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# Benefits of soy germ isoflavones in postmenopausal women with contraindication for conventional hormone replacement therapy

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**Abstract**

*Objective:* To evaluate the effects of isoflavones on vasomotor symptoms and blood lipids in postmenopausal women with contraindication for conventional hormone replacement therapy (HRT). *Methods:* This prospective, double-blind and placebo-controlled study included 50 postmenopausal women randomly divided into two groups: 25 women on soy germ isoflavones (60 mg per day, capsules) and 25 women on placebo. Inclusion criteria included: non-vegetarian, non-asian women whose last menstruation dated at least 12 months prior to the beginning of the study, with FSH > 40 mIU/ml, hot flushes and contraindication for HRT, not using tamoxifen or antibiotic and no disease of the gastrointestinal tract. For 6 months, the Kupperman menopausal index (KMI), the vaginal cytological maturation value (MV) and both hormonal and lipid profiles were assessed. The *t*-test and analysis of variance (ANOVA) were employed to compare the two groups. *Results:* In both groups, a decreased KI rate was observed. However, isoflavone was significantly superior to placebo in reducing hot flushes (44% versus 10%, respectively) ($P < 0.05$). After 6 months, the isoflavone group showed increased estradiol levels with unchanged FSH, LH, and vaginal cytology, and a reduction of 11.8% in LDL and an increase of 27.3% in HDL ($P < 0.05$). In the placebo group, just a reduction in MV was observed after 6 months ($P < 0.05$). *Conclusions:* Soy germ isoflavone exerted favorable effects on vasomotor symptoms and lipid profile, showing itself to be an interesting alternative therapy for the postmenopausal women with contraindication for conventional HRT.


*Keywords:* Soy germ; Isoflavone; Menopause; Hot flushes; Lipid profile

## 1. Introduction

Hormone replacement therapy (HRT) is recommended in the relief of vasomotor symptoms, treatment of vaginal atrophy, and prevention of osteoporosis [1]. In spite of the well-known advantages of HRT, approximately 70% of the women drop out after the first year of treatment [2]. One of the main causes of this low compliance rate is irregular bleeding. Other reasons include mastalgia, nausea, migraine, weight gain, and hydric retention, besides the fear of breast cancer. These effects have lead some women to be reserved and opt for natural forms of treatment. Moreover, there are women for whom HRT is not

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indicated. In these cases, very little can be offered to relieve their climacteric symptoms [3,4]. For all these reasons, the development of alternative therapies, that can bring the benefits of HRT with no side effects nor contraindications, has been subject of interest [1–6].

Phytoestrogens are naturally found in some vegetables and are structurally and functionally similar to estradiol [7]. There are four major classes of phytoestrogens: isoflavones, found in soy beans and their by-products; lignanes, found in whole cereals and oleaginous plants; flavonoids, found in some fruits and vegetables; cumestranes, found in bean sprouts and alfalfa [8]. The phytoestrogens with the most powerful estrogenic action are genistein, daidzein, and glycitein that belong to the class of isoflavones and are found in the soy germ. They are non-steroid compounds that weakly bind to estrogenic receptors (less than 1% of estradiol binding affinity) and have a selective action, that is, they exhibit estrogenic activity in some tissues and antioestrogenic in others [5,9].

Most clinical evidences on the use of isoflavones are epidemiologic and were obtained in areas of high soy consumption [9]. Less than 20% of the Japanese women present hot flushes as compared with 80% of the European women. This is partly attributed, to the differences observed in their diets [8]. Isoflavones have been demonstrated to decrease both the severity and the frequency vasomotor symptoms in menopausal women [10–14]. Albertazzi et al. in a double-blind, placebo-controlled trial, observed that 60 g per day of isolated soy protein (dietary supplement), as compared to a placebo, reduced 50% of the vasomotor symptoms [3].

