Manipulation of the Flaxseed Inhibits TNF-α and IL-6 production in ovarian-induced osteoporosis

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Introduction

- Ovarian hormone deficiency is a major risk factor for osteoporosis in postmenopausal women.[1,2]. Estrogen replacement therapy (ERT) has long been used to alleviate postmenopausal symptoms and lowers the risk of osteoporosis. However, estrogen treatment is associated with a higher risk of certain types of cancer or contraindications.[3,4]

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Introduction

- Phytoestrogens, are compounds found in plants and plant products that possess some estrogenic or antiestrogenic activity.
- These phytoestrogens may act as estrogen antagonists in mammary gland and in contrasts they act as estrogen agonists in bone.[7]
- Lignans, one type of phytoestrogen, are diphenolic compounds similar in structure to endogenous non-steroid hormones and are hypothesized to act *in vivo* to alter hormone metabolism and subsequent bone metabolism[8].

Introduction

- Flaxseed, one of the edible plant foods is the highest rich source of lignans,
- Flaxseed is also a rich source of polyunsaturated fatty acid (PUFA), especially linolenic acid (18:3 n-3).[10] α-linolenic acid (ALA)
- It may decrease the rate of bone resorption by inhibiting the biosynthesis of cytokines such as prostaglandins, interleukins and tumor necrosis factors.[11] .

Introduction

- Oxygen-derived free radicals, resulting from excessive production of reactive oxygen species perturb the normal redox balance of osteogenesis including bone formation and resorption.
- These findings indicate that free radicals have marked capacity to degenerate the bone metabolism and enhance osteoclast formation and bone resorption.
- Oxidative stress, is involved in the pathogenesis of bone loss in female rats due to chronic inflammatory diseases, aging, and osteoporosis.[12]

Introduction

- Lignans present in flaxseed may possess antioxidant properties. Therefore, flaxseed may reduce the rapid rate of bone loss experienced by postmenopausal women, in part, by enhancing antioxidant status and exerting a positive effect on bone. All cells can utilize glucose for energy production.
- flaxseed oil has been shown to decrease TNF-α and IL-1 in human peripheral blood mononuclear cells.
- Modulation of the dietary n-6 to n-3 ratio has been shown to be beneficial in various clinical inflammatory diseases[17-18] and animal models of bone metabolism. [19-21]

Aim of study

- The aim of study is to examine the effect of dietary intake of flaxseed and/or flax oil as therapeutic functional foods on pro-inflammation cytokines induced in ovariectomized rats model osteoporosis.

Material &Methods.

- **Experiment procedure.**

  Forty eight, three months old female sprag-dawly rats were randomly divided into 6 groups: group 1-sham + control diet; Group 2-OVX rats + basal diet; Group 3 - OVX + 20% of whole FS; Group 4- OVX + 40% FS; Group 5 - OVX + 5% FO; Group 6 - OVX + 10% FO. All OVX rats underwent bilateral ovariectomy. The experiment was continued for two months.

- **Methods**.

  Serum bone alkaline phosphatase (B-ALP), interleukin -6 (IL-6), tumor necrosis factor- alpha (TNF- α), calcium (Ca), phosphorous (P) and magnesium (Mg) were measured.

Results

- **Results:** A significantly increase of serum IL-6 and TNF- α concentrations were observed between OVX when compared with Group 1, while no significant difference in the activity of B-ALP, serum Ca, P and Mg among all groups. A remarkable significant decrease of serum levels of IL-6 and TNF-α was observed in rats that fed FS (group 3 and 5) and FO (Group 5 and 6).

Table 1 - Composition of the control diet based on AIN 93 slandered diet.

Component	Corn	Flax			
		Flax powder 10%	Flax powder 20%	Flax oil 5%	Flax oil 10%
Casein	200	200	200	200	200
Cornstarch	367.50	167.5	0	367.50	367.48
Dyetrose	132	132	132	132	132
Sucrose	100	100	100	100	100
Cellulose	50	50	15	50	50
Corn oil	100	100	100	50	0
Flaxseed powder	0	200	400	0	0
Flaxseed oil	0	0	0	50	100
Butylhydroquinone	0	0.02	0.02	0.02	0.02
l-Cystine	3.0	3.0	3.0	3.0	3.0
Choline bitartrate	2.5	2.5	2.5	2.5	2.5
Mineral mix2	35	35	35	35	35

