

## Effects of Flaxseed (*Linum usitatissimum*) on Postmenopausal Symptoms and its Clinical Parameters

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### Abstract

Menopause is the irreversible and permanent cessation of menstruation after one year of amenorrhea. Common symptoms include vaginal dryness, hot flushes, night sweating, and bone pain. Traditionally *Linum usitatissimum* (Flaxseeds) has been used for the treatment of postmenopausal symptoms. However, the effect of this medicinal herb on the satiety hormone; leptin and body weight in menopausal women has not been elucidated well. This study was designed to evaluate the effect of flaxseeds on serum estrogen, progesterone, leptin, and malondialdehyde, body mass index and blood pressure in healthy women. Moreover, the flaxseed effect on climacteric symptoms was also investigated. The study was an open-label interventional clinical trial. It was a six-weeks (short duration) oral administration of 1000 mg flaxseed powder twice daily by menopausal women. Serum levels of estrogen, progesterone, and leptin hormones as well as total plasma malondialdehyde were determined pre-and-post flaxseed intervention. Clinical symptoms and bothersome complaints of postmenopausal women such as hot flushes, vaginal dryness, bone pain, and night sweating were also evaluated. Furthermore, blood pressure elements and body mass index were also measured. The results showed that *Linum usitatissimum* seed powder significantly reduced vaginal dryness, hot flushes, bone pain, and night sweating in menopausal women. The same dose of flaxseed had no significant effects on serum estrogen and progesterone. However, it significantly decreased serum malondialdehyde and increased serum leptin. Flaxseed had a non-significant effect on body mass index and blood pressure. In conclusion *Linum usitatissimum* seed had significant effect in relieving vasomotor symptoms and increasing serum levels of leptin in menopausal women.

**Keywords:** Climacteric, Estrogen, Progesterone, Leptin, *Linum usitatissimum*, Malondialdehyde, Menopause, Progesterone.

### آثار بذور الكتان (*Linum usitatissimum*) على أعراض سن اليأس والمعايير السريرية في النساء بعد سن اليأس

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### الخلاصة

سن اليأس هو مرحلة انتهاء دورات الحيض بصورة دائمة ويتم التشخيص بذلك بعد مرور سنة كاملة من دون دورة شهرية. الأعراض الشائعة لهذه المرحلة هي جفاف المهبل، هبات الحرارة، التعرق الليلي والالام العضام. تم تقليدياً استخدام بذور الكتان لعلاج أعراض المصحوبة بالسن اليأس. ولكن لم يتم توضيح تأثيرها على الهرمون الشبع الليبتين ومؤشر كتلة الجسم. لذلك تم تصميم هذا البحث لتقييم تأثير بذور الكتان على نسبة هورمون الأستروجين و البروجسترون و الليبتين و عامل الأأكسدة مالونديالدهايد و مؤشر كتلة الجسم و الضغط الدم في مجموعة من النساء في السن اليأس. تم تصميم البحث على شكل تداخلي قبل و بعد تناول المادة. تضمنت الدراسة تناول 1000 ملغم من مسحوق البذور لدى المشاركين في الدراسة مرتين باليوم لمدة ستة أسابيع. تم تحليل نسبة الدم لهورمون الأستروجين و البروجسترون و الليبتين وكذلك نسبة مالونديالدهايد قبل و بعد تناول البذور. وتم تقييم الأعراض السريرية و المعاناة المزجة لهذه الحالة منها الهبات الحرارة، جفاف المهبل، التعرق الليلي والالام العضام و كذلك ضغط الدم وقياس مؤشر كتلة الجسم. أظهرت النتيجة بأن بذور الكتان خفضت شدة التعرق الليلي في النساء المشاركات في البحث. حيث لم يوجد تأثير كبير على نسبة الأستروجين و البروجسترون و لكن انخفضت نسبة مالونديالدهايد و ارتفعت نسبة الليبتين في الدم. لم يحدث تغير كبير في مؤشر كتلة الجسم و ضغط الدم لدى المشاركات في البحث. نستنتج من ذلك بأن لبذور الكتان تأثير كبير وواضح على تقليل وارتياح من الأعراض الحركية الوعائية وتخفيض عامل الأأكسدة و ارتفاع نسبة هورمون الشبع الليبتين في الدم عند المرأة في السن اليأس.

