve in UPDRS (-3.3 ± 10.0 vs. +4.4 ± 14.9, P = 0.02). Furthermore, co-supplementation decreased high-sensitivity C-reactive protein (hs-CRP) (-0.3 ± 0.6 vs. +0.3 ± 0.3 μg/mL, P < 0.001), and increased total antioxidant capacity (TAC) (+65.2 ± 68.7 vs. +16 ± 52.4 μmol/L, P = 0.003) and glutathione (GSH) concentrations (+41.4 ± 80.6 vs. -19.6 ± 55.9 μmol/L, P = 0.001) compared with the placebo. Additionally, co-supplementation meaningfully decreased insulin (-2.1 ± 4.9 vs. +1.4 ± 6.2 μIU/mL, P = 0.01), homeostasis model of assessment-estimated insulin resistance (-0.7 ± 1.8 vs.+0.3 ± 1.6, P = 0.02) and Beta cell function (-5.9 ± 13.9 vs. +5.7 ± 25.5, P = 0.03), and increased quantitative insulin sensitivity check index (+0.009 ± 0.02 vs. -0.006 ± 0.03, P = 0.03) compared with the placebo. Overall, our study demonstrated that omega-3 fatty acids and vitamin E co-supplementation in people with PD had favorable effects on UPDRS, hs-CRP, TAC, GSH and markers of insulin metabolism.

KEYWORDS: Inflammation; Oxidative stress; Parkinson's disease; Supplementation

Mol Cell Biochem. 2017 Aug;432(1-2):33-39. doi: 10.1007/s11010-017-2995-z. Epub 2017 Mar 20.

Secoisolariciresinol diglucoside attenuates cardiac hypertrophy and oxidative stress in monocrotaline-induced right heart dysfunction.

Puukila S[1], Fernandes RO[2,3], Türck P[2], Carraro CC[2], Bonetto JHP[2], de Lima-Seolin BG[2], da Rosa Araujo AS[2], Belló-Klein A[2], Boreham D[4], Khaper N[5].

Pulmonary arterial hypertension (PAH) occurs when remodeling of pulmonary vessels leads to increased pulmonary vascular resistance resulting in increased pulmonary arterial pressure. Increased pulmonary arterial pressure results in right ventricle hypertrophy and eventually heart failure. Oxidative stress has been implicated in the pathogenesis of PAH and may play a role in the regulation of cellular signaling involved in cardiac response to pressure overload. Secoisolariciresinol diglucoside (SDG), a component from flaxseed, has been shown to reduce cardiac oxidative stress in various pathophysiological conditions. We investigated the potential protective effects of SDG in a monocrotaline-induced model of PAH. Five- to six-week-old male Wistar rats were given a single intraperitoneal injection of monocrotaline (60 mg/kg) and sacrificed 21 days later where heart, lung, and plasma were collected. SDG (25 mg/kg) was given via gavage as either a 21-day co-treatment or pre-treatment of 14 days before monocrotaline administration and continued for 21 days. Monocrotaline led to right ventricle hypertrophy, increased lipid peroxidation, and elevated plasma levels of alanine transaminase (ALT) and aspartate transaminase (AST). Co-treatment with SDG did not attenuate hypertrophy or ALT and AST levels but decreased reactive oxygen species (ROS) levels and catalase and superoxide dismutase activity compared to the monocrotaline-treated group. Pre-treatment with SDG decreased right ventricle hypertrophy, ROS levels, lipid peroxidation, catalase, superoxide dismutase, and glutathione peroxidase activity and plasma levels of ALT and AST when compared to the monocrotaline group. These findings indicate that pre-treatment with SDG provided better protection than co-treatment in this model of right heart dysfunction, suggesting an important role for SDG in PAH and right ventricular remodeling.

KEYWORDS: Antioxidants; Cardiac hypertrophy; Monocrotaline; Oxidative stress; Pulmonary arterial hypertension; Secoisolariciresinol diglucoside

J Am Coll Nutr. 2017 Nov-Dec;36(8):646-653. doi: 10.1080/07315724.2017.1342213. Epub 2017 Sep 18.

Influence of Flaxseed Lignan Supplementation to Older Adults on Biochemical and Functional Outcome Measures of Inflammation.

Di Y[1], Jones J[2], Mansell K[1], Whiting S[1], Fowler S[2], Thorpe L[3], Billinsky J[1], Viveky N[1], Cheng PC[1], Almousa A[1], Hadjistavropoulos T[4], Alcorn J[1].

Evidence from the literature suggests that dietary flaxseed lignans have the ability to modulate inflammation, which is recognized as the underlying basis of multiple chronic human diseases in older adults. Our objective was to determine the effects of oral lignan supplementation on biochemical and functional indicators of inflammation as well as safety and tolerability in older healthy adults. We designed a randomized, double-blind, placebo-controlled clinical trial in older healthy adults (60-80 years) to assess flaxseed lignan-enriched complex (~38% secoisolariciresinol diglucoside [SDG]; 600 mg SDG dose) oral supplementation effects on biochemical and functional indicators of inflammation and safety and tolerability in older healthy adults after 6 months of once-daily oral administration. The clinical trial confirmed that plasma concentration of total flaxseed lignans (free and conjugated forms) secoisolariciresinol (SECO), enterodiol (ED), and enterolactone (ENL) were significantly associated with daily oral supplementation of flaxseed lignan-enriched complex ($p < 0.05$). A significant decrease in systolic blood pressure (SBP; from a mean of 155 ± 13 mm Hg at baseline to 140 ± 11 mm Hg at 24 weeks) was observed in lignan-supplemented participants stratified into an SBP ≥140 mm Hg subcategory ($p = 0.04$). No differences were found between treatment or placebo groups in terms of cognition, pain, activity, physical measurements (calf, waist, and upper arm circumstances), and grip strength. With respect to blood inflammatory markers, lipid profiles, and biochemical parameters, no significant differences were found between treatment and placebo groups at the end of the 6-month supplementation. No adverse effects were reported during supplementation. These data further support the safety and tolerability of long-term flaxseed lignan-enriched complex supplementation in older adults and identify an ability to favorably modulate SBP, an important risk factor in cardiovascular disease.

KEYWORDS: Inflammation; flaxseed lignans; older adults; safety; systolic blood pressure

J Diabetes Complications. 2017 Sep;31(9):1394-1400. doi: 10.1016/j.jdiacomp.2017.06.010. Epub 2017 Jun 28.

Clinical and metabolic response to flaxseed oil omega-3 fatty acids supplementation in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial.

Soleimani Z[1], Hashemdokht F[2], Bahmani F[2], Taghizadeh M[2], Memarzadeh MR[3], Asemi Z[4].

BACKGROUND: Data on the effects of flaxseed oil omega-3 fatty acids supplementation on wound healing and metabolic status in subjects with diabetic foot ulcer (DFU) are scarce.

OBJECTIVE: This study was conducted to evaluate the effects of flaxseed oil omega-3 fatty acids supplementation on wound healing and metabolic status in subjects with DFU.

METHODS: The current randomized, double-blind, placebo-controlled trial was conducted among 60 subjects (aged 40-85years old) with grade 3 DFU. Subjects were randomly allocated into two groups (30 subjects each group) to receive either 1000mg omega-3 fatty acids from flaxseed oil supplements or placebo twice a day for 12weeks.

