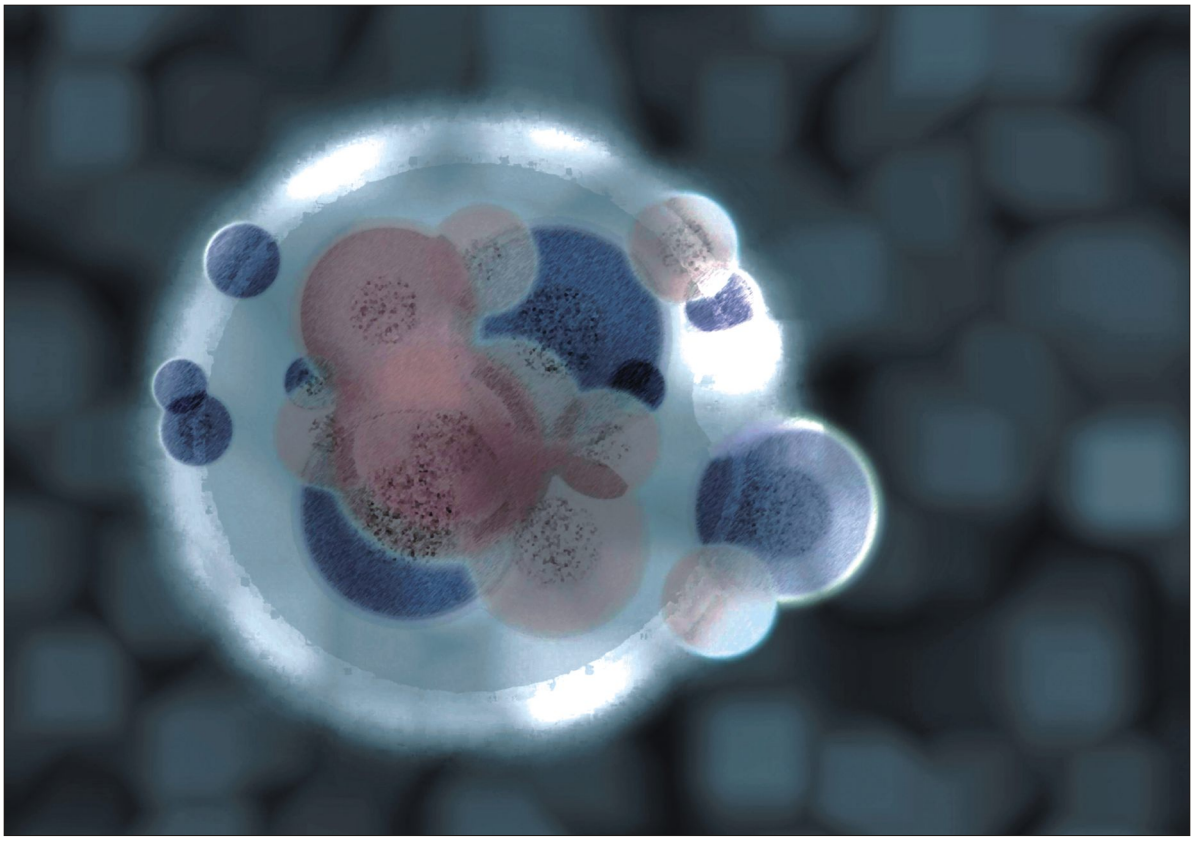

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Research Article
Nutritional Supplement Prepared from Whole Meal Wheat Flour, Soya Bean Flour, Flaxseed and Anise Seeds for Alleviating the Menopausal Symptoms