الكلمات المفتاحية: سن اليأس، الأستروجين، البروجسترون، الليبتين، مالونديالدهايد

### Introduction

Menopause is a naturally occurring phenomenon that is not related to a pathological condition. It is characterized by hormonal changes, permanent and irreversible cessation of menstruation.

A woman who has experienced twelve consecutive months of amenorrhea is confirmed to be diagnosed as menopause. The typical age for menopause to occur in most women is 45-52 years<sup>(1,2)</sup>.

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The majority of women experience complicated symptoms, such as hot flushes, night sweats “i.e. vasomotor symptoms”, disturbance of sleep and sexual dysfunction, mood change, weight gain, bone pain, and cognitive impairment. Furthermore, menopause has an impact on other body systems such as genitourinary, cardiovascular, and psychogenic<sup>(3)</sup>. Menopause-associated symptoms such as vulvovaginal atrophy, atrophic vaginitis, or urogenital atrophy which are recently named as genitourinary syndrome of menopause usually last five to seven years although they may persist longer. These health consequences of menopause are thought to be caused by the lack of estrogens during menopause<sup>(4,5)</sup>.

Typically, the primary treatment for menopausal symptoms is hormonal therapy. However, due to the adverse effects associated with the use of hormones, most women cannot use this approach<sup>(6)</sup>. Herbal products enriched with estrogen are frequently used in relieving menopause symptoms. Phytoestrogenic herbs elevate the level of estrogen in menopause women and can attenuate the frequency of vasomotor symptoms via escalation of the estrogen level and regulating the hormonal balance<sup>(7,8)</sup>.

Phytoestrogens can be found in grains, vegetables, and fruits of many medicinal plants. Flaxseed (*Linum usitatissimum*); is regarded as a well-known and enriched source of phytoestrogens, it is a member of the genus *Linum* in the family *Linaceae*. *Linum usitatissimum* oil has been traditionally used for the treatment of menopause symptoms. It has a unique nutrient profile that contains omega-3 fatty acids, lignans,  $\alpha$ -linolenic acid, protein, and fiber<sup>(9)</sup>. Hypo estrogenic state during menopause age is proven to enhance metabolic dysfunction thus leading to higher body mass<sup>(10)</sup>. A preclinical study proposed the anti-obesity effect of flaxseed in an animal model of metabolic syndrome via a mechanism in which flaxseed is capable of removing leptin resistance then enhance lipolysis and fatty acid oxidation and inhibiting lipogenesis<sup>(11)</sup>. Leptin is a protein mainly synthesized in adipose tissue, and its production is associated with total body fat<sup>(12)</sup>, it acts as a satiety hormone by acting on the hypothalamic centers, and suppressing appetite and food intake, thereby regulating body weight homeostasis<sup>(13,14)</sup>. In the previous studies, various levels of leptin have been recorded in postmenopausal women when compared with premenopausal women, some have increased<sup>(15)</sup>, equal<sup>(16)</sup>, or decreased leptin levels<sup>(17)</sup>, these discrepancies may be associated with concomitant changes in body mass index (BMI), body composition, and insulin sensitivity along with declining endogenous estradiol levels<sup>(14)</sup>. The effect of this medicinal herb on the satiety hormone; leptin and body weight in menopausal women has not been elucidated well.