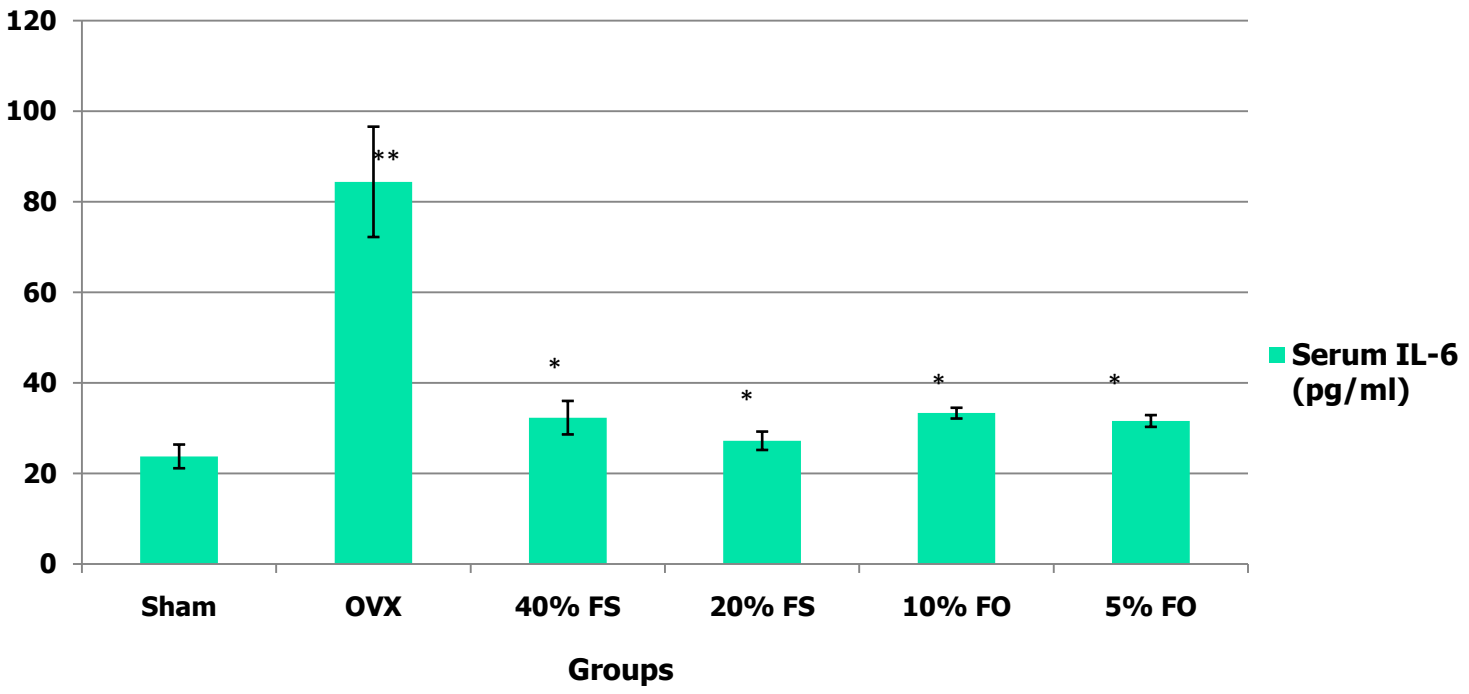
Table 2: Effects of ovariectomized, whole flaxseed and flax oil on food intake, body weight and relative weight organs

Parameters	Sham	OVX	FS		FO	
			10%	20%	5%	10%
Food intake (g/day/rat) P<	10.84 ±0.41	15.38 ±0.40 0.001	13.16 ±0.21 0.008	11.07 ±0.49 0.003	12.05 ±0.63 0.01	11.04 ±0.82 0.004
Bodyweight(g) Initial Final P<	155.4±5.03 210±6.98	154.6±9.04 242.6±10.93 0.0001	154.0±8.14 245.4±8.33 0.0001	154.2±6.73 265.2±9.69 0.0001	154±8.97 235.6±7.82 0.0001	154.2±8.54 234.4±10.39 0.0001
Organs weight (g/100g b.wt) Uterus Livers	0.32 ±0.03 5.22 ±0.356	0.21 ±0.05 4.90 ±0.293	0.19 ±0.03 5.40 ±0.174	0.18 ±0.04 5.86 ±0.122	0.20 ±0.04 4.74 ±0.29	0.19 ±0.06 4.60 ±0.354

Table (3): The levels of biochemical parameters in ovariectomy rats, feeding whole flaxseed and flax oil, 2 months treatment