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Abstract

Background and Objective: Menopause is a physiological phenomenon in women's life. The decrease of estrogen hormone level leads to appearance of uncomfortable physical and psychological symptoms that have a negative impact on all aspects of female's daily life. This study aimed to help the female's body to adapt to diminish estrogen hormone around the time of the menopause by cookies, prepared from whole meal wheat flour, soy bean flour, anise seeds and flaxseed. **Materials and Methods:** 51 volunteer's Egyptian females complaining of menopausal symptoms participated in this study. Chemical analysis of supplement was carried out. Detailed gynecological, obstetric, drugs intake and dietary history were recorded. Menopausal symptoms evaluation was carried out using the Menopause Rating Scale (MRS) for evaluation of somatic, psychological and urogenital symptoms. Relevant anthropometric measurements and blood pressure were reported. Female sex hormones were evaluated. **Results:** Chemical analysis of the cookies showed that the supplement was enriched in protein, total phenols, fiber and minerals contents. Clinically, the waist circumference, blood pressure and MRS score decreased significantly, while female sex hormone levels improved, Estradiol showed significant increase at the end of the intervention. **Conclusion:** The consumption of bakery products prepared from soya flour, flaxseed and anise as a diet therapy helps in ameliorating the severity of the menopausal symptoms.

Key words: Soya flour, flaxseed, anise seed, dietary supplement, menopause

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Menopause is a natural physiological phenomenon that occurs as a result of decrease in the ovaries' production of the female sex hormones estradiol and progesterone[1]. Average age of natural menopause is between 40 and 51 years[2]. First, the menstrual cycles remain regular with change in the blood flow due to fluctuation in hormonal release, however ovulation may not occur each cycle, this menopausal transitional phase can last for several years. This is followed by irregular menstruation with change in severity and length. Finally, menstrual cycle cessations become permanently[3].

The fall in the level of circulating estradiol impacts all females' tissue from skin to organ resulting in decline in the physical, emotional and mental compliance that significantly disrupt women's life. The most common menopausal symptoms are hot flashes (felling of hotness, skin redness, sweating, sense of difficult rapid breathing), night sweating, heart palpitation, weight gain, difficult concentration, sleep disorders, poor memory, inability to concentrate, anxiety, depression, mood swings, headaches or migraines, dizziness, lack of energy, breast pain and tenderness, joint pain, back pain, vaginal dryness, painful intercourse, urinary incontinence and urgency, tingling extremities, dry itching skin and digestive problems. The average duration of symptoms can last up to 15 years and many women continue with symptoms into their 70s. Night sweats can interfere with sleep and lead to sleep deprivation, mood changes and chronic fatigue[4].

The management of menopause has changed considerably since the publication of the Women's Health Initiative (WHI) in 2002 which was conducted to address major health issues causing morbidity (cardiovascular disease, cancer and osteoporosis) and mortality in postmenopausal women[5]. Hormone replacement therapy by estrogen (HRT) increases the risk of heart disease, hypertension, breast cancer, uterine cancer, vaginal bleeding which lead to anemia, blood clots, fluid retention, gall bladder disease, acute liver disease, Pancreatic disease, stroke, bloating, weight gain, irritability, depression, headaches, migraine and endometriosis[6]. Many women reject the risks associated with hormone replacement therapy to treat their menopause symptoms and instead seek relief from non prescription therapies and alternative sources[7].

During the perimenopausal period of life, what females eat can influence how their body respond to the changes it goes through, as wrong diets can worse certain symptoms[8]. Healthy diet and functional foods consumption have been on the rise as consumers became more oriented with foods that contain only natural ingredients, as they are related to better quality of life[9].

The estrogenic activities of soy isoflavones play an important role in women health-enhancing properties as it mimics the actions and functions of estrogens on their body[10]. Some foods made from soy include tofu, tempeh, miso, soybean oil, soy sauce, soy protein isolate, soy protein concentrate, soy flour and soy milk. Flaxseed is rich in lignans which have estrogenic activities as well as antioxidant and anticancer activities[11,12].

AIM OF THE WORK

Several previous studies discussed the negative impact of menopause on medical and psychological status of the women at the perimenopausal period, that burden their life. Interference of this incapacity may be a key facet to improve female's quality of life at this biological time transition, guarantee a durable and active role in society.

Our main objective was to help the female's body to adapt to diminish estrogen hormone around the time of the menopause and how to ultimately take control of their symptoms to be relieved by natural safety products.

MATERIALS AND METHODS

The study was conducted through a project funded by National Research Centre (NRC) Egypt, 2016-2019: entitled "Dietary therapy and alternative medicine for alleviating the menopausal symptoms".

