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The Effect of Herbal Extract (EstroG-100) on Pre-, Peri- and Post-Menopausal Women: A Randomized Double-blind, Placebo-controlled Study

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This clinical research study was designed to evaluate the efficacy of a new herbal product, EstroG-100, containing a mixture of standardized extracts of *Cynanchum wilfordii*, *Phlomis umbrosa* and *Angelica gigas*, on menopausal symptoms. This randomized double-blind, placebo-controlled trial was performed for 12 weeks with 64 pre-, peri- and postmenopausal White Hispanic, White non-Hispanic and African American women who were randomly allocated to either the EstroG-100 group ($n = 31$) or the placebo group ($n = 33$). Primary end-points were the mean change in scores of the Kupperman menopause index (KMI) that evaluates 11 symptoms, and the mean change in scores of vaginal dryness. The mean KMI score was significantly reduced in the EstroG-100 group from 29.5 ± 7.4 at baseline to 11.3 ± 5.8 ($p < 0.01$) compared with change of the placebo group (29.2 ± 6.6 at baseline vs 23.7 ± 7.7 at week 12). The constituting symptoms of vasomotor, paresthesia, insomnia, nervousness, melancholia, vertigo, fatigue and rheumatic pain were significantly improved in the EstroG-100 group in comparison with the placebo group ($p < 0.05$). Statistically significant improvement in vaginal dryness in the EstroG-100 group was also observed compared with that of the placebo group ($p < 0.05$). In conclusion, EstroG-100 significantly improved the menopausal symptoms of pre-, peri- and post-menopausal women without weight gain or any serious side effects. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: menopausal symptom; vaginal dryness; EstroG-100; *Cynanchum wilfordii*; *Phlomis umbrosa*; *Angelica gigas*.

INTRODUCTION

The results of the Women's Health Initiative (WHI), a multi-center, randomized, double-blind placebo-controlled study involving 16608 post-menopausal women, have changed the approach to the management of menopausal symptoms. The WHI showed an increased risk of breast cancer by 26%, heart disease by 29% and stroke by 41%, in participants who took hormone replacement therapy (HRT) for the relief of menopausal symptoms, compared with those in the placebo group (Anon. Writing Group for the Women's Health Initiative Investigators, 2002). As an alternative, botanical dietary supplements have been reported to have weaker effects than HRT, but appear to be safer (Bai *et al*., 2007; Verhoeven *et al*., 2005). Many dietary supplements are widely available for menopausal symptoms but most lack the scientific evidence to support their use.

EstroG-100 is a botanical dietary supplement that has gained much attention in recent years. The Korea Food and Drug Administration (KFDA) has registered these herbs as non-toxic food materials based on the fact that they have been used as safe foods for herbal remedies for several hundred years in both Korea and China. A single-dose toxicity, a bacterial reverse mutation test, a chromosomal aberration test and a micronucleate test performed by a GLP laboratory in Korea showed the approximate lethal dose of EstroG-100 to be greater than 4000 mg/kg and EstroG-100 to have no genetic toxicity (data not shown). Numerous studies, both *in vitro* and *in vivo*, as well as the previous clinical research performed with Korean women, have confirmed the safety and efficacy of EstroG-100. According to reports on Korean herbs to the WHO, *Cynanchum wilfordii* and *Phlomis umbrosa* have hepatoprotective and antihepatotoxic activity, respectively (Shin, 1985; Kim and Park, 1994). In a previous human study conducted in South Korea, it was observed that a combination of EstroG-100, vitamins and minerals improved various menopausal symptoms (Lee *et al*., 2005). This study examined the effect of EstroG-100 on pre-, peri- and post-menopausal symptoms in non-Asian American women.