Based on many clinical and pre-clinical studies, this plant has also been suggested to have an ameliorative effect on postmenopausal symptoms<sup>(18,19)</sup>. One of the speculated mechanisms is through the modulation of oxidative stress. A decrease in estrogen production in menopause women, obesity and aging causing an imbalance in oxidative stress<sup>(20-22)</sup>. Malondialdehyde as a marker of oxidative stress is elevated in post menopause compared to their premenopausal peer, it can be used as a marker of cardiovascular risk<sup>(23)</sup>.

Although advanced work on the beneficial action of flaxseed have been conducted however, the flaxseed antioxidant effect on improving clinical symptoms and oxidative stress in menopause women remain to be elucidated and there is no enough research to support a recommendation for its use. Therefore, this study was designed to evaluate the potential effects of flaxseeds on serum estrogen, progesterone, the satiety hormone leptin, and malondialdehyde and to investigate the climacteric symptoms in postmenopausal women using flaxseed powder for six weeks.

## Subjects and Methods

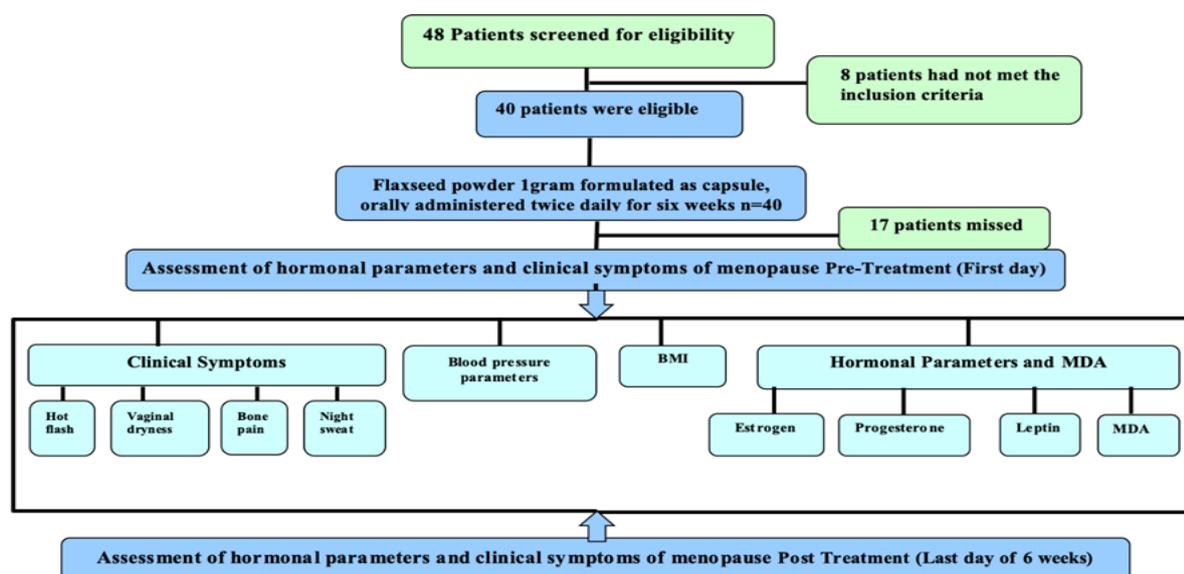
### Study design and setting

The study was an open-label interventional clinical trial; it was conducted at the outpatient's unit in Maternity Teaching Hospital in Erbil/Kurdistan Region. The duration of the study was eight months from July 2020 to February 2021 including patient recruitment, follow up and data analysis. It was carried out under the Declaration of Helsinki and its amendments to the Ethical Guidelines for Human Studies and the currently adopted regulations of the Iraqi Ministry of Health. Approval of this study was obtained before its onset from the Ethical Committee of Hawler Medical University. All the women included were informed about the nature and scope of the study and written informed consent was obtained from each before participation in the study. Eligible women diagnosed as menopausal by senior gynecologists were selected. A total of 48 patients were screened for eligibility. Forty patients were eligible for inclusion. Twenty-three patients completed the six-weeks study, seventeen patients were dropped out from the study (Figure 1).