Subjects: This study was conducted in the nutrition and food science department of NRC from November 2016 to May 2017. Fifty-one women in the perimenopause stage, suffering from symptoms of menopause participated as volunteers in this study, with mean age 46.72±0.62 years, the research was given ethical approval from Ethical Committee of National Research Centre (Registration Number is 16/110). The participants consumed daily (80 g) of the supplement made with substituting wheat flour with 30% soy flour and addition of Flaxseed and anise seed, in the form of cookies (Table 1) with weekly follow up for 8 weeks. All participants' females were subjected to:

- Signed written informed consents to participate in the research project after they had been given a full explanation of the study
- Full medical history and medical examination, detailed gynecological and obstetric history and blood pressure measurement (it was measured 3 times and the mean was recorded)

Table 1: Composition of the supplement (g/100 g)

Raw materials	Formula (%)
Whole meal wheat flour	45
Defatted soy bean flour	30
Skim milk	10
Anise seeds	5
Flaxseed	5
Corn oil	5

- Abdominal obesity assessment by minimal waist and hip measurements
- Menopause Rating Scale (MRS) Evaluation Form[13]: The questionnaire has an option to check the degree of severity of symptoms. The three dimensions (sub-scales) are psychological, somato-vegetative and urogenital subscale. The total score is the sum of the three sub-scales scores

Somatic symptoms: Hot flushes, episodes of sweating, Heart discomfort (unusual awareness of heart beat, tightness), Sleep problems (difficulty in falling asleep, difficulty in sleeping through, waking up early), Joint and muscular discomfort.

Psychological symptoms: Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings), irritability (feeling nervous, inner tension and feeling aggressive), anxiety (inner restlessness, feeling panicky) and physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness).

Urogenital symptoms: Sexual complains (change in sexual desire, in sexual activity and satisfaction), bladder symptoms (bladder incontinence, difficulty in urinating, increased frequency of urination) and dryness of vagina (sensation of burning in the vagina, difficulty with sexual intercourse):

- All subjects were informed not to consume soya products or to use hormonal replacement therapy and they followed their usual diet throughout the study
- Collecting detailed data about nutritional intake and habit using the (Anonymous)[14] computer program
- Blood sampling and biochemical analysis: Blood samples were drawn from the patients and were allowed to clot at the room temperature, centrifuged and sera were separated. Biochemical parameters were performed on fasting sera that were stored at -70°C until used. Quantitative determination of Follicle Stimulating Hormone (FSH) concentration in participants' sera by FSH ELISA kit supplied by Chemux BioScience Inc, South San Francisco, USA., catalog number 10001[15]. Quantitative determination of Estradiol (E2) concentration by E2 ELISA kit supplied by Chemux BioScience Inc, South San Francisco, USA, catalog number 10009[16]. Quantitative determination of progesterone concentration by progesterone ELISA kit supplied by Chemux BioScience Inc, South San Francisco, USA, catalog number 10004[17]. Quantitative determination of Free Testosterone concentration by Free Testosterone ELISA kit supplied by IBL INTERNATIONAL GMBH, Hamburg, Germany, catalog number EFT127[18].

CHEMICAL COMPOSITION OF THE SUPPLEMENT

Analytical methods: Formula was prepared by mixing the ingredients according to Table 1 and the suitable amount of water were added according to (AACC)[19], to be formed as cookies. These formulas were baked in an electrical oven (Mondial Formi, Model No: 4T 40/60, Italy) at 200°C for about 20 min. Weight, volume, Specific volume, diameter, thickness and spread ratio of the cookies were recorded.

Moisture, ash, crude protein, fat and crude fiber contents were determined in raw materials [whole meal wheat flour (WWF), defatted soybean flour (DSF), skim milk (SM), Flaxseed and anise] and the cookies according to the methods outlined in AOAC[20]. Carbohydrates were calculated:

Carbohydrates = 100-Protein %+Fat %+Ash %+Crude fiber %

Statistical analysis: Data were analyzed using the Statistical Package for the Social Sciences version 16 (SPSS Inc., Chicago, IL). The categorical variables were expressed as rates (in percentage and frequency); while numerical data were expressed as Mean±SD and SE. Two tailed student t-test was used to compare the results before and after intervention. p-values less than 0.05 were considered statistically significant.