RESULTS: After the 12-week intervention, compared with the placebo, omega-3 fatty acids supplementation resulted in significant decreases in ulcer length (-2.0±2.3 vs. -1.0±1.1cm, P=0.03), width (-1.8±1.7 vs. -1.0±1.0cm, P=0.02) and depth (-0.8±0.6 vs. -0.5±0.5cm, P=0.01). Additionally, significant reductions in serum insulin concentrations (-4.4±5.5 vs. +1.4±8.3 μIU/mL, P=0.002), homeostasis model of assessment-estimated insulin resistance (-2.1±3.0 vs. +1.0±5.0, P=0.005) and HbA1c (-0.9±1.5 vs. -0.1±0.4%, P=0.01), and a significant rise in the quantitative insulin sensitivity check index (+0.01±0.01 vs. -0.005±0.02, P=0.002) were seen following supplementation with omega-3 fatty acids compared with the placebo. In addition, omega-3 fatty acids supplementation significantly decreased serum high sensitivity C-reactive protein (hs-CRP) (-25.5±31.5 vs. -8.2±18.9μg/mL, P=0.01), and significantly increased plasma total antioxidant capacity (TAC) (+83.5±111.7 vs. -73.4±195.5mmol/L, P<0.001) and glutathione (GSH) concentrations (+60.7±140.2 vs. -15.5±129.7μmol/L, P=0.03) compared with the placebo.

CONCLUSIONS: Overall, omega-3 fatty acids supplementation for 12weeks among subjects with DFU had beneficial effects on parameters of ulcer size, markers of insulin metabolism, serum hs-CRP, plasma TAC and GSH levels. In addition, flaxseed oil omega-3 fatty acids may have played an indirect role in wound healing due to its effects on improved metabolic profiles.

Obes Surg. 2017 Oct;27(10):2663-2671. doi: 10.1007/s11695-017-2704-8.

Unsaturated Fatty Acids Improve Atherosclerosis Markers in Obese and Overweight Non-diabetic Elderly Patients.

de Oliveira PA[1,2,3], Kovacs C[4], Moreira P[4], Magnoni D[4], Saleh MH[4], Faintuch J[5].

BACKGROUND: Several studies have demonstrated the benefits of replacing trans and saturated fats with unsaturated fatty acids on cardiovascular diseases. We aimed to demonstrate the effect of polyunsaturated and monounsaturated fat supplementation on the biochemical and endothelial markers of atherosclerotic disease in obese or overweight non-diabetic elderly patients.
METHOD: Seventy-nine patients were randomly divided into three groups: flaxseed oil, olive oil, and sunflower oil; patients in each group received 30 mL of oil for 90 days. Patients were subjected to anthropometric and bioimpedance assessments; biochemical and endothelial evaluations were performed through ultrasonography of the brachial artery and carotid artery for endothelium-dependent dilation and intima-media thickness assessment, respectively, before and after the intervention. The participants' usual diet remained unchanged.

RESULTS: The flaxseed oil group had improved ultra-sensitive C-reactive protein levels (p = 0.074) and reduced carotid intima-media thickness (CIMT) (p = 0.028); the olive oil group exhibited an improved apolipoprotein (Apo)B/ApoA ratio (p = 0.021), reduced CIMT (p = 0.028), and improved flow-mediated vasodilation (FMV) (p = 0.054); and similarly, the sunflower oil group showed an improved ApoB/ApoA ratio (p = 0.024), reduced CIMT (p = 0.048), and improved FMV (p = 0.001**).**

CONCLUSION: Unsaturated fatty acid supplementation using the three vegetable oils attenuated pro-inflammatory properties and improved prothrombotic conditions. Therefore, introducing or replacing saturated and trans fat with unsaturated fatty acids is beneficial for cardiovascular risk reduction in obese or overweight non-diabetic elderly people. Further studies are needed to determine which unsaturated fat best prevents cardiovascular disease in elderly patients.

KEYWORDS: Atherosclerosis; Carotid intima-media thickness; Elderly; Inflammation; Obesity; Unsaturated fatty acids; Vascular endothelium; Vascular stiffness

Iran J Kidney Dis. 2016 Jul;10(4):197-204.

Effects of Omega-3 Fatty Acid Supplementation on Inflammatory Cytokines and Advanced Glycation End Products in Patients With Diabetic Nephropathy: a Randomized Controlled Trial.

Mirhashemi SM, Rahimi F, Soleimani A, Asemi Z[1].

INTRODUCTION: This study was performed to evaluate the effects of omega-3 fatty acid supplementation on inflammatory cytokines and advanced glycation end products (AGEs) in patients with diabetic nephropathy (DN).

MATERIALS AND METHODS: This randomized double-blind placebo-controlled trial was done on 60 patients with DN who were randomly divided into 2 groups to receive either 1000 mg/d of omega-3 fatty acid from flaxseed oil (n = 30) or placebo (n = 30) for 12 weeks. The primary outcome variables were tumor necrosis factor-α, receptor tumor necrosis factor-α and growth differentiation factor 15. Fasting blood samples were taken at the onset and the end of the study to quantify the related markers.

RESULTS: Compared with the placebo, omega-3 fatty acid supplementation resulted in a significant decrease in serum AGEs (-2.3 ± 2.8 AU versus 0.2 ± 2.5 AU, P = .001). Despite a significant reduction in serum level of receptor for AGEs (-0.1 ± 0.3 AU, P = .02) in the omega-3 fatty acid group, no significant difference was found between the two groups in terms of their effects on the receptor for AGEs. Supplementation with omega-3 fatty acid had no significant effect on the inflammatory cytokines as compared with the placebo.

CONCLUSIONS: Our study demonstrated that omega-3 fatty acid supplementation among DN patients had favorable effects on AGEs and the receptor for AGEs.

Phytother Res. 2016 Aug;30(8):1339-44. doi: 10.1002/ptr.5635. Epub 2016 May 6.

Flaxseed Supplementation in Metabolic Syndrome Management: A Pilot Randomized, Open-labeled, Controlled Study.

Yari Z[1], Rahimlou M[2], Poustchi H[3], Hekmatdoost A[1].

The aim of this study was to evaluate the efficacy of flaxseed supplementation plus lifestyle modification in comparison with lifestyle modification alone in the management of metabolic syndrome (MetS). A randomized controlled clinical trial was conducted on 44 patients with MetS. Participants were assigned to receive either the lifestyle advice and 30-g brown milled flaxseed daily or only the lifestyle advice as the control group. The percentage of individuals with MetS decreased from baseline by 50% and 82% in the control and intervention group, respectively. The reversion rate of central obesity was higher in the flaxseed group (36%) than control group (13%). Moreover, greater reduction in insulin resistance was observed in flaxseed group in comparison with control group ($p < 0.001$). Body weight, waist circumference, and body mass index decreased significantly in both groups with a significantly greater reduction in flaxseed group in comparison with controls ($p < 0.05$). There were no significant changes in blood pressure in any groups. Our results indicate that co-administration of flaxseed with lifestyle modification is more effective than lifestyle modification alone in management of MetS; whether these effects will be sustained with longer treatment durations remains to be determined.