A soy-rich diet seems to be beneficial for the cardiovascular system due to its favorable effect on the lipid profile [15–18]. Some studies have demonstrated a HDL elevation and a LDL reduction of about 10% [19]. In vitro reduction has been observed in thromboxane and platelet aggregation, resulting in a lower prothrombotic tendency of the isoflavones and coronary vasodilation [9,20,21]. The incidence of breast cancer, colon cancer, endometrial cancer, and ovary cancer is lower in Asia than in Western countries [8]. In cultures of breast malign cells, isoflavones have shown a dose-dependent antiproliferative effect [16]. Other mechanisms that could prevent malign tumors by using a soy diet include the inhibition of the tyrosinequinase system, the suppression on angiogenesis and antioxidant effects [6].

Based on these favorable effects, the addition of soy products to the diet, would be advisable [6,22]. Most of the studies of soy derived dietary supplements have demonstrated a moderate oestrogenic effect [8]. However, there is a great difficulty in modifying the western woman's alimentary habit. Soy germ isoflavones are found in the form of gelatin capsules, but few investigations using this form have been conducted. Further studies are necessary to confirm the effectiveness and safety of this alternative therapy [3,22].

The purpose of this investigation was to evaluate the effects of gelatin capsules of soy germ isoflavones on the climacteric symptoms and the lipid profile in menopausal women with, contraindications or intolerance to conventional hormonal replacement therapy.

## 2. Patients and methods

This clinical prospective, randomized, double-blind, and placebo-controlled trial included 50 menopausal Brazilian women. Inclusion criteria: last menstruation dated at least 12 months prior to the beginning of the study, FSH $>$ 40 mIU/ml, symptoms of estrogenic privation (hot flushes) and contraindications or intolerance to conventional HRT. Exclusion criteria: vegetarian and macrobiotic diets, Asians, smokers, alcoholics, history of chronic gastrointestinal diseases, use of HRT, tamoxifen or antibiotics taken within the preceding 6 months. Prior to the study, the thyroid stimulator hormone (TSH), free tyroxine (T4) and antibody thyreoperoxidase (TPO-AB) levels were measured to exclude thyroid dysfunctions that could interfere in the sintomatology. Informed consent was obtained from all patients and the study was approved by the Research Ethics Committee of Botucatu Medical School—UNESP.

The initial evaluation consisted of anamnesis, general and gynecological physical exam, and oncotic colpocytology. Data included information on: age, menarche, time since menopause, parity, intestinal habits, HRT contraindication, weight, height, and arterial pressure. The patients were then randomly assigned to one of two groups: G1, oral isoflavones ($n$ = 25) or G2, oral placebo ($n$ = 25). The examining doctor, as well as and the patients, had no

previous knowledge of group assignment. The only unblended person was the pharmacist responsible for the manipulation of the capsules. Thus, 25 patients orally received 60 mg of isoflavones in the form of four capsules per day of 500 mg of soy germ (Isosoy®, Herborisa®, Brazil) divided into two takings, for 6 months. Each capsule contained, as natural components of soy germ, 56 mg of lipids, 202 mg of protein, 141 mg of carbohydrates, and 19 mg of fiber (energy value = 2 kcal). All soy germ was extracted from the same crop of grains. The other 25 patients received four lactose capsules per day. The capsules were packed in white, opaque bottles, which were labeled with code numbers by the pharmacist to prevent identification by the participants of the study groups. Follow-up duration was 6 months, with evaluations at 2, 4, and 6 months.

At the baseline interview and at each follow-up session, the Kupperman menopausal index (KMI) was obtained. This index is the sum of the severity scores (from 0: absent to 3: most severe) given to 11 of the most common menopausal complaints (hot flushes, paresthesia, insomnia, nervousness, melancholy, vertigo, weakness, arthralgia, headaches, palpitation, and formication). Paresthesia, insomnia and nervousness are multiplied by 2 while hot flushes is multiplied by 4 [23]. Weight variation was monitored by the body mass index (BMI = weight/height$^2$) [24]. For the diagnosis of obesity, the criteria used were those of the World Health Organization (1997) that considered BMI $\geq$ 30 kg/m$^2$. The waist/hip ratio (WHR) was used to indirectly evaluate the distribution of body fat distribution, considered as gynecoid when WHR < 0.8, and androgenic when WHR > 0.8 [25].