RESULTS

Chemical composition of raw materials and cookies: Chemical composition of WWF, DSF, SM, flaxseed, anise and cookies were determined and presented in Table 2-3. The obtained results showed that moisture content of selected samples ranged between 2.69-12.88%. DSF characterized by its higher crude protein, ash and total phenols (as tannins = 5796.98 mg/100 g). Anise was characterized by its higher crude fiber; while flaxseed was higher in fat content and lower in carbohydrate content. WWF had the highest carbohydrate content. Chemical analysis of the cookies showed that the supplement was enriched in

Table 2: Chemical composition of raw materials and cookies

Samples	Moisture (%)	Ash (%)	Protein (%)	Fat (%)	Fiber (%)	Total carbohydrate
Whole meal wheat flour	12.88±0.135	1.74±0.151	11.71±0.189	2.66±0.03	3.29±0.11	80.60±1.04
Defatted soybean flour	7.33±0.08	7.46±0.06	42.40±0.17	5.39±0.09	2.82±0.06	41.93±1.16
Skim milk	2.69±0.02	4.55±0.09	22.11±0.19	3.02±0.07	-	70.32±0.83
Flaxseed	6.46±0.07	3.12±0.05	20.17±0.13	37.54±0.22	6.37±0.09	32.80±0.26
Anise	7.84±0.09	6.83±0.10	19.92±0. 10	7.34±0.09	13.35±0.15	52.56±0.33
Soya cookies	20.52±0.13	2.88±0.02	15.98±0.11	6.16±0.03	3.21±0.03	71.77±0.96

Table 3: Minerals and phenols content in dry tested samples

Samples	P (mg/100 g)	K (mg/100 g)	Ca (mg/100 g)	Mg (mg/100 g)	Na (mg/100 g)	Fe (mg/100 g)	Total phenol l (As tannin)
Soy beans flour	327	200	423	561	147	102	5796.98
Soya cookies	299	196	461	582	169	148	7321.68

Table 4: Frequency and percentage of menopausal symptoms score before and after intervention

Menopausal evaluation questionnaires	Score	Frequency basal	Frequency after intervention	Percentage basal	Percentage after intervention
MRS	1	-	6	-	11.8
	2	9	6	17.60	11.8
	3	9	15	17.60	29.4
	4	33	24	64.70	47.1
Somatic subscale	1	3	6	5.90	11.8
	2	3	12	5.90	23.5
	3	15	24	29.40	47.1
	4	30	9	58.80	17.6
Psychological subscale	1	3	6	5.90	11.8
	2	6	9	11.80	17.6
	3	9	15	17.60	29.4
	4	33	21	64.70	41.2
Urogenital subscale	1	6	9	11.80	17.6
	2	-	3	-	5.9
	3	18	15	35.30	29.4
	4	27	24	52.90	47.1

Total MRS and subscales (Psych., Somatic, Urogenital) 1 = No 2 = Mild 3 = Moderate 4 = sever

Fig. 1: Soya supplement

protein, total phenols, fiber and minerals contents (calcium, magnesium and iron). These results were in agreement with Hussein *et al.*[21].

Physical characteristics of snacks: The physical characteristics of the cookies were evaluated using rapid Visco Analyser-4 according to AACC[19], demonstrated that the weight was (17.78 g), volume was (23.66 cm^3) and specific volume was (1.33 cm^3 g^{-1}).

Sensory attributes: The sensory evaluation of cookies as a function of replaced WWF with DSF, SM, flaxseed and anise revealed all characteristics color, flavor, taste, crispiness and appearance were acceptable with overall acceptability 87% Fig. 1.

Data presented as frequency and percentage of menopausal symptoms at base line stage and after 2 months of intervention showed in Table 4, mean and p-value of menopausal symptoms score before and after soya cookies consumption in Table 5. All participants showed significant improvement in somatic menopausal symptoms (Hot flushes, episodes of sweating, Heart discomfort, Sleep disturbances, Joint and muscular discomfort), urogenital symptoms (Sexual complains, bladder symptoms and dryness of vagina) and psychological symptoms (Depression,

irritability, anxiety and mental exhaustion) after intervention, especially in somatic and psychological subscales.