KEYWORDS: central obesity; flaxseed; insulin resistance; metabolic syndrome

Hypertension. 2016 Oct;68(4):1031-8. doi: 10.1161/HYPERTENSIONAHA.116.07834. Epub 2016 Aug 15.

Dietary Flaxseed Reduces Central Aortic Blood Pressure Without Cardiac Involvement but Through Changes in Plasma Oxylipins.

Caligiuri SP[1], Rodriguez-Leyva D[1], Aukema HM[1], Ravandi A[1], Weighell W[1], Guzman R[1], Pierce GN[2].

In the year-long FlaxPAD clinical trial (Flaxseed for Peripheral Artery Disease), dietary flaxseed generated a powerful reduction in brachial systolic and diastolic blood pressure in patients with peripheral artery disease. Oxylipins were implicated as potential mechanistic mediators. However, the ability of flaxseed to impact central aortic hypertension, arterial stiffness, or cardiac performance was not investigated. Additionally, the relationship between central blood pressure (cBP) and oxylipins was not elucidated. Therefore, radial tonometry and pulse wave analysis were used to measure cBP and cardiac function in the FlaxPAD population (n=62). Plasma oxylipins were analyzed with high-performance liquid chromatography mass spectrometry. In patients with high blood pressure at baseline, the average decrease in central systolic and diastolic blood pressures versus placebo was 10 and 6 mm Hg, respectively. Flaxseed did not significantly impact augmentation index or other cardiac function indices. Alternatively, the data support several specific oxylipins as potential mediators in the antihypertensive properties of flaxseed. For example, every 1 nmol/L increase in plasma 16-hydroxyeicosatetraenoic acid increased the odds of higher central systolic and diastolic blood pressures by 12- and 9-fold, respectively. Every 1 nmol/L increase in plasma thromboxane B2 and 5,6-dihydroxyeicosatrienoic acid increased the odds of higher cBP by 33- and 9-fold, respectively. Flaxseed induced a decrease in many oxylipins, which corresponded with a reduced risk of elevated cBP. These data extend the antihypertensive properties of flaxseed to cBP without cardiac involvement but rather through oxylipins. This study provides further support for oxylipins as therapeutic targets in hypertension.

CLINICAL TRIAL REGISTRATION: URL: http://www.clinicaltrials.gov. Unique identifier: NCT00781950.

J Clin Lipidol. 2016 Mar-Apr;10(2):386-93. doi: 10.1016/j.jacl.2015.12.017. Epub 2015 Dec 29.

A randomized-controlled clinical trial investigating the effect of omega-3 fatty acids and vitamin E co-supplementation on markers of insulin metabolism and lipid profiles in gestational diabetes.

Taghizadeh M[1], Jamilian M[2], Mazloomi M[3], Sanami M[1], Asemi Z[4].

BACKGROUND: Limited data are available that evaluated the effects of combined omega-3 fatty acids and vitamin E supplementation on glucose homeostasis parameters and lipid concentrations in gestational diabetes (GDM).

OBJECTIVES: The present study was designed to determine the effects of omega-3 fatty acids and vitamin E co-supplementation on glucose homeostasis parameters and lipid concentrations among women with GDM who were not on oral hypoglycemic agents.

METHODS: This prospective randomized, double-blind, placebo-controlled clinical trial was carried out among 60 patients with GDM. Patients were randomly allocated to take either 1000-mg omega-3 fatty acids from flaxseed oil plus 400-IU vitamin E supplements (n = 30) or placebo (n = 30) for 6 weeks.

Fasting blood samples were obtained from at the beginning of the study and after 6-week intervention to quantify related variables.

RESULTS: After 6 weeks of intervention, changes in fasting plasma glucose (-11.8 ± 11.0 vs +1.5 ± 11.9 mg/dL, P < .001), serum insulin concentrations (-1.8 ± 6.9 vs +5.8 ± 12.1 μIU/mL, P = .004), homeostasis model of assessment-estimated insulin resistance (-0.8 ± 1.6 vs +1.4 ± 2.8, P = .001), homeostasis model of assessment-estimated beta cell function (-0.2 ± 27.7 vs +22.8 ± 48.2, P = .02), and quantitative insulin sensitivity check index (+0.01 ± 0.02 vs -0.01 ± 0.02, P = .01) in the omega-3 fatty acids plus vitamin E group were significantly different from the changes in these indicators in the placebo group. Changes in serum triglycerides (+10.8 ± 41.5 vs +34.2 ± 35.5 mg/dL, P = .02), VLDL-cholesterol (+2.1 ± 8.3 vs +6.8 ± 7.1 mg/dL, P = .02), low-density lipoprotein (LDL)-cholesterol (+11.6 ± 18.8 vs +1.7 ± 15.9 mg/dL, P = .03) and HDL-cholesterol concentrations (+1.9 ± 8.7 vs -2.4 ± 7.7 mg/dL, P = .04) were significantly different between the supplemented women and placebo group. However, after controlling for baseline total cholesterol levels, maternal age, and BMI at baseline, the changes in serum LDL-cholesterol concentrations were not significantly different between the 2 groups. We did not find any significant effect of joint omega-3 fatty acids and vitamin E supplementation on total cholesterol concentrations.

CONCLUSIONS: Overall, we demonstrated that omega-3 fatty acids and vitamin E co-supplementation in GDM women had beneficial effects on glucose homeostasis parameters, serum triglycerides, VLDL-cholesterol, and HDL-cholesterol concentrations, but it did not influence total-cholesterol and LDL-cholesterol levels.

KEYWORDS: Gestational diabetes; Omega-3 fatty acids; Pregnant women; Supplementation; Vitamin E

Int J Food Sci Nutr. 2016 Jun;67(4):461-9. doi: 10.3109/09637486.2016.1161011. Epub 2016 Mar 17.

Flaxseed supplementation in non-alcoholic fatty liver disease: a pilot randomized, open labeled, controlled study.

Yari Z[1], Rahimlou M[2], Eslamparast T[1], Ebrahimi-Daryani N[3], Poustchi H[4], Hekmatdoost A[1].

A two-arm randomized open labeled controlled clinical trial was conducted on 50 patients with non-alcoholic fatty liver disease (NAFLD). Participants were assigned to take either a lifestyle modification (LM), or LM +30 g/day brown milled flaxseed for 12 weeks. At the end of the study, body weight, liver enzymes, insulin resistance and hepatic fibrosis and steatosis decreased significantly in both groups (p< 0.05); however, this reduction was significantly greater in those who took flaxseed supplementation (p < 0.05). The significant mean differences were reached in hepatic markers between flaxseed and control group, respectively: ALT [-11.12 compared with -3.7 U/L; P< 0.001], AST [-8.29 compared with -4 U/L; p < 0.001], GGT [-15.7 compared with -2.62 U/L; p < 0.001], fibrosis score [-1.26 compared with -0.77 kPa; p = 0.013] and steatosis score [-47 compared with -15.45 dB/m; p = 0.022]. In conclusion, flaxseed supplementation plus lifestyle modification is more effective than lifestyle modification alone for NAFLD management.