The study was a six-week oral administration of 1000mg flaxseed powder twice daily, the dose was selected based on the previous studies with modification<sup>(24-26)</sup> (Figure 1). Flaxseed powder was prepared by grinding the seeds, then a capsule dosage form was prepared from the milled powder, it was given with full instruction. The duration of the study was eight months including patient enrollment, intervention, follow up and laboratory investigations. Weight (in kilograms) and height (in centimeters) were measured while

participants were wearing light clothing and no shoes. Blood pressures (BP) were recorded in a sitting position with a standard mercury

sphygmomanometer after minutes of rest. All the participants have been instructed to eat flaxseed-free diet.



**Figure 1.** Flow chart of the study design. BMI; body mass index, MDA; Malondialdehyde.

***Inclusion criteria***

The included participants in this study were the postmenopausal women (last menstrual bleeding was at least 1 year before) who were diagnosed by a gynecologist, who had not taken any hormonal therapy, supplements, vitamins, phytoestrogens six months before the recruitment. Women between the ages range of 47 to 59 years were included in the study. All the participants have been informed to eat flaxseed-free diet.

***Exclusion criteria***

Patients who underwent oophorectomy, hysterectomy, or patients with chronic disease such as hypertension, diabetes mellitus, thyroid disease (hypothyroidism / hyperthyroidism) or cardiovascular disease, cancer, and women who received hormone replacement therapy were excluded.

***Blood sample***

Five milliliters of blood samples were drawn from each patient in the morning. Blood samples have been taken before (first day) and after the treatment (last day after six weeks) to determine estrogen, progesterone, leptin hormones, and malondialdehyde (MDA) levels in the post-menopausal women. Venous blood samples were drawn into plain tubes without anticoagulants. The blood was allowed for 30 minutes to clot and after centrifugation for 5 minutes at 3000 rpm; the serum was collected in a plain tube and kept frozen for analysis.

***Outcome measures***

Serum levels of estrogen, progesterone, and leptin hormones were determined pre-and post-treatment (i.e. at day 1 and at day 42) using an Enzyme-linked immunosorbent assay (ELISA) kit. Additionally, antioxidant status was observed, and particularly the concentration of total plasma MDA was determined pre-and post-treatment. Clinical symptoms and bothersome complaints of post menopause women such as bone pain, vaginal dryness, night sweat and hot flushes were also evaluated pre and post-flaxseed intervention. Bone pain was measured by using visual analogue scale (VAS). While hot flushes and night sweat were measured based on women own self-reports, the women were provided with a diary and instructed to record the time when hot flushes and night sweat occur with its severity rating mild, moderate and severe (27). Furthermore, blood pressure elements and BMI were also measured twice. To monitor patient adherence to the study protocol and appearance of possible adverse effects, weekly telephone calls were done to all the participants.

***Statistical analysis***

All Data were expressed as mean ± standard error of means (M ± SEM) and statistical analysis was carried out using statistically available software (SPSS, version 24). A Chi-square test for the association was used to compare proportions. The student's t-test was used to compare two means. A P-value of less than 0.05 was considered statistically significant.

Parameters	Flaxseed treated-participants n=23
Age (year) ± SD	57.13±2.89
Body mass index (kg/m <sup>2</sup> ) ± SD	27.72±0.36
Duration of menopause period (month) ± SD	6.25 ±1.1
Estrogen (pg./ml)	39.48±16.71
Progesterone (ng/ml)	0.33±0.03

**Results**

1-The basic characteristics of the participants has been summarized in Table (1).

**Table1. Basic characteristics of the participants n=23.**

2-Effects of *Linum usitatissimum* on serum estrogen and progesterone level in post-menopause women. After six weeks of daily administration of *Linum usitatissimum* powder for women presenting with menopausal symptoms, flaxseed has no significant effect on estrogen and progesterone level as shown in Table(2).