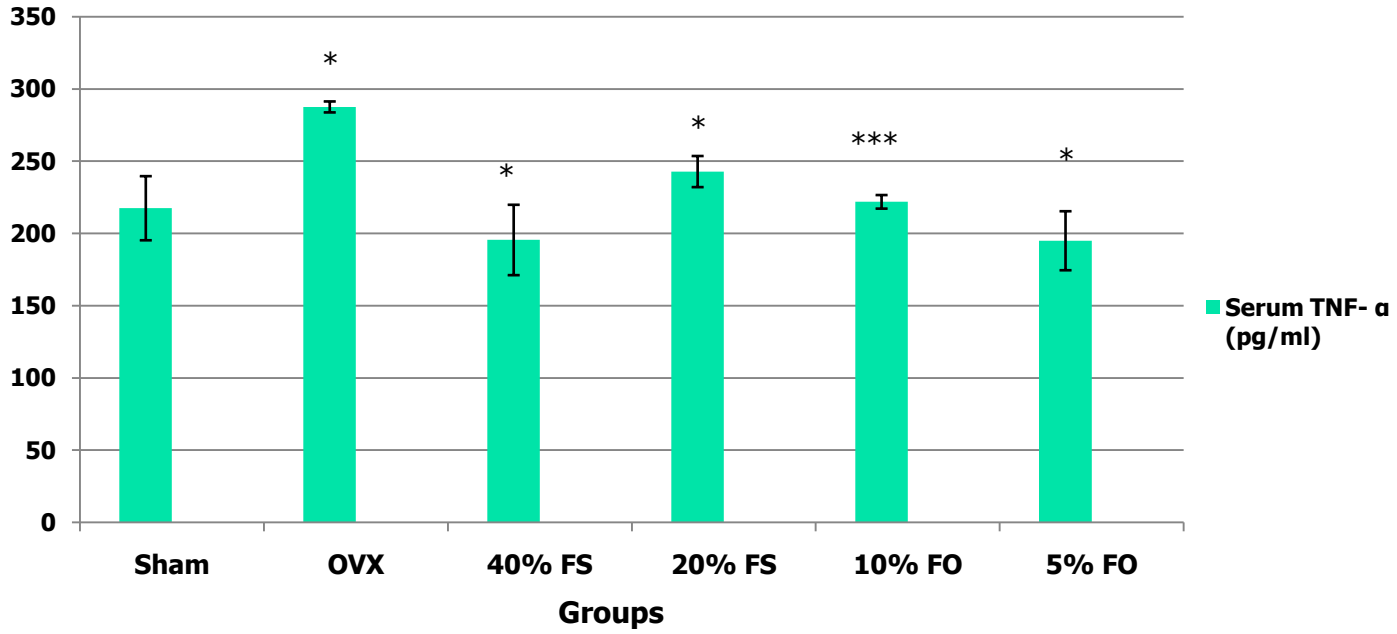
	Group 1	Group 2	Group 3 Flaxseed 10%	Group 4 Flaxseed 20%	Group 5 Flax oil 5%	Group 6 Flax oil 10%
S. Ca (mg/dl)	11.00 ±0.21	11.15 ±0.28	10.54 ±0.33	11.23 ±0.21	11.08 ±0.20	11.15 ±0.34
S. P (mg/dl)	4.61 ±0.16	5.13 ±0.26	45.17 ±0.14	4.73 ±0.17	4.94 ±0.16	4.75 ±0.12
S. Mg (mg/dl)	2.65 ±0.04	2.61 ±0.02	2.62 ±0.07	2.65 ±0.14	2.65 ±0.04	2.61 ±0.04
S.B-ALP(pg/ml)	21.14 ±1.56	20.30 ±0.51	21.78 ±1.84	22.48 ±1.30	18.94 ±0.85	19.08 ±1.31

Figure 2 - Effect of dietary whole flaxseed (FS) and flax oil (FO) on interlukin-6 (IL-6) for 2 mo in ovariectomized rats.



FS gps (20% and 40%) vs OVX gp & FO gps (5% and 10%) vs OVX gp for 2 mo. The plotted data represent the mean ± S.E. for each dietary treatment group. *p<0.05 and **p<0.01

Figure 2 - Effect of dietary whole flaxseed (FS) and flax oil (FO) on tumor necrosis factor- α (TNF-α) for 2 mo in ovariectomized rats.



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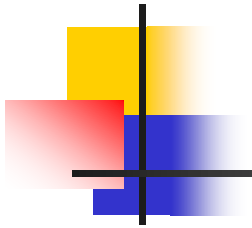
In conclusion

- This study is encouraging and may be promising for consumption of FS lignans as a potential alternative therapy to prevent osteoporosis associated ovarian deficient-women.
- However, the biological effects observed can attribute to particular contents, as many compounds are present in FS. Further studies are needed to demonstrate their efficacy in humans by using bioactive components of FS and to clarify their mechanism of action.



Thank You