KEYWORDS: Clinical trial; flaxseed; hepatic fibrosis; liver enzymes; non-alcoholic fatty liver disease

Nutrients. 2016 Mar 4;8(3):136. doi: 10.3390/nu8030136.

Effect of Flaxseed Intervention on Inflammatory Marker C-Reactive Protein: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.

Ren GY[1,2], Chen CY[3,4], Chen GC[5], Chen WG[6], Pan A[7], Pan CW[8], Zhang YH[9], Qin LQ[10], Chen LH[11].

Functional food-flaxseed and its derivatives (flaxseed oil or lignans) are beneficial for human health, possibly because of their anti-inflammatory effects. C-reactive protein (CRP), a sensitive marker of inflammation was chosen to evaluate the anti-inflammatory effects of flaxseed. We searched randomized controlled trials from PubMed and the Cochrane Library in October 2015 and conducted a meta-analysis to evaluate the effectiveness of flaxseed and its derivatives on CRP. The mean differences (net change) in CRP (mg/L) concentrations were pooled with a random- or a fixed-effects model depending on the results of heterogeneity tests. Overall, flaxseed interventions had no effects on reduction of CRP ($p = 0.428$). The null effects were consistent in the subgroup analysis with multiple studies and population characteristics. Significant heterogeneity was observed in most of the analyses. Meta-regression identified baseline body mass index (BMI) as a significant source of heterogeneity (P-interaction = 0.032), with a significant reduction in CRP of 0.83 mg/L (95% confidence interval -1.34 to -0.31; $p = 0.002$) among subjects with a BMI of ≥30 kg/m^2. In conclusion, our meta-analysis did not find sufficient evidence that flaxseed and its derivatives have a beneficial effect on reducing circulating CRP. However, they may significantly reduce CRP in obese populations.

KEYWORDS: C-reactive protein; flaxseed; meta-analysis; randomized controlled trials

Curr Pharm Des. 2016;22(2):214-20.

Prevention and treatment of atherosclerosis with flaxseed-derived compound secoisolariciresinol diglucoside.

Prasad K[1], Jadhav A.

Atherosclerosis is the primary cause of coronary artery disease, heart attack, strokes, and peripheral vascular disease. Alternative/complimentary medicines, although are unacceptable by medical community, may be of great help in suppression, slowing of progression and regression of atherosclerosis. Numerous natural products are in use for therapy in spite of lack of evidence. This paper discusses the basic mechanism of atherosclerosis, risk factors for atherosclerosis, and prevention, slowing of progression and regression of atherosclerosis with flaxseed-derived secoisolariciresinol diglucoside (SDG). SDG content of flaxseed varies from 6mg/g to 18 mg/g. Flaxseed is the richest source of SDG. SDG possesses antioxidant, antihypertensive, antidiabetic, hypolipidemic, anti-inflammatory and antiatherogenic activities. SDG content of some commonly used food has been described. SDG in very low dose (15 mg/ kg) suppressed the development of hypercholesterolemic atherosclerosis by 73 % and this effect was associated with reduction in serum total cholesterol, LDL-C, and oxidative stress, and an increase in the levels HDL-C. A summary of the effects of flaxseed and its components on hypercholesterolemic atherosclerosis has been provided. Reduction in hypercholesterolemic atherosclerosis by flaxseed, CDC-flaxseed, flaxseed oil, flax lignan complex and SDG are 46 %, 69 %, 0 %, 34 % and 73 % respectively in dietary cholesterol -induced rabbit model of atherosclerosis. SDG slows the progression of atherosclerosis in animal model. Long-term use of SDG regresses hypercholesterolemic atherosclerosis. It is interesting that regular diet following high cholesterol diet accelerates in this animal model of atherosclerosis. In conclusion SDG suppresses, slow the progression and regresses the atherosclerosis. It could serve as an alternative medicine for the prevention, slowing of progression and regression of atherosclerosis and hence for the treatment of coronary artery disease, stroke and peripheral arterial vascular diseases.

Crit Rev Food Sci Nutr. 2016 Aug 17;56(11):1826-43. doi: 10.1080/10408398.2013.789823.

Bioactivation of Phytoestrogens: Intestinal Bacteria and Health.

Landete JM[1], Arqués J[1], Medina M[1], Gaya P[1], de Las Rivas B[2], Muñoz R[2].

Phytoestrogens are polyphenols similar to human estrogens found in plants or derived from plant precursors. Phytoestrogens are found in high concentration in soya, flaxseed and other seeds, fruits, vegetables, cereals, tea, chocolate, etc. They comprise several classes of chemical compounds (stilbenes, coumestans, isoflavones, ellagitannins, and lignans) which are structurally similar to endogenous estrogens but which can have both estrogenic and antiestrogenic effects. Although epidemiological and experimental evidence indicates that intake of phytoestrogens in foods may be protective against certain chronic diseases, discrepancies have been observed between in vivo and in vitro experiments. The microbial transformations have not been reported so far in stilbenes and coumestans. However, isoflavones, ellagitanins, and lignans are metabolized by intestinal bacteria to produce equol, urolithins, and enterolignans, respectively. Equol, urolithin, and enterolignans are more bioavailable, and have more estrogenic/antiestrogenic and antioxidant activity than their precursors. Moreover, equol, urolithins and enterolignans have anti-inflammatory effects and induce antiproliferative and apoptosis-inducing activities. The transformation of isoflavones, ellagitanins, and lignans by intestinal microbiota is essential to be protective against certain chronic diseases, as cancer, cardiovascular disease, osteoporosis, and menopausal symptoms. Bioavailability, bioactivity, and health effects of dietary phytoestrogens are strongly determined by the intestinal bacteria of each individual.

KEYWORDS: Phytoestrogens; enterodiol; enterolactone; equol; microbiota; urolithin

Nutr J. 2015 Jul 28;14:71. doi: 10.1186/s12937-015-0059-3.

Potential protective properties of flax lignan secoisolariciresinol diglucoside.

Imran M[1], Ahmad N[2], Anjum FM[3], Khan MK[4], Mushtaq Z[5], Nadeem M[6], Hussain S[7].

Lignans are a group of phytonutrients which are widely distributed in the plant kingdom. Flaxseed is the richest source of providing lignan precursor such as secoisolariciresinol diglucoside (SDG). This article reviews the studies relevant to experimental models in animals and humans demonstrating the possible nutraceutical actions of SDG to prevent and alleviate lifestyle-related diseases. A local and international web-based literature review for this project was carried out to provide information relating to the study. The major key word "SDG" was selected to gather information using the electronic databases pertaining to the current state of flaxseed lignans composition, bioactive compounds, metabolism and to find out their role in terms of chemopreventive action. The extraction methods vary from simple to complex depending on separation, fractionation, identification and detection of the analytes. The majority of studies demonstrate that SDG interferes with the development of different types of diseases like cardiovascular, diabetic, lupus nephritis, bone, kidney, menopause, reproduction, mental stress, immunity, atherosclerosis, hemopoietic, liver necrosis and urinary disorders due to its various biological properties including anti-inflammatory, antioxidant, antimutagenic, antimicrobial, antiobesity, antihypolipidemic and neuroprotective effects. Moreover, SDG has a defending mediator against various cancers by modulating multiple cell signaling pathways. As discussed in this review, SDG has shown therapeutic potential against a number of human diseases and can be recommended for discerning consumers.