**Table2. Effect of *Linum usitatissimum* powder on serum estrogen and progesterone levels in post-menopause women (n=23). Non-significant P-value is ≥ 0.05**

Parameters	Pre- Flaxseed intervention (mean±SE)	Post-Flaxseed intervention (mean±SE)	p. value
Estrogen (pg/ml)	39.48 ± 16.71	33.32 ± 13.62	0.408
Progesterone(ng/ml)	0.33 ± 0.03	0.35 ± 0.03	0.577

3-The effect of *Linum usitatissimum* on Leptin and malondialdehyde in women presented with post-menopausal symptoms. Daily administration of 1000 mg *Linum usitatissimum* powder for six weeks

significantly increased serum leptin level and significantly decreased serum malondialdehyde as showed in the Table(3).

**Table3. Effect of daily administration of *Linum usitatissimum* powder on serum leptin and malondialdehyde level in post-menopause women for six weeks (n=23).**

Parameters	Pre-Flaxseed intervention (mean±SE)	Post-Flaxseed intervention (mean±SE)	p. value
Leptin (ng/ml)	53.13 ± 7.16	73.84 ± 6.42	0.004 **
Malondialdehyde(nmol/ml)	77.43 ± 15.30	40.80 ± 6.44	0.007 **

\*\*indicates significant P-value is <0.01

4-Effect of *Linum usitatissimum* on body mass index in postmenopausal women. Flaxseed powder had no significant effect on the body mass index

(BMI) after six weeks of daily administration in women presenting with menopausal symptoms in Table(4).

**Table4. The effect of *Linum usitatissimum* on body mass index in women presented with post-menopausal symptoms.**

Parameters	Pre- Flaxseed intervention (mean±SE)	Post-Flaxseed intervention (mean±SE)	p. value
Body mass index(kg/m <sup>2</sup> )	27.72 ± 0.36	27.75 ± 0.38	0.668

Non-significant P-value is ≥ 0.05

5-Effect of *Linum usitatissimum* on Diastolic blood pressure, Systolic blood pressure, Mean blood pressure, and Heart rate in post-menopausal women. Six weeks of daily administration of flaxseeds

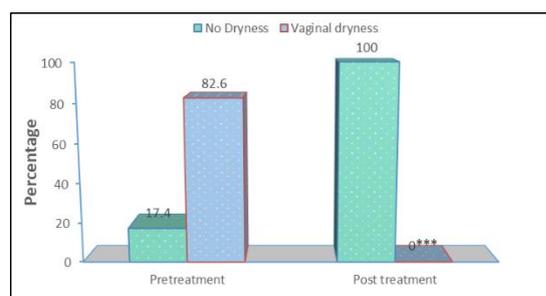
powder showed no significant effects on diastolic blood pressure, systolic blood pressure, mean blood pressure, and heart rate Table(5) in post-menopausal women.

**Table5. Effect of Linum usitatissimum on Diastolic blood pressure, Systolic blood pressure, Mean blood pressure, and Heart rate before and after treatment (n=23).**

Parameters	Pre- Flaxseed intervention (mean±SE)	Post-Flaxseed intervention (mean±SE)	p. value
Diastolic blood pressure (mmHg)	67.82 ± 1.21	69.69 ± 1.09	0.257
Systolic blood pressure (mmHg)	120.73 ± 2.31	121.52 ± 2.23	0.350
Mean blood pressure (mmHg)	85.39 ± 1.47	86 ± 1.30	0.320
Heart rate (b/min)	71.34 ± 1.38	71.08 ± 0.87	0.871