Hormonal colpocytological evaluation was performed at baseline and after 6 month. Vaginal smears were collected from the mid-third of the vaginal lateral wall. In a total of 100 exfoliation cells, parabasal cells (P), intermediary cells (I), and superficial cells (S) were counted and results were expressed as the maturation value (MV) of Meisels [26]. All examinations were interpreted by the same cytopathologist without prior knowledge of the subjects' data.

FSH, LH, and estradiol levels were assessed at baseline and at 6 months by electrochemiluminescence with the Elecsys® 2010 System (Roche® Diagnostics, Mannheim, Germany). The following were considered normal menopause values: FSH between 25.0 and 134.8 mIU/ml, LH between 7.7 and 58.5 mIU/ml, and estradiol between <10.0 and 39.5 pg/ml.

Triglycerides (TG), total cholesterol (TC), HDL, and LDL were measured at baseline, and at 3 and 6 months. Measurements were processed by the automatic biochemical analyzer, RAXT (Technicon®, USA). Total cholesterol, HDL and the triglycerides levels were quantified by colorimetry while LDL was calculated using the formula of Friedewald, where total cholesterol is subtracted from the sum of HDL and triglycerides divided by 5. Normality rates were: TC < 200 mg/dl, HDL > 35 mg/dl, LDL < 130 mg/dl, and TG < 170 mg/dl.

Transvaginal ultrasonography was performed to evaluate endometrial thickness at baseline and 6 months by the same operator. Sonochrome® (GE®, USA) with a 7.5 MHz endovaginal transducer was used to obtain morphologic images of the uterus and the ovaries. The endometrial thickness, at sagital incidence, measured from a basal layer to the other, was considered normal in the menopause when <5 mm.

For the calculation of sample size, the confidence interval was 95%, case/control ratio was 1:1, and expected amelioration was 40% of the treated cases. Averages were compared by the *t*-test and analysis of variance (ANOVA). Differences in case frequency were analyzed by either the chi-square test or Fisher's test whenever necessary. Data were expressed as mean ± standard deviation. Statistical tests were two-tailed, significance level was set at 5%, and data were calculated with Software SPSS version (8.5).

## 3. Results

Baseline clinical, colpocytologic, ultrasonographic, and laboratory data regarding the groups of patients on isoflavones and on placebo were statistically compared and are shown in Tables 1 and 2. The groups were observed to be homogeneous regarding the following variables: age, menarche, parity, menopause, body mass index, waist/hip ratio, Kupperman menopausal index, maturation value, and endometrial thickness (Table 1). Statistically significant differences in baseline hormonal values were not observed between groups. On the other hand, the lipid profile analysis revealed that the patients randomized to the isoflavones group exhibited elevated baseline

Table 1
Comparison of the clinical characteristics, colpocytology, and initial ultrasonography among the patients of the isoflavone group (G1) ($n$ = 25) and the placebo group (G2) ($n$ = 25) (mean ± standard deviation)

| Variáveis | G1 (isoflavone) | G2 (placebo) | $P$ value* |
|---|---|---|---|
| Age (years) | 53.70 ± 5.45 | 52.90 ± 5.11 | 0.63 |
| Menarce (years) | 13.05 ± 1.54 | 13.50 ± 1.79 | 0.39 |
| Parity (children $n$ ) | 3.25 ± 2.55 | 3.05 ± 1.32 | 0.75 |
| Menopause (years) | 48.35±3.44 | 47.90 ± 3.46 | 0.68 |
| BMI (kg/m$^2$) | 27.97 ± 4.92 | 30.01 ± 5.64 | 0.23 |
| WHR | 0.88 ± 0.05 | 0.87 ± 0.05 | 0.40 |
| KMI | 21.10 ± 6.11 | 20.05 ± 6.14 | 0.50 |
| MV (%) | 38.85 ± 21.69 | 45.53 ± 20.52 | 0.40 |
| Endometrium (mm) | 0.40 ± 0.09 | 0.37 ± 0.08 | 0.30 |

BMI: body mass index; WHR: waist/hip ratio; KMI: Kupperman menopausal index; MV: maturation value.
* ANOVA.

values of total cholesterol and LDL, when compared to the placebo group ($P < 0.05$) (Table 2).