Br J Nutr. 2015 Aug 14;114(3):406-17. doi: 10.1017/S0007114515001786. Epub 2015 Jul 2.

Dietary modulation of the gut microbiota--a randomised controlled trial in obese postmenopausal women.

Brahe LK[1], Le Chatelier E[2], Prifti E[2], Pons N[2], Kennedy S[2], Blædel T[1], Håkansson J[3], Dalsgaard TK[4], Hansen T[5], Pedersen O[5], Astrup A[1], Ehrlich SD[2], Larsen LH[1].

The gut microbiota has been implicated in obesity and its progression towards metabolic disease. Dietary interventions that target the gut microbiota have been suggested to improve metabolic health. The aim of the present study was to investigate the effect of interventions with Lactobacillus paracasei F19 or flaxseed mucilage on the gut microbiota and metabolic risk markers in obesity. A total of fifty-eight obese postmenopausal women were randomised to a single-blinded, parallel-group intervention of 6-week duration, with a daily intake of either L. paracasei F19 (9.4 × 1010 colony-forming units), flaxseed mucilage (10 g) or placebo. Quantitative metagenomic analysis of faecal DNA was performed to identify the changes in the gut microbiota. Diet-induced changes in metabolic markers were explored using adjusted linear regression models. The intake of flaxseed mucilage over 6 weeks led to a reduction in serum C-peptide and insulin release during an oral glucose tolerance test (P< 0.05) and improved insulin sensitivity measured by Matsuda index (P< 0.05). Comparison of gut microbiota composition at baseline and after 6 weeks of intervention with flaxseed mucilage showed alterations in abundance of thirty-three metagenomic species (P< 0.01), including decreased relative abundance of eight Faecalibacterium species. These changes in the microbiota could not explain the effect of flaxseed mucilage on insulin sensitivity. The intake of L. paracasei F19 did not modulate metabolic markers compared with placebo. In conclusion, flaxseed mucilage improves insulin sensitivity and alters the gut microbiota; however, the improvement in insulin sensitivity was not mediated by the observed changes in relative abundance of bacterial species.

KEYWORDS: Flaxseed mucilage; Gut microbiota; Metagenomics; Obesity-related disease; Probiotics

Br J Nutr. 2015 Aug 14;114(3):406-17. doi: 10.1017/S0007114515001786. Epub 2015 Jul 2.

Dietary modulation of the gut microbiota--a randomised controlled trial in obese postmenopausal women.

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Abstract

The gut microbiota has been implicated in obesity and its progression towards metabolic disease. Dietary interventions that target the gut microbiota have been suggested to improve metabolic health. The aim of the present study was to investigate the effect of interventions with Lactobacillus paracasei F19 or flaxseed mucilage on the gut microbiota and metabolic risk markers in obesity. A total of fifty-eight obese postmenopausal women were randomised to a single-blinded, parallel-group intervention of 6-week duration, with a daily intake of either L. paracasei F19 (9.4 × 1010 colony-forming units), flaxseed mucilage (10 g) or placebo. Quantitative metagenomic analysis of faecal DNA was performed to identify the changes in the gut microbiota. Diet-induced changes in metabolic markers were explored using adjusted linear regression models. The intake of flaxseed mucilage over 6 weeks led to a reduction in serum C-peptide and insulin release during an oral glucose tolerance test (P< 0.05) and improved insulin sensitivity measured by Matsuda index (P< 0.05). Comparison of gut microbiota composition at baseline and after 6 weeks of intervention with flaxseed mucilage showed alterations in abundance of thirty-three metagenomic species (P< 0.01), including decreased relative abundance of eight Faecalibacterium species. These changes in the microbiota could not explain the effect

of flaxseed mucilage on insulin sensitivity. The intake of L. paracasei F19 did not modulate metabolic markers compared with placebo. In conclusion, flaxseed mucilage improves insulin sensitivity and alters the gut microbiota; however, the improvement in insulin sensitivity was not mediated by the observed changes in relative abundance of bacterial species.

KEYWORDS: Flaxseed mucilage; Gut microbiota; Metagenomics; Obesity-related disease; Probiotics

Holist Nurs Pract. 2015 May-Jun;29(3):151-7. doi: 10.1097/HNP.0000000000000085.

The effects of flaxseed on menopausal symptoms and quality of life.

Cetisli NE[1], Saruhan A, Kivcak B.

The purpose of this study was to analyze the effects of flaxseed on menopausal symptoms and quality of life throughout the menopausal period. The empirical research was conducted in an obstetrics and gynecology outpatient department of a university hospital and involved 140 menopausal women who were divided into 4 groups. The menopausal symptoms decreased and the quality of life increased among the women who used flaxseed for 3 months.

Rev Recent Clin Trials. 2015;10(1):61-7.

Effect of flaxseed on blood lipid level in hyperlipidemic patients.

Torkan M, Entezari MH[1], Siavash M.

INTRODUCTION: Hyperlipidemia is one of the most important risk factors of ischemic heart disease. Previous studies showed that flaxseedhas the potential to improve lipid profiles. In this study we investigated the effects of flaxseed powder intake on lipid profiles of patients with hyperlipidemia.

MATERIALS AND METHODS: This study was a randomized controlled clinical trial. Seventy patients with hyperlipidemia participated in the research. After detailed diet and lifestyle education, blood samples were collected from the participants. Patients with hyperlipidemia were randomly divided in to two intervention and control groups. The intervention group received 30 g of raw flaxseed powder every day for 40 days. Serum lipids were measured again in two groups after that time. Activity and food intakes of two groups were recorded.

RESULTS: In the intervention group, weight and body mass index were considerably reduced. Total cholesterol was reduced in the intervention group and increased in the control group, both of which were significant. Low density lipoprotein significantly increased in the control group and reduced in intervention group; also, triglyceride was increased in the control group and reduced in the intervention group, which were significant Table 1.

CONCLUSION: Based on the findings obtained in this research, flaxseed powder intake desirably reduced serum lipids. The differences between two groups on the basis of analysis of covariance test were significant. In all cases except for the HDL-c, this is an effective intervention. Therefore, flaxseed may be regarded as a useful therapeutic food for reducing hyperlipidemia.

Rev Recent Clin Trials. 2015; 10(1):61-7.

Effect of flaxseed on blood lipid level in hyperlipidemic patients.

Torkan M, Entezari MH1, Siavash M.

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Nutr J. 2015 Jan 10;14:5. doi: 10.1186/1475-2891-14-5.

Impact of weight loss diet associated with flaxseed on inflammatory markers in men with cardiovascular risk factors: a clinical study.

Cassani RS, Fa ssini PG[1], Silvah JH, Lima CM, Marchini JS.

BACKGROUND: Flaxseed has received attention for its anti-inflammatory and antioxidant role. The present study hypothesizes if flaxseedadded to a weight loss diet could improve the lipid and metabolic profiles and decrease risk factors related to cardiovascular disease.