Non-significant P-value is ≥ 0.05

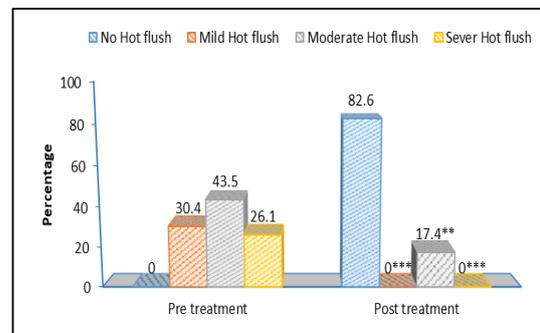
6-The effect of Linum usitatissimum on vaginal dryness in postmenopausal women. Daily administration of Linum usitatissimum powder for six weeks significantly reduced vaginal dryness (p-value = 0.001) in women presented with postmenopausal symptoms as showed in Figure (2).



**Figure 2. Effect of Linum usitatissimum on vaginal dryness in postmenopausal women (n=23).**

\*\*\*indicates significant P-value is ≤ 0.001

7-The effect of Linum usitatissimum on Hot flush in post-menopausal women. After six weeks of daily administration, Linum usitatissimum powder significantly reduced the frequency of hot flushes (p-value = 0.001) in post-menopausal women presented with a history of a hot flush (Figure 3).



**Figure 3. The effect of Linum usitatissimum on symptoms of a hot flush in post-menopausal women (n=23).** \*\*indicates significant P-value is ≤ 0.01 and \*\*\*indicates significant P-value is ≤ 0.001.

8-The effect of Linum usitatissimum on bone pain in post-menopausal women using visual analogue scale (VAS).

Linum usitatissimum significantly reduced bone pain measured by visual analogue scale (VAS) in menopausal women who presented with a history of bone pain after six weeks of daily use of flaxseed powder as shown in Table(5).

**Table5. Effect of Linum usitatissimum on bone pain in post-menopause women (n=23).**

Symptoms		Severe	Moderate	Mild	P-Value
		(n) %	(n) %	(n) %	
Bone pain (measured by VAS)	Pre-Flaxseed intervention	(4) 17.4	(12) 52.2	(7) 30.4	0.005**
	Post-Flaxseed intervention	(1) 4.3	(5) 21.7	(9) 39.1	

\*\*indicates significant P-value is ≤ 0.01

9-The effect of Linum usitatissimum on night sweating in post-menopausal women. Daily ingestion of flaxseed for six weeks significantly reduced the symptoms of the night

sweating in women who presented with menopausal symptoms as showed in Table(6).

**Table6. Effect of Linum usitatissimum powder on night sweating in post-menopausal women (n=23).**

Symptoms		Severe	Moderate	Mild	p.value
		(n) %	(n) %	(n) %	
Night sweating measured by women's own self-reports)	Pre-Flaxseed intervention	(8) 34.8	(9) 39.1	(6) 39.1	0.001***
	Post-Flaxseed intervention	(1) 4.3	(2) 8.7	0	

\*\*\*indicates significant P-value is ≤ 0.001

## Discussion

More than two-thirds of the women in the menopause period have some symptoms such as hot flush, night sweating, vaginal dryness, and sleep disturbances are due in part “not entirely” to estrogen depletion<sup>(28)</sup>. These symptoms are frequent and may be severe that can cause considerable emotional distress. Many treatment approaches exist to alleviate these bothersome symptoms, including hormone replacement therapy, non-hormone drug treatment, and plant-based therapies such as soybean, lentils as a source of isoflavones, and flaxseed, vegetables, grains, fruits as lignans phytoestrogen sources<sup>(29)</sup>. Safety concerns regarding hormone replacement therapy have developed an interest in the use of phytoestrogens in the management of complaints associated with menopause age. Flaxseed extract is the main origin of lignan phytoestrogen named secoisolariciresinol diglucoside. After ingestion and in the colon, it is converted into enterodiol and enterolactone; the active mammalian lignans<sup>(30)</sup>. In the previous studies when postmenopausal women used a flaxseed supplement diet, their menopausal symptoms were decreased and their quality of life has improved<sup>(24)</sup>.