The percent of the frequency consumption of different food items was summarized on Table 6. Reported frequencies of food intake habit of the participants depended on their economic status, food likes and dislikes.

Table 5: Mean±SD and p-value of menopausal symptoms score before and after intervention

	Mean±SE	t. test	p-value
MRS1	20.65±1.34	11.95	0.00
MRS2	14.41±1.10		
Somatic1	8.59±0.460	13.436	0.00
Somatic2	5.47±0.379		
Psych1	7.76±0.601	8.865	0.00
Psych2	5.41±0.455		
Urogenital1	4.53±0.440	6.103	0.00
Urogenital2	3.65±0.394		

1: Menopausal symptoms score before intervention 2: Menopausal symptoms score after intervention, significant at $p \leq 0.05$

Table 6: Percent of the frequency consumption of different food items for the studied sample

	Daily intake	
	Less than three times/day	Three times or more/day
Food items	Sample (%)	
Bread bakery products	33.20	66.80
Milk and dairy products	54.60	45.40
	Weekly intake	
	Less than three times/week	Three times or more/week
Food items	Sample (%)	
Chicken, meat and fish	29.65	70.35
Eggs	35.60	64.40
Legume	63.78	36.22
Vegetables	47.85	52.15
Fruits	48.28	51.72
Sweet, pastries	62.61	37.39
Beverages	75.46	24.54

Table 7 showed Mean±SE of age, relevant anthropometric parameters, blood pressure and blood sex hormonal profile among menopausal subjects at the basal and at the end of the study (after 8 weeks) of dietary therapy. Central obesity represented by Waist and hip measurements decreased significantly ($p<0.01$) at the end of the intervention. Blood pressure values were within normal ranges as patients were under medical control; however systolic blood pressure (SBP) and diastolic blood pressure (DBP) decreased significantly after dietary therapy. FSH, progesterone and free testosterone were decreased significantly at $p<0.01$ after dietary therapy. Estradiol (E2) showed significant increased at the end of the study.

DISCUSSION

Data of this study showed that the supplement prepared from soy flour and flaxseed was enriched in protein, total phenols, fiber and minerals contents. Clinically, the blood pressure, central obesity and MRS score decreased significantly. Consumers became more aware regarding health and nutrition. So, modification of bakery products is an important method used to add value to healthy foods[22]. Functional food demand increased last few years as it has disease preventing or heath promoting properties which provide basic nutrients benefits without changing the eating habits of the consumers[23].

Biscuit and cookies are popular snack food with easy availability at low cost, but traditional types couldn't consider as healthy foods, especially when prepared by refined wheat flour, refined sugar and saturated fat. Refined wheat flour (when used as the main ingredient of cookies) is deficient in the essential amino acid lysine, fiber, minerals and vitamins[24].

Fortification of bakery products by soy flour successfully enriched them with protein and vitamins (vit. A and D), soy

Table 7: Mean±SE of age, anthropometric parameters, blood pressure and biochemical parameters of the participants at the basal and last visit of the dietary therapy (No = 51)

Anthropometric parameters	Basal	Last	Change (%)	p-value
Ages (year)	46.72±0.62			
Menarche age (year)	13.61±0.14			
Waist (cm)	89.88±1.13	85.15±0.99	-5.26	0.001
Hip (cm)	113.79±1.65	108.18±1.55	-4.93	0.001
Waist hip ratio	0.78±0.01	0.76±0.01	-2.56	0.001
SBP (mmHg)	138.24±1.79	130.88±1.29	-5.32	0.001
DBP (mmHg)	82.06±1.69	74.12±1.17	-9.68	0.001
FSH (mIU mL^{-1})	74.76±8.57	40.76±4.42	-45.48	0.001
Estradiol (E2) (pg mL^{-1})	57.09±3.69	78.84±2.64	+38.09	0.001
Progesterone (ng mL^{-1})	1.0353±2.17	1.9588±4.04	+89.20	0.048
Free testosterone (pg mL^{-1})	1.49±0.16	1.23±0.14	-17.45	0.002

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FSH: Follicle stimulating hormone, significant at $p \leq 0.05$

flour is an excellent source of essential amino acids lysine, linoleic fatty acids, minerals, fiber and phytoestrogen which provide several functional advantages to cookies[25]. Addition of flax seed to the supplement improved its nutritional value by increasing the bioavailability of carbohydrate, protein, vitamins, minerals and improved the dough volume and texture of the cookies. This is in agree with ref.[26-28] who stated that bakery products when fortified with flax seed resulted in better nutritious and quality products.