METHODS: In a prospective, single blinded 42 days protocol, subjects were allocated into two groups with low carbohydrates intake: GriceLC (35% of carbohydrate and 60g of raw rice powder per day) and GflaxLC (32% of carbohydrate and 60g of flaxseed powder per day). Blood pressure, anthropometric measures and serum levels of isoprostane, C-reactive protein, Tumor Necrosis Factor-alpha, glucose, lipidic profile, uric acid, adiponectin, leptin and insulin were measured at baseline and at the end of interventions. Serum and urinary enterodiol and enterolactione were also measured.

RESULTS: A total of 27 men with cardiovascular risk factors were evaluated, with mean age of 33 ± 10 years to GriceLC and 40 ± 9 years to GflaxLC. Both groups experienced weight loss and systolic blood pressure reduction. A decrease in inflammatory markers (CRP and TNF-α) was observed after flaxseed intake (mean decrease of 25% and 46% for GflaxLC respectively). All groups also showed improvement in levels of total cholesterol, LDL-c, uric acid and adiponectin. Only GflaxLC group showed a decrease in triglyceride levels.

CONCLUSION: This study suggests that flaxseed added to a weight loss diet could be an important nutritional strategy to reduce inflammation markers such as CRP and TNF-α.

TRIAL REGISTRATION: ClinicalTrials.gov NCT02132728.

Rev Recent Clin Trials. 2015; 10(1):61-7.

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Food Chem Toxicol. 2014 Aug;70:163-78. doi: 10.1016/j.fct.2014.05.009. Epub 2014 May 21.

α-Linolenic acid: nutraceutical, pharmacological and toxicological evaluation.

Kim KB[1], Nam YA[2], Kim HS[2], Hayes AW[3], Lee BM[4].

α-Linolenic acid (ALA), a carboxylic acid with 18 carbons and three cis double bonds, is an essential fatty acid needed for human health and can be acquired via regular dietary intake of foods that contain ALA or dietary supplementation of foods high in ALA, for example flaxseed. ALA has been reported to have cardiovascular-protective, anti-cancer, neuro-protective, anti-osteoporotic, anti-inflammatory, and antioxidative effects. ALA is the precursor of longer chain omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), but its beneficial effects on risk factors for cardiovascular diseases are still inconclusive. The recommended intake of ALA for cardiovascular health is reported to be 1.1-2.2g/day. Although there are limited toxicological data for ALA, no serious adverse effects have been reported. The evidence on an increased prostate cancer risk in association with dietary ALA is not conclusive. Based on the limited data currently available, it may be concluded that ALA may be beneficial as a nutraceutical/pharmaceutical candidate and is safe for use as a food ingredient.

KEYWORDS: Nutraceutic; Safety; α-Linolenic acid

Pak J Pharm Sci. 2013 Jan;26(1):199-208.

Flaxseed - a miraculous defense against some critical maladies.

Akhtar S[1], Ismail T, Riaz M.

Presence of omega-3, omega-6 rich oil, alpha-linoleic acid, dietary fibers, secoisolariciresinol diglucoside, protein and minerals in flaxseed constitute a very strong basis for the utilization of flaxseed in various food preparations as a curative agent. An extensive body of literature illustrates that flaxseed has gained a significant position in the domain of nutritional sciences owing to its pivotal role as an antioxidant agent. The review discusses at length, numerous health benefits of flaxseed typically focusing its preventive role against cardiovascular diseases, cancer, diabetes and enhancement of spatial memory. Massive increase in the size of population with a special emphasize to the developing countries, there is an urge for exploration of the alternative dietary resources that can meet the dietary and nutritional needs of forthcoming generations. With respect to its remarkable nutritional importance, the review in question enables researchers engaged in nutritional sciences to further investigate the therapeutic value of flaxseed functional components and their dietary application in various food products and availability in processed foods as well as in the human cell line.

Nutr Hosp. 2012 Sep-Oct;27(5):1598-604. doi: 10.3305/nh.2012.27.5.5907.

Flaxseed energy and macronutrients balance.

Gonçalves de Oliveira C[1], Rodrigues Ferreira Cruz AC, Mayumi Nakajima V, Bressan J, de C Gonçalves Alfenas R, Mattes RD, Brunoro Costa NM.

BACKGROUND/OBJECTIVES: Flaxseed has functional properties in the reduction of the risk of chronic non-communicable diseases such as cardiovascular disease, diabetes and cancer. Regardless of its high energy density, the consumption of flaxseed tends to promote body weight maintenance. The purpose of this study was to evaluate energy and macronutrient balance after flaxseed consumption.

SUBJECTS/METHODS: Twenty four healthy volunteers were allocated into 3 experimental groups, when they consumed flaxseed (FS), defatted flaxseed flour (FF), or flaxseed oil (FO). During the control period they were provided a diet without flaxseed products for 7-9 days. Following that diets containing 70 g of one of the flaxseed products were consumed for another 7-9 day- period. Test foods were consumed exclusively in the laboratory and fecal excretion was collected during the study. There was a higher energy excretion ($P < 0.05$) in the FF and FS groups, compared to their control and FO group.

RESULTS: The excretions of total lipid and the PUFA α-linolenic acid were higher in FS group ($P < 0.05$).

CONCLUSIONS: The intake of 70 g/day of FS and FF raised lipid and energy excretion, which may mitigated the effect of flaxseedconsumption on body weight.

Recent Pat Food Nutr Agric. 2010 Nov;2(3):181-6.

Food applications for flaxseed and its components: products and processing.

Giada Mde L[1].

Flaxseed is the richest plant source of omega-3 fatty acid (α-linolenic acid) and the phytohormone lignans. It is also an essential source of high-quality protein and dietary fiber. Additionally, flaxseed has potential to be a source of phenolic compounds. Because of the beneficial physiological effects of its components, this seed is considered a functional food. It can contribute to the reduction of several diseases such as diabetes mellitus, arteriosclerosis and cancer. Food products and processing with regards to flaxseed are presented in this article. The article also presents some promising patents on food applications for flaxseed and its components. In addition, some potential opportunity areas are also discussed along with the impact of the use of this seed and its components in foods.

BMC Microbiol. 2010 Apr 16;10:115. doi: 10.1186/1471-2180-10-115.

Production of enterodiol from defatted flaxseeds through biotransformation by human intestinal bacteria.

Wang CZ[1], Ma XQ, Yang DH, Guo ZR, Liu GR, Zhao GX, Tang J, Zhang YN, Ma M, Cai SQ, Ku BS, Liu SL.

BACKGROUND: The effects of enterolignans, e.g., enterodiol (END) and particularly its oxidation product, enterolactone (ENL), on prevention of hormone-dependent diseases, such as osteoporosis, cardiovascular diseases, hyperlipemia, breast cancer, colon cancer, prostate cancerand menopausal syndrome, have attracted much attention. To date, the main way to obtain END and ENL is chemical synthesis, which is expensive and inevitably leads to environmental pollution. To explore a more economic and eco-friendly production method, we explored biotransformation of enterolignans from precursors contained in defatted flaxseeds by human intestinal bacteria.