The health benefits of flax meal are due to its alpha-linolenic acid<sup>(31)</sup>, fiber<sup>(32)</sup>, and lignan<sup>(33)</sup>. The high omega-3 and protein content also make flaxseed meals unique and superior to other fiber supplements and food ingredients<sup>(26)</sup>.

The mammalian lignans are believed to work by binding to estrogen receptors on cell membranes. they show low estrogenic activity or anti-estrogenic activity with potentially pharmacological advantages<sup>(34)</sup>.

In the current study, intake of one gm flaxseed for six weeks showed no significant effect on total serum estrogen and serum progesterone. However, in a clinical study, menopause women consuming 10g ground flaxseed daily for 7 weeks significantly reduced serum level of 17- beta-estradiol and estrone sulfate and increasing serum prolactin concentrations<sup>(35)</sup>.

Additionally, in another clinical intervention, Haggans et al showed that 10g flax consumption daily for 7 weeks significantly increases the 2-hydroxy estrone/16- $\alpha$  hydroxy estrone ratio in urine and the 2-hydroxy estrone excretion levels were higher of 10 g/day flax group compare to the control group, this difference in the result may be mostly due to the dosage of flaxseed and the duration of therapy<sup>(36)</sup>.

Effects on the other endogenous sex hormones were not statistically significant this finding suggested that flaxseed affects certain circulating sex hormone levels in favor of prevention of breast cancer since a high ratio of 2-hydroxylation to 16-  $\alpha$  hydroxylation pathway estrogen metabolites have been associated with reduced breast cancer risk<sup>(37)</sup>.

In this study, after six weeks of flaxseed intake, flaxseed increased the serum level of leptin in post-menopause women, when compared with pre-treatment serum level. This rise in serum leptin levels in post-menopausal women could be related to flaxseed high content of omega-3- 3 fatty acid and  $\alpha$ -linolenic acid which increases leptin expression<sup>(26,38)</sup>. McCullough et al reported that consumption of flaxseed significantly increased plasma and adipose levels of  $\alpha$ -linolenic acid and consequently leptin levels were elevated in animals (rabbits) taking a diet supplemented with 10 % flaxseed (10gm flaxseed /100gm regular rabbit diet in that study. Changes in leptin expression by flaxseed supplementation are inversely correlated with the risk of atherosclerosis and effects on lipid metabolism through reducing total cholesterol, LDL, and increasing HDL levels<sup>(38)</sup>. A systematic review and meta-analysis of randomized controlled trials on the effect of flaxseed supplementation on circulating adiponectin and leptin concentration in adults reported that flaxseed supplementation had no significant effect on adiponectin and leptin levels in adults<sup>(39)</sup>.

Although in the current study consumption of 1000 mg of flaxseed powder has no significant effect on BMI. However, a meta-analysis that included 45 randomized placebo-controlled trials showed a significant reduction in body weight, BMI, and waist circumference following long-term supplementation of flaxseed i.e. more than 12 weeks, in doses  $\geq 30$  g/day durations, this controversial finding might be related to the smaller quantity and shorter duration of flaxseed consumed in the present study. Flaxseed consumption decreases BMI due to the presence of dietary fiber, as flaxseed is a rich source of dietary fiber both soluble as well as insoluble fibers. Dietary fibers from flaxseed were found to have a direct relation to health in particular in body weight regulation through diminished nutrient absorption<sup>(40,41)</sup>. Additionally, a recent in vivo study conducted by Luo et al. has elucidated the mechanism of the ant obesity effect of flaxseed polysaccharide via inducing satiety due to removal of leptin resistance and enhancing lipid metabolism through the AMP-Activated Protein Kinase (AMPK) signaling pathway and suppression of lipogenesis<sup>(11)</sup>.