MATERIALS AND METHODS

Study plant. The dried roots of *Cynanchum wilfordii* Hemsley (harvested in Kyungbuk, Korea) were purchased from Samhong Co., *Phlomis umbrosa* Turcz (collected in Kyungbuk, Korea) from Ungok Traditional

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Medicine Co. and *Angelica gigas* Nakai (harvested in Chungbuk, Korea) from Jechun Herbal Medicine Co. The three herbs were mixed in a ratio (w/w) of *C. wilfordii*: *P. umbrosa*: *A. gigas*, 32.5: 32.5: 35.0. The mixture was extracted with a ten-fold volume of water for 8 h at 95 °C. The extract was then filtered through 10 μm pore size and the filtrate was concentrated up to 30 brix at 60 °C under 600 mmHg. The concentrate was dried, and the extracted powder was used for the preparation of EstroG-100. The powder contained 0.002% cinnamic acid originated from *C. wilfordii* root, 0.08% shanzhiside methylester from *P. umbrosa* root and 0.57% nodakenin from *A. gigas* root which were analysed by HPLC.

Clinical study material. The EstroG-100 tablets in the clinical study comprised 257.05 mg of EstroG-100 powder, corn starch 164.56 mg, microcrystalline cellulose 186 mg, hydroxypropyl methyl cellulose 50 mg, titanium dioxide 15 mg, silicon dioxide 6.2 mg, magnesium stearate 6.2 mg, glycerin mono fatty acid ester 5 mg and lac color 5 mg. The placebo tablet was the same as the treatment tablet except that the EstroG-100 powder was replaced with corn starch. Clinical study and placebo materials were the same in size and color, and separately formulated into 695 mg purple tablets.

Participants. Participants in the study were recruited by advertisement in newspapers and by signs posted at the study location. The criteria for eligibility was any woman with moderate or severe menopausal symptoms (score greater than or equal to 20), identified by a simplified questionnaire with the Kupperman menopause index (KMI) (Kupperman *et al.*, 1953). Participants were excluded from the study if they had any of the following conditions: concurrent use of dietary supplement for menopause symptoms, any suspicion of breast or endometrial malignancy, history of using estrogen or progestin-containing products in the past 3 months, psychoactive drugs, BMI greater than 40 kg/m^2, irregular gynecological bleeding one year after menopause, hysterectomy, uncontrolled hypertension, thyroid disease, diabetes mellitus, history of hormone-dependent (gynecological) cancer, drug and alcohol abuse, mental disorder, abnormality in renal and liver functions, personal or family history of breast cancer in a first degree relative, and history of clotting disorder such as deep vein thrombosis.

Eligibility was re-examined with the results of laboratory, mammogram and pelvic ultrasound tests. The registered participants were reminded that they should not take estrogen- or progestin-containing products or menopausal symptoms related supplements during the course of this study. In addition, the enrolled participants were informed to maintain their current life style and dietary habits.

Design/Ethics. This study was conducted as a randomized, double-blind, placebo-controlled trial for 12 weeks. This study was carried out according to International Conference on Harmonization/WHO Good Clinical Practice standards (ICH-GCP). This research was registered and approved by Sterling IRB, Atlanta, GA, USA (IRB#3192; NETESTROG-100-001). Written informed consent was obtained from all participants enrolled in the study.

Intervention/Blinding. Qualified participants were provided with either EstroG-100 or placebo tablet bottles. The tablet bottles were packaged identically, so that neither the research team nor the participants were able to differentiate them by appearance. Participants were instructed to take one tablet twice a day orally for 12 weeks. Each bottle contained a 6-week supply of either EstroG-100 or placebo, and the empty bottle was replaced when participants were seen at the 6-week follow up visit.

Primary outcome measurement/Objective. The primary endpoints that were assessed were the mean changes in scores of self-scored Kupperman menopause index (KMI), the mean change in scores of each symptom of the questionnaire from KMI, and the mean change in scores of vaginal dryness. The KMI includes hot flash or cold sweat (vasomotor), numbness and tingling (paresthesia), difficulty sleeping (insomnia), nervousness, feeling blue or depressed (melancholia), dizzy spells (vertigo), tired feelings (fatigue), rheumatic pain (arthralgia and myalgia), headaches, pounding of the heart (palpitation) and sensation of crawling on the skin (formication). Each participant came in to the center for three visits for the measurement of primary endpoints and biochemical/hematological analysis.

Sample size. There were no previous studies on the efficacy of EstroG-100 with respect to postmenopausal symptoms for American women. The sample size was postulated to be 72 from statistical significance level of 0.05, power of test of 0.8 and estimated standard deviation and difference of KMI between groups. Initially it was decided to have a total of 72 subjects in the study but it ended with 64 subjects due to more than an expected number of disqualifications and drop outs.

Randomization. The qualified participants were randomly allocated by permuted-block randomization (block size = 2, allocation ratio = 1:1) in accordance with the previously randomized allocation table generated by a computer-based fixed randomization at www.randomization.com. Each bottle was labeled with its randomized number. Participants were given a bottle in the order of return date after they completed the necessary screening examination and were given clearance by the principal investigator.

Adverse events. For the detection of adverse events, each subject was interviewed by the physician at every visit. In addition, participants were contacted every 2 weeks via telephone for any adverse event monitoring as well as compliance with the study.

Statistical analysis. Examination variables for effectiveness and safety were treated with an intent-to-treat (ITT) analysis. All enrolled participants who had taken the test material at least once, visited the center at week 6, and complied with the dosage of protocol over 50% per 12 weeks treatment, were included in the analysis. The last-observation-carried-forward method was used for missing data. In order to evaluate effectiveness, the study group was tested for normality. Significance of difference was tested by independent *t*-test. For any data that did not show normality, the Wilcoxon rank sum test was applied. SAS for Windows 9.1 (SAS, Cary, NC) was

used for the analysis. All data were summarized as mean ± SD, and values of $p < 0.05$ were considered statistically significant.

RESULTS

Participants

Participant screening, enrollment and completion are shown in Fig. 1. The total number of participants who consented was 104. Forty participants did not meet the inclusion criteria. The effectiveness and safety of EstroG-100 were evaluated in 61 participants out of 64 total participants who were enrolled in the study and complied with the dosage protocol. Participants consisted of three African Americans and 58 White Hispanic/non-Hispanic Americans. Three participants were terminated before the second visit to the center for week 6 follow up and they were not included in the evaluation. Two participants could not be reached for the week 6 visit and were terminated from the study. One participant was terminated from the study after 1 week of being on the study due to a discrepancy in the mammogram report: the research team received two different mammogram reports 1 week apart with the second report being abnormal. One participant was terminated from the study at the 6-week visit due to vaginal spotting after 1 week of taking the pills. As the participant reported this during the week 6 visit, she was allowed to complete the week 6 KMI questionnaire but was terminated from the study subsequently. She was later found to be a participant of the placebo group.

Of the total participants, 33 participants were in the placebo group and 31 participants were in the EstroG-100 group. Excluding the three participants who were terminated from the study, the average age of the 29 participants in the EstroG-100 group was 53.2 ± 5.7 (range 45–64), while that in the placebo group was 54.1 ± 5.9 (range 42–70). The last menstrual period (LMP) varied from 0 to 336 months, and the average LMP of the EstroG-100 group was 61.0 months and that of the placebo group was 45.7 months. At the baseline of the study, there were no significant differences on basic physical profiles, serum hormone concentrations, and serum metabolic profiles between the treatment group and the placebo group (Table 1).

The compliance rate (%) for test material was 97.2 ± 2.1 for the EstroG-100 group and 96.6 ± 2.2 for the placebo group. The study lasted from 26 May 2009 when the first visit of the first participant was made to 29 January 2010 when the last visit of the last participant was made.

Results

The mean KMI score was significantly reduced in the EstroG-100 group from 29.5 ± 7.4 at baseline to 13.6 ± 7.6 at week 6 and to 11.31 ± 5.8 at week 12. The placebo group showed changes from 29.2 ± 6.6 at baseline to 23.3 ± 9.0 at week 6 and to 23.7 ± 7.7 at week 12 ($p < 0.01$). The decrease in KMI score at week 12 was 18.1 ± 8.5 in the treatment group and was 5.5 ± 5.3 in the placebo group. The improvement was statistically significant in the treatment group compared with the placebo group ($p < 0.01$).

As shown in Table 2, for the each constituting symptom of KMI, the mean scores for vasomotor, insomnia, nervousness, melancholia, vertigo and fatigue were significantly lower in the EstroG-100 group at weeks 6 and 12 compared with baseline ($p < 0.01$), and the

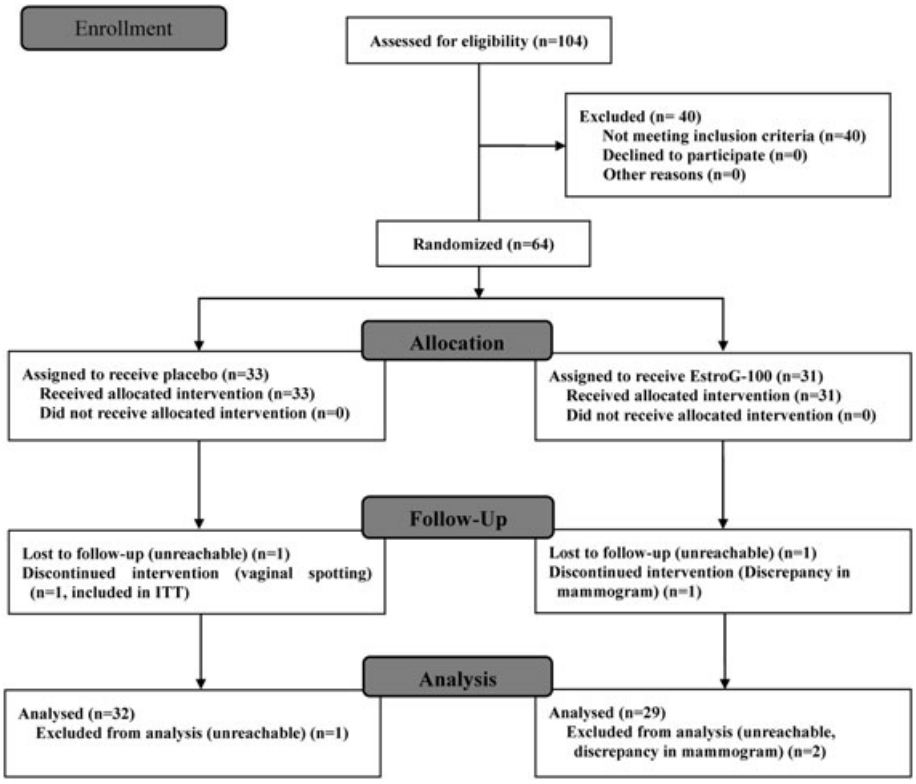

Figure 1. Study flow diagram.

Table 1. Basic characteristics of subjects

	EstroG-100	Placebo	Total
FSH (mIU/mL)	50.95 ± 36.48	71.97 ± 40.52	68.10 ± 39.77
E2 (pg/mL)	55.26 ± 51.78	40.83 ± 38.27	46.39 ± 45.39
Osteocalcin (ng/mL)	18.61 ± 8.01	20.21 ± 9.12	20.19 ± 8.58
Alkaline phosphatase (IU/L)	73.93 ± 15.86	79.47 ± 29.47	78.85 ± 23.96
hGh (ng/mL)	1.16 ± 2.26	0.56 ± 0.66	0.63 ± 1.64
Fasting glucose (mg/dL)	88.90 ± 9.65	91.97 ± 6.72	90.51 ± 8.32
Cholesterol (mg/dL)	212.55 ± 30.94	217.19 ± 25.49	217.62 ± 28.07