The analysis of the Kupperman menopausal index mean values showed a significant reduction in both groups, starting at 2 months of follow-up (Fig. 1). When hot flushes were separately evaluated in the isoflavones group, a significant reduction was observed starting at the 4th month of follow-up ($P < 0.05$) (Table 3). In 44% of the patients (11/25) in the isoflavones group, these symptoms completely disappeared, whereas in 36% (9/25) of these women they improved partially, and in 20% (5/25) they remained unchanged. In the placebo group, 12% (3/25) of the patients reported total relief of the hot flushes, whereas 28% (7/25) reported a discrete amelioration and 60% (15/25) reported no improvement.

At month 6, the average of the vaginal cells maturation value remained unchanged in the patients on isoflavones whereas, in the placebo group, it was significantly reduced as compared to baseline values ($P < 0.05$) (Fig. 2). Throughout follow-up, no changes were observed in the values of body mass index, waist/hip ratio and arterial pressure, in both groups. At transvaginal ultrasonography, no variations were observed in the endometrial thickness average values. However, three patients (two on isoflavones and one on placebo) had a discreet vaginal bleeding during the study, with endometrial measures greater than 5.0 mm. Diagnostic hysteroscopy was performed and revealed two cases of atrophyc endometrium and one case of endometrial polyp.

Table 4 shows the FSH, LH, and estradiol average values in both groups at baseline and at 6 months of follow-up. At the end of the study, the average values of estradiol were significantly higher in G1 than in G2 ($P < 0.05$), while FSH and LH remained unchanged. The lipid profile analysis revealed that the average values of total cholesterol and LDL that were initially high in the isoflavones group were reduced after 6 months whereas HDL significantly increased ($P < 0.05$), and triglycerides remained unchanged. The placebo group showed no changes in those parameters (Fig. 3).

The contraindications for conventional hormonal replacement therapy, at enrollment, were: breast cancer in 38% (19/50), cardiovascular disease with acute myocardium infarction in 16% (8/50), deep vein thrombosis in 12% (6/50) and recent endometrial cancer in 10% (5/50) of the cases. The 12% (6/50) of the remaining cases reported intolerance to conventional HRT

Table 2
Comparison of the initial laboratorial characteristics among the patients of the isoflavone group (G1) ($n$ = 25) and the placebo group (G2) ($n$ = 25) (mean ± standard deviation)

| Variáveis | G1 (isoflavone) | G2 (placebo) | $P$ value* |
|---|---|---|---|
| FSH (mIU/ml) | 76.79 ± 19.37 | 75.21 ± 28.75 | 0.80 |
| LH (mIU/ml) | 30.68 ± 8.51 | 33.96 ± 21.84 | 0.50 |
| Estradiol (pg/ml) | 15.80 ± 7.28 | 14.61 ± 5.98 | 0.30 |
| Total cholesterol (mg/dl) | 229.65 ± 31.58 | 203.75 ± 25.08 | <0.05 |
| HDL (mg/dl) | 43.95 ± 11.31 | 48.10 ± 12.96 | 0.28 |
| LDL (mg/dl) | 151.50 ± 39.22 | 130.50 ± 23.57 | <0.05 |
| Triglycerids (mg/dl) | 150.35 ± 94.38 | 139.00 ± 68.93 | 0.20 |
| Glycemia (mg/dl) | 102.25 ± 28.24 | 95.01 ± 12.59 | 0.30 |

* ANOVA.

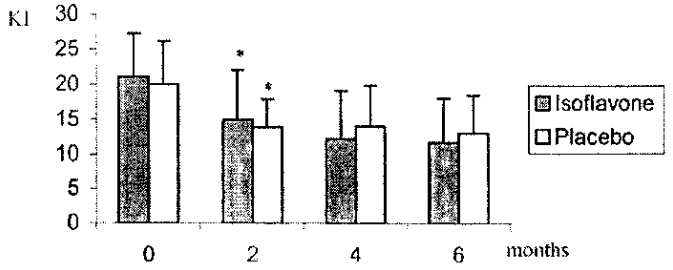


Fig. 1. Comparison of the mean values of the Kupperman menopausal index (KMI) among the patients of the isoflavone group (G1) ($n = 25$) and the placebo group (G2) ($n = 25$) (mean ± standard deviation). *Significantly different from baseline within group ($P < 0.05$) (Paired $t$-test)