The menopause transition period is accompanied by dysregulation of lipid metabolism and production of many adipocytokines, proinflammatory cytokines, and reactive oxygen species which cause lipid peroxidation<sup>(42)</sup>. The current study aimed to attenuate the deleterious effect of oxidative consequences of this metabolic alteration by flaxseed. Administration of flaxseed in this study to women presented with symptoms of menopause showed a statistically significant reduction in malondialdehyde serum level. The result is

consistent with the finding of other studies that demonstrated the antioxidant potential of flaxseed and its phenolic components<sup>(43-45)</sup>.

It was found that the phenolic compounds (lignans, phenolic acid, flavonoids, phenylpropanoids, and tannins) of flaxseeds are excellent in preventing the excess of free radicals and avoiding their pathological effects. Phenolic compounds exert their antioxidant effect by acting as reducing agents, hydrogen donors, singlet oxygen quenchers, or metal chelators<sup>(45)</sup>.

Furthermore, the reduction in malondialdehyde serum level could be achieved through the flaxseed-rich content of the  $\alpha$ -linolenic acid, because  $\alpha$ -linolenic acid can be stored in adipose tissue, and some of its beneficial actions may be due to its effects on the adipose tissue.

Consumption of 1000 mg flaxseed for six weeks showed a non-significant change in mean blood pressure, systolic blood pressure, and diastolic blood pressure in normotensive post-menopause women. However, in a coronary heart disease high-risk population consuming a diet with alpha-linolenic acid there was a decrease in diastolic blood pressure, and increase serum triacylglycerol concentration<sup>(46)</sup>. Additionally, in patients with hypertension flaxseed consumption reduces blood pressure by altering circulating oxylipins "derived from polyunsaturated fatty acids regulate vascular tone" via an  $\alpha$ -linolenic acid-induced inhibition of soluble epoxide hydrolase<sup>(47)</sup>.

Wilkinson et al., (2005) measured the diet-related change in blood pressure and total peripheral resistance responses to a diet high in flaxseeds, they recorded a non-significant change in systolic and diastolic blood pressure<sup>(48)</sup>. However, in patients with peripheral arterial disease intake of 30g of milled flaxseed per day for six months resulted in significant decreases in both systolic and diastolic blood pressure<sup>(49)</sup>. Whereas this result disagreed with the meta-analysis carried out by Khalesi et al (2015) who recorded an improvement in diastolic blood pressure after consuming whole flaxseed for twelve weeks' duration<sup>(50)</sup>.

Daily consumption of 1000 mg flaxseed for six weeks in women presenting with menopausal symptoms showed a significant reduction in frequency and duration of menopausal symptoms such as hot flashes and night sweat, this effect was not consistent with the clinical studies conducted on postmenopausal women in which the participants had been allocated in different groups for consuming flaxseed, the results of those studies showed that consumption of a flaxseed-rich diet is not more effective than a placebo in alleviating the climacteric symptoms of postmenopausal women<sup>(51,19)</sup>.

In the current study, all the post-menopausal women had less dry vagina when they have taken 1000 mg of flaxseed powder for six weeks. A similar result was observed in postmenopausal women who

have taken 1 g of milled flaxseed daily for 24 weeks<sup>19</sup>. This is because flaxseed is rich in phytoestrogen and omega 3, that combat vaginal dryness.

In the current study, flaxseeds showed a significant reduction in bone pain in post-menopausal women. This was in agreement with the study of Griel et al (2007) who reported that the  $\alpha$ -linolenic acid and omega-3 fat found in flaxseed promotes bone health by preventing excessive bone turnover<sup>(52)</sup>.

## Conclusion

Menopause is characterized by significant bothersome clinical symptoms, endocrine and metabolic changes. Flaxseed had significant efficacy in attenuating climacteric symptoms, decreasing oxidative stress, and increasing serum levels of leptin in menopausal women. However, no significant changes have been seen in estrogen and progesterone level. Further studies are required to elucidate the mechanism of action of flaxseed and its constituents in alleviation of symptoms of menopause.

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