Anise seed was added for its carminative effect (decreased flatulence), as a treatment for abdominal colic and sleeplessness[29].

Japanese and Chinese women, who consume daily a soy-rich diet, record less morbidity with heart disease, less mortality with breast cancer and less complaining of vasomotor symptoms than European and American women[30-31].

Soy foods affectivity studies in decreasing vaginal and vasomotor symptoms have been conducted worldwide and have recommend the utility of soya foods enriched in variable isoflavones amounts. Soybeans contain genistein and daidzein. They are known as being estrogenic, aiding to control hot flashes and other symptoms of menopause. They have also an anti-Aging and anti-angiogenic (they help in prevent the growth of new blood vessels to nourish the developing tumors) effects[32-33].

Ground flaxseed can be integrated into all baked like breads, cookies and muffins, or it has been used in cereals and nutritional bars[34]. Soya flour and Flax were used in this study because a synergistic relationship is thought to exist between the two ingredients. Soy and flax health benefits increase when they are used together in food products and they protect against many same diseases[35].

Clinical research is interesting in women aging and age-related decline of mental and physical compliance related to menopause. Menopause rating scale was applied to assess the symptoms severity, soya cookies were effective in decreasing the frequency and severity of these symptoms which annoy subjects and interfere with sleep leading to mood changes, depression and chronic fatigue. Data of this study revealed significant decrease in the abdominal obesity which was reported in the decreased value of the minimal waist circumference. Abdominal obesity likely to have a negative impact on health where there is a strong correlation between central obesity and cardiovascular disease, Alzheimer's disease[36] and type 2 diabetes[37].

The results of this study indicated that the soya cookies had positive significant effect on E2, negative effect on FSH, progesterone and free testosterone. A meta-analysis study by Hooper *et al.*[38] revealed that isoflavone rich soy products consumption for 4 weeks or more may decrease the serum levels of FSH and LH in premenopausal women and raise estradiol level in post-menopausal women. Previous studies had shown a decrease in E2 levels after consumption of soy food, some studies had revealed no change in its level. Others studies had demonstrated significant increase, no change or decrease in the levels of testosterone after use of soy products[39-44]. There are several reasons why this conflict in different studies, such as subject have hormonal disturbances or not, day of sample withdrawn for hormones assay as the subjects had irregular or absent menstruation, menopausal women classification into pre- peri- or post-menopausal stage, whether soya product was introduced into the usual diet or its effect with different nutrients examined not just of the isoflavone related effect, different types of soy foods and presence of polycystic ovaries syndromes.

CONCLUSION

In conclusion, menopausal symptoms are common. This study discovers the possible synergistic effect of Soya bean flour, flaxseed and anise combination to form a natural bakery product in the form of cookies that can be beneficial for alleviating the somatic menopausal symptoms, urogenital symptoms and psychological symptoms after intervention, especially in somatic and psychological subscales. Diet therapy is a must in the management of menopause annoying symptoms. Bakery products are safe, easily prepared and not expensive.

SIGNIFICANCE STATEMENT

This study revealed the importance of and the healthy beneficial effect of using functional foods in the form of dietary supplements as a dietary strategy to reduce the menopausal symptoms. This study discovers the possible synergistic effect of Soya bean flour, flaxseed and anise combination to form a bakery product in the form of cookies that can be beneficial for alleviating the menopausal symptoms in Egyptian females in the peri-menopausal phase of life. This study will help the physicians and the researcher to uncover the role of diet supplement significant in improvement the somatic menopausal symptoms, urogenital symptoms and psychological symptoms after intervention, especially in somatic and psychological subscales. Thus, a new theory on these nutrients combination and possibly other combinations, may be arrived at.

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