RESULTS: We cultured fecal specimens from healthy young adults in media containing defatted flaxseeds and detected END from the culture supernatant. Following selection through successive subcultures of the fecal microbiota with defatted flaxseeds as the only carbon source, we obtained a bacterial consortium, designated as END-49, which contained the smallest number of bacterial types still capable of metabolizing defatted flaxseeds to produce END. Based on analysis with pulsed field gel electrophoresis, END-49 was found to consist of five genomically distinct bacterial lineages, designated Group I-V, with Group I strains dominating the culture. None of the individual Group I-V strains produced END, demonstrating that the biotransformation of substrates in defatted flaxseeds into END is a joint work by different members of the END-49 bacterial consortium. Interestingly, Group I strains produced secoisolariciresinol, an important intermediate of END production; 16S rRNA analysis of one Group I strain established its close relatedness with Klebsiella. Genomic analysis is under way to identify all members in END-49 involved in the biotransformation and the actual pathway leading to END-production.

CONCLUSION: Biotransformation is a very economic, efficient and environmentally friendly way of mass-producing enterodiol from defatted flaxseeds.

Br J Nutr. 2010 Apr;103(7):929-38. doi: 10.1017/S0007114509992753. Epub 2009 Dec 15.

Health effects with consumption of the flax lignan secoisolariciresinol diglucoside.

Adolphe JL[1], Whiting SJ, Juurlink BH, Thorpe LU, Alcorn J.

Flaxseed is the richest source of the lignan secoisolariciresinol diglucoside (SDG). After ingestion, SDG is converted to secoisolariciresinol, which is further metabolised to the mammalian lignans enterodiol and

enterolactone. A growing body of evidence suggests that SDG metabolites may provide health benefits due to their weak oestrogenic or anti-oestrogenic effects, antioxidant activity, ability to induce phase 2 proteins and/or inhibit the activity of certain enzymes, or by mechanisms yet unidentified. Human and animal studies identify the benefits of SDG consumption. SDG metabolites may protect against CVD and the metabolic syndrome by reducing lipid and glucose concentrations, lowering blood pressure, and decreasing oxidative stress and inflammation. Flax lignans may also reduce cancer risk by preventing pre-cancerous cellular changes and by reducing angiogenesis and metastasis. Thus, dietary SDG has the potential to decrease the incidence of several chronic diseases that result in significant morbidity and mortality in industrialised countries. The available literature, though, makes it difficult to clearly identify SDG health effects because of the wide variability in study methods. However, the current evidence suggests that a dose of at least 500 mg SDG/d for approximately 8 weeks is needed to observe positive effects on cardiovascular risk factors in human patients. Flaxseed and its lignan extracts appear to be safe for most adult populations, though animal studies suggest that pregnant women should limit their exposure. The present review discusses the potential health benefits of SDG in humans, with supporting evidence from animal studies, and offers suggestions for future research.

Int J Food Sci Nutr. 2009;60 Suppl 6:126-36.

Effect of flaxseed gum on reduction of blood glucose and cholesterol in type 2 diabetic patients.

Thakur G1, Mitra A, Pal K, Rousseau D.

The effects of ingestion of flaxseed gum on blood glucose and cholesterol, particularly low-density lipoprotein cholesterol, in type 2 diabetes were evaluated. Flaxseed gum was incorporated in wheat flour chapattis. Sixty patients of type 2 diabetes were fed a daily diet for 3 months, along with six wheat flour chapattis containing flaxseed gum (5 g), as per the recommendations of the American Diabetic Association. The control group (60 individuals) consumed an identical diet but the chapattis were without gum. The blood biochemistry profiles monitored before starting the study and at monthly intervals showed fasting blood sugar in the experimental group decreased from 154 ± 8 mg/dl to 136 ± 7 mg/dl (P=0.03) while the total cholesterol reduced from 182 ± 11 mg/dl to 163 ± 9 mg/dl (P=0.03). Results showed a decrease in low-density lipoprotein cholesterol from 110 ± 8 mg/dl to 92 ± 9 mg/dl (P=0.02). The study demonstrated the efficacy of flax gum in the blood biochemistry profiles of type 2 diabetes.

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Curr Top Nutraceutical Res. 2007;5(4):177-181.

The Effect of Flaxseed Supplementation on Hormonal Levels Associated with Polycystic Ovarian Syndrome: A Case Study.

Nowak DA[1], Snyder DC, Brown AJ, Demark-Wahnefried W.

Flaxseed is a rich source of lignan and has been shown to reduce androgen levels in men with prostate cancer. Polycystic ovarian syndrome (PCOS), a common endocrine disorder among women in their reproductive years, also is associated with high levels of androgens and is frequently accompanied by hirsutism, amenorrhea and obesity. This clinical case study describes the impact of flaxseed supplementation (30 g/day) on hormonal levels in a 31-year old woman with PCOS. During a four month period, the patient consumed 83% of the flaxseed dose. Heights, weights, and fasting blood samples taken at baseline and 4-month follow-up indicated the following values: BMI (36.0 vs. 35.7m/kg(2)); insulin (5.1 vs. 7.0 uIU/ml); total serum testosterone (150 ng/dl vs. 45 ng/dl); free serum testosterone (4.7 ng/dl vs. 0.5 ng/dl); and % free testosterone (3.1% vs. 1.1%). The patient also reported a decrease in hirsutism at the completion of the study period. The clinically-significant decrease in androgen levels with a concomitant reduction in hirsutism reported in this case study demonstrates a need for further research of flaxseed supplementation on hormonal levels and clinical symptoms of PCOS.

Forum Nutr. 2005;(57):100-11.

Health effects of phytoestrogens.

Branca F[1], Lorenzetti S.

Phytoestrogens are naturally occurring plant-derived phytochemicals, whose common biological roles are to protect plants from stress or to act as part of a plant's defense mechanism. Although composed of a wide group of nonsteroidal compounds of diverse structure, phytoestrogens have been shown to bind estrogen receptors and to behave as weak agonist/antagonist in both animals and humans. Phytoestrogens include mainly isoflavones (IF), coumestans, and lignans. These compounds are known to be present in fruits, vegetables, and whole grains commonly consumed by humans. IF are found in legumes--mainly soybeans--whereas flaxseed is a major source of lignans, and coumestans are significantly present in clover, alfalfa and soybean sprouts. 8-Prenyl flavonoids are common in vegetables. Bioavailability of IF requires an initial hydrolysis of the sugar moiety by intestinal beta-glucosidases to allow the following uptake by enterocytes and the flow through the peripheral circulation. Following absorption, IF are then reconjugated mainly to glucuronic acid and to a lesser degree to sulphuric acid. Gut metabolism seems key to the determination of the potency of action. Several epidemiological studies correlated high dose consumptions of soy IF with multiple beneficial effects on breast and prostate cancers, menopausal symptoms, osteoporosis, atherosclerosis and stroke, and neurodegeneration. For the relief of menopausal symptoms a consumption of 60 mg aglycones/day has been suggested; for cancer prevention a consumption between 50 and 110 mg aglycones/day is considered beneficial to reduce risks of breast, colon and prostate cancer; to decrease cardiovascular risk a minimum intake of 40-

60 mg aglycones/day, together with about 25 g of soy protein has been suggested. For improvement in bone mineral density, 60-100 mg aglycones/day for a period of at least 6-12 months could be beneficial.