Table 3
Comparison of the mean values of the hot flushes in the Kupperman menopausal index (KMI) among the patients of the isoflavone group (G1) ($n = 25$) and the placebo group (G2) ($n = 25$) (mean ± standard deviation)

| Variables/time (months) | G1 (isoflavone) | G2 (placebo) | Sig* |
|---|---|---|---|
| Basal (M1) | 7.0 ± 1.8 | 6.4 ± 2.4 | G1 = G2 |
| 2 months (M2) | 4.8 ± 3.3 | 5.6 ± 2.3 | G1 = G2 |
| 4 months (M3) | 3.4 ± 3.2 | 5.2 ± 2.7 | **G1 < G2** |
| 6 months (M4) | 3.0 ± 2.1 | 5.2 ± 2.5 | **G1 < G2** |
| Sig** | M1 > M2 > (M3 = M4) | M1 = M2 = M3 = M4 | |

* Significantly different between groups (G1 > G2) ($P < 0.05$) (ANOVA).
** Significantly different from baseline within group ($P < 0.05$) (Paired $t$-test).

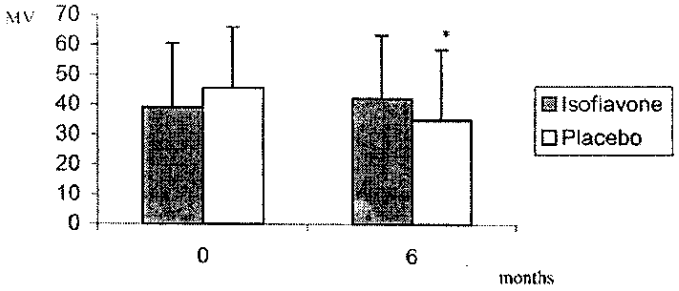


Fig. 2. Comparison of the mean maturation values (MV) among the patients of the isoflavone group (G1) ($n = 25$) and the placebo group (G2) ($n = 25$) (mean ± standard deviation). *Significantly different from baseline within group ($P < 0.05$) (Paired $t$-test).

Table 4
Comparison of the FSH (mIU/ml), LH (mIU/ml) and estradiol ($E_2$, pg ml) values among the patients of the isoflavone group (G1) ($n = 25$) and the placebo group (G2) ($n = 25$) (mean ± standard deviation)

| Time/Variables | Basal | | 6 months | |
|---|---|---|---|---|
| | G1 | G2 | G1 | G2 |
| FSH (mIU/ml) | 76.8 ± 13.4 | 75.2 ± 28.7 | 77.7 ± 19.6 | 82.5 ± 30.7 |
| LH (mIU/ml) | 30.7 ± 8.51 | 33.9 ± 21.8 | 30.6 ± 9.7 | 34.4 ± 16.7 |
| $E_2$ (mIU/ml) | 15.8 ± 7.3 | 14.6 ± 6.0 | 17.7 ± 6.7* | 12.3 ± 3.8 |

* Significantly different between groups (G1 > G2) ($P < 0.05$) (ANOVA).

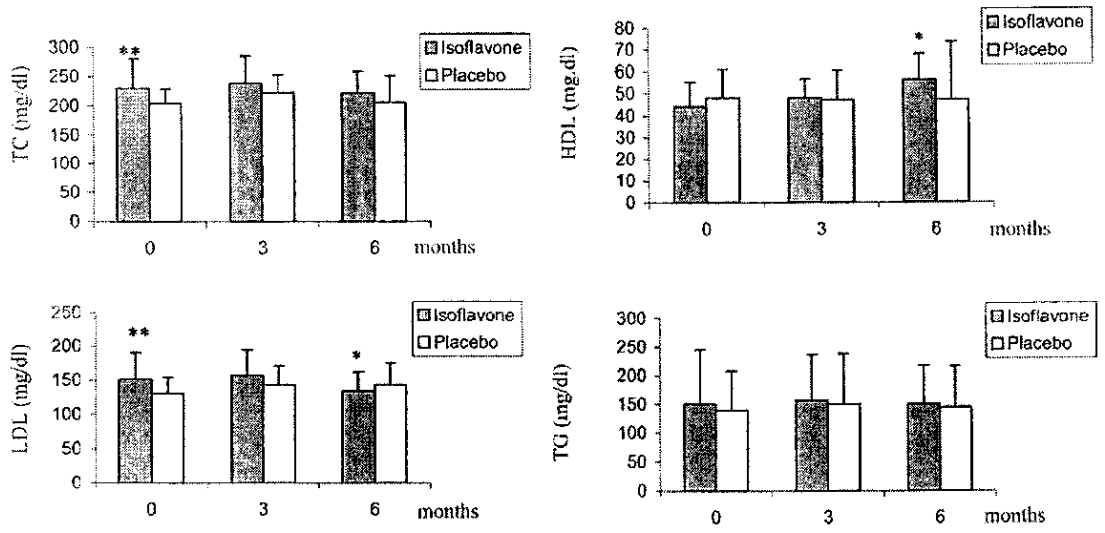


Fig. 3. Comparison of the total cholesterol (TC, mg/dl), HDL (mg/dl), LDL (mg/dl) and triglycerides (TG, mg/dl) values among the patients of the isoflavone group (G1) ($n = 25$) and the placebo group (G2) ($n = 25$) (mean ± standard deviation). *Significantly different from baseline within group ($P < 0.05$) (Paired $t$-test) **Significantly different between groups (G1 > G2) ($P < 0.05$) (ANOVA).

with edema, mastalgia, weight gain, and difficulty to control bleeding while the other 12% (6/50) did not want conventional HRT due to the fear of breast cancer caused by family history. During follow-up, three patients on isoflavone reported constipation, two reported flatulence and two reported nausea. In the group on placebo, two patients reported constipation and flatulence. There was no patient drop out.

## 4. Discussion

Isoflavones are found in the glycosilated form and biologically inactive in the nature. Following the intake of isoflavones, a complex enzymatic conversion mechanism occurs in the gastrointestinal tract that results in the formation of heterocyclic phenols structurally similar to 17-β-estradiol [7,8]. Due to this factor, the concentrations of the different phytoestrogen metabolites and their clinical effects vary from individual to individual even when the amount of isoflavones administered is controlled, making difficult to determine the ideal dose. An intake of 20–100 mg per day is recommended [2,22,27]. In the present study, capsules containing 60 mg of soy germ in the glycosilated natural form, which is the most bioavailable form, were used. Few are the studies in which this form of isoflavones has been used. Most frequently, either capsules of soy isoflavone extract, which are not so bioavailable, or whole soy diet supplementation have been used. The concentrations of isoflavones in soybeans based diets also vary, as they depend on the quality of the grains, growth, and soil conditions, and the soy bean processing. In 60 g of soy, an average of 70 mg of isoflavones are found, 40 mg of genistein, and 30 mg of daidzein [3] whereas from 60 g of soy germ, 1392 mg of isoflavones are found, 672 mg daidzein, 185 mg denistein, and 534 mg glycitein [28].

In this study, a reduction in the frequency of typical climacteric problems was demonstrated by the significant decrease in the total sum of the Kupperman menopausal index observed in both groups, suggesting a placebo effect. However, when hot flushes were separately analyzed, the reduction in hot flushes was statistically significant among the women that received soy germ isoflavone when compared to the placebo. Hot flushes are common in the transition to menopause and are related to hypoestrogenism. Hot flushes completely disappeared in 44% of the women

in the isoflavones group and in 10% of those in the placebo group. These results are in agreement with other authors that observed an improvement of the vasomotor symptoms with dietary soy supplementation [3,10–14,29]. In a recent study, Han et al. demonstrated a significant reduction in the Kupperman menopausal index after 4 months on 100 mg capsules of soy isoflavone extract [12]. Faure et al., using soy isoflavone extract (70 mg per day), also demonstrated a 61% reduction in the frequency of hot flushes versus a 21% reduction obtained with placebo in climacteric women [13]. On the other hand, Van Pattern et al. evaluated the beneficial effects of a soy beverage containing 90 mg of isoflavones on menopausal women with breast cancer and verified no amelioration of hot flushes among the patients on isoflavones as compared to those on placebo after 12 months of follow-up. The authors recommend further studies to evaluate the safety and effectiveness of isoflavones in women with breast cancer [30]. Clinical researches are limited to observation studies that show an inverse relationship between breast cancer and isoflavones used [31,32]. Maškarinec et al. evaluated the effects of 100 mg of isoflavones on mammographic density, a predictor of breast cancer risk, and observed no mammographic changes after 12 months, suggesting isoflavones exert no estrogenic effect on the breasts [33]. To Mishra et al., controlled trials are necessary to draw further conclusions [34].

Dislipidemy, arterial hypertension and central obesity are associated with a high risk for cardiovascular disease (CVD) in menopausal women. During this present study, no changes were observed in the body mass index and the waist/hip ratio after 6 months of isoflavones or placebo. In addition, no variations in arterial pressure were observed, in spite of the fact that 40% (10/25) of the women in the isoflavones group and 32% (8/25) of those in the placebo group had chronic hypertension controlled by therapeutic anti-hypertensives. Kleijn et al. evaluated the diets of 939 menopausal women diets, participants to the Framingham Offspring Study. They demonstrated that those on a phytoestrogen-rich diet, the waist/hip ratio and triglycerides levels were significantly lower as compared to those on a soy-poor diet. They concluded that a high intake of phytoestrogens on menopause seems to be associated with a favorable metabolic profile for CVD [18].

In the isoflavones group, average baseline values of total cholesterol and LDL were significantly higher in the group on placebo. In the users of 60 mg of isoflavones, there was a significant reduction of 11.8% in the average values of LDL and a rise of 27.3% in HDL, with a small decrease in total cholesterol after 6 months. Anderson et al. conducted a meta-analysis to evaluate the lipid profile in 38 studies of soy-rich diets. They found an average LDL reduction of 12.9% but no significant change in HDL [19]. However, other investigators demonstrated increases in the average HDL values that varied from 3.7 to 28.6% [15,35]. Han et al. observed a reduction in total cholesterol and LDL and unchanged HDL and triglycerides in women using 100 mg per day of soy isoflavone extract in capsules as compared to women on placebo [12]. On the other hand, Dewell et al. did not verify changes in the lipid profile of patients with hypercholesterolemia on 150 mg of soy supplement [17].

At 6 months of follow-up, the average maturation value was unchanged in the isoflavone users, suggesting maintenance of the vaginal epithelium whereas in the patients on placebo a significant reduction in the average value of vaginal maturation was observed. There is a lot of controversy over the beneficial effects of phytoestrogens on vaginal cytology. In a pioneer study, Wilcox et al. demonstrated an improvement in vaginal maturation with 45 g of soy in the diet [36]. Dalais et al. observed a significantly increased vaginal maturation index in the menopausal women receiving soy supplementation [10]; but no significant improvement of the vaginal mucosa was demonstrated in others studies [5,11,12,37].

At the end of this investigation, a significant elevation in the estradiol average values was observed in the patients on isoflavones as compared to those on placebo. However, these values remained below 20 pg/ml. Isoflavones, as non-steroid compounds, seem to exert estrogen-like hormonal effects when ingested in high doses [38]. Cassidy et al. demonstrated an increase in estradiol levels in peri-menopausal women on 45 mg per day of isoflavones [39]. Duncan et al. showed a reduction in estrone values, with unchanged estradiol levels in menopausal women on an isoflavone-rich diet [37]. In other investigations, no changes in hormonal levels were observed [11,12,40].

In the present work, no changes in endometrial thickness as measured at transvaginal ultrasonography

were observed in both groups. Studies evaluating the effects of isoflavones on the endometrium have shown that their use in the form of supplements or capsules, do not change endometrial thickness in menopausal women [11,12,37,38,41]. Phytoestrogen seem to have an anti-estrogenic and anti-proliferative effect on the endometrial tissue [38].

There is still not enough evidence for the use of phytoestrogens as a replacement for conventional HRT [1,2,16]. However, in this investigation, isoflavones in capsules of soy germ, at the dose of 60 mg per day, exerted favorable effects on vasomotor symptoms and lipid profile, suggesting this may be an interesting alternative therapy for menopausal women with contraindications or intolerance to conventional HRT.

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