American Journal of Clinical Nutrition Volume 79, Issue 2, February 2004, Pages 318-325

Supplementation with flaxseed alters estrogen metabolism in postmenopausal women to a greater extent than does supplementation with an equal amount of soy

Brooks, J.D., Ward, W.E., Lewis, J.E., Hilditch, J., Nickell, L., Wong, E., Thompson, L.U.

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Background: Phytoestrogens, which are abundant in flaxseed and soy, have chemical structures resembling those of endogenous estrogens and have been shown to exert hormonal effects, thereby affecting chronic diseases. Objective: We compared the effects of consuming equal amounts of flaxseed or soy on estrogen metabolism and biochemical markers of bone metabolism in postmenopausal women.

Design: In a parallel design, the diet of postmenopausal women (n = 46) was supplemented with either a placebo, soy (25 g soy flour), or flaxseed (25 g ground flaxseed) muffin for 16 wk. Blood and 24-h urine samples were collected at baseline and at the endpoint. Urine samples were analyzed for phytoestrogens, estrogen metabolites (2-hydroxyestrone, 16α-hydroxyestrone), and serum hormones (estradiol, estrone, estrone sulfate). Serum and urine samples were also analyzed for biochemical markers of bone metabolism.

Results: Urinary concentrations of 2-hydroxyestrone, but not of 16α-hydroxyestrone, increased significantly in the flaxseed group (P = 0.05). In the flaxseed group, the ratio of 2-hydroxyestrone to 16α-hydroxyestrone was positively correlated with urinary lignan excretion (r = 0.579, P = 0.02). In the soy and placebo groups, no significant correlation was observed. No significant change in serum hormones or biochemical markers of bone metabolism was observed within or between the treatment groups.

Conclusions: Supplementation with flaxseed modifies urinary estrogen metabolite excretion to a greater extent than does supplementation with an equal amount of soy. This modification by flaxseed is associated with an increase in urinary lignan excretion. Despite the shift in estrogen metabolism to favor the less biologically active estrogens, a negative effect on bone cell metabolism was not observed.

Nutr Cancer. 2001;39(1):58-65.

Flaxseed consumption influences endogenous hormone concentrations in postmenopausal women.

Hutchins AM[1], Martini MC, Olson BA, Thomas W, Slavin JL.

Lignans, similar in structure to endogenous sex steroid hormones, may act in vivo to alter hormone metabolism and subsequent cancer risk. The objective of this study was to examine effects of dietary

intake of a lignan-rich plant food (flaxseed) on serum concentrations of endogenous hormones and binding proteins (estrone, estrone sulfate, 17 beta-estradiol, sex hormone-binding globulin, progesterone, prolactin, dehydroepiandrosterone sulfate, dehydroepiandrosterone, androstenedione, testosterone, and free testosterone) in postmenopausal women. This randomized, crossover trial consisted of three seven-week feeding periods, during which 28 postmenopausal women, aged 52-82 yr, consumed their habitual diets plus 0, 5, or 10 g of ground flaxseed. Serum samples collected during the last week of each feeding period were analyzed for serum hormones using standard diagnostic kits. The flaxseed diets significantly reduced serum concentrations of 17 beta-estradiol by 3.26 pg/ml (12.06 pmol/l) and estrone sulfate by 0.09 ng/ml (0.42 nmol/l) and increased prolactin by 1.92 micrograms/l (0.05 IU/ml). Serum concentrations of androstenedione, estrone, sex hormone-binding globulin, progesterone, testosterone, free testosterone, dehydroepiandrosterone, and dehydroepiandrosterone sulfate were not altered with flaxseed feeding. In this group of postmenopausal women, consuming flaxseed in addition to their habitual diets influenced their endogenous hormone metabolism by decreasing serum 17 beta-estradiol and estrone sulfate and increasing serum prolactin concentrations.

Cancer Epidemiol Biomarkers Prev. 2000 Oct;9(10):1113-8.

Flaxseed influences urinary lignan excretion in a dose-dependent manner in postmenopausal women.

Hutchins AM[1], Martini MC, Olson BA, Thomas W, Slavin JL.

Dietary estrogens, such as lignans, are similar in structure to endogenous sex steroid hormones and may act in vivo to alter hormone metabolism and subsequent cancer risk. The objective of this study was to examine the effect of dietary intake of a lignan-rich plant food (flaxseed) on urinary lignan excretion in postmenopausal women. This randomized, cross-over trial consisted of three 7-week feeding periods during which 31 healthy postmenopausal women, ages 52-82 years, consumed their habitual diets plus 0, 5, or 10 grams of ground flaxseedper day. Urine samples collected for 2 consecutive days during the last week of each feeding period were analyzed for lignan content (enterodiol, enterolactone, and matairesinol) by isotope dilution gas chromatography/mass spectrometry. Compared with the 0-gram flaxseeddiet, consumption of 5 or 10 grams of flaxseed significantly increased excretion of enterodiol by 1,009 and 2,867 nmol/day, respectively; significantly increased excretion of enterolactone by 21,242 and 52,826 nmol/day, respectively; and significantly increased excretion of total lignans (enterodiol + enterolactone + matairesinol) by 24,333 and 60,640 nmol/day, respectively. Excretion of matairesinol was not significantly altered by flaxseed consumption. Consumption of flax, a significant source of dietary estrogens, in addition to their habitual diets increased excretion of enterodiol and enterolactone, but not matairesinol, in a dose-dependent manner in this group of postmenopausal women. Urinary excretion of lignan metabolites is a dose-dependent biomarker of flaxseed intake within the context of a habitual diet.

An open-label study on the effect of flax seed powder (Linum usitatissimum) supplementation in the management of diabetes mellitus.

Mani UV1, Mani I, Biswas M, Kumar SN.

Diabetes mellitus is characterized by hyperglycemia and associated with aberrations in the metabolism of carbohydrate, protein, and lipid that result in development of secondary complications. Extensive studies have indicated that nutritional therapy plays a pivotal role in the controlling or postponing of

development of these secondary complications. Several functional foods have been shown to possess hypoglycemic and hypolipidemic properties. Flax seed (FS) is a functional food that is rich in omega 3 fatty acids and antioxidants and is low in carbohydrates. In exploratory studies, FS was incorporated in recipes, which resulted in a reduction in the glycemic index of the food items. These observations prompted us to investigate the efficacy of FS supplementation in type 2 diabetics (n = 29). Subjects were assigned to the experimental (n = 18) or the control group (n = 11) on the basis of their desire to participate in the study. The experimental group's diet was supplemented daily with 10 g of FS powder for a period of 1 month. The control group received no supplementation or placebo. During the study, diet and drug intake of the subjects remained unaltered. The efficacy of supplementation with FS was evaluated through a battery of clinico-biochemical parameters. Supplementation with FS reduced fasting blood glucose by 19.7% and glycated hemoglobin by 15.6%. A favorable reduction in total cholesterol (14.3%), triglycerides (17.5%), low-density lipoprotein cholesterol (21.8%), and apolipoprotein B and an increase in high-density lipoprotein cholesterol (11.9%) were also noticed. These observations suggest the therapeutic potential of FS in the management of diabetes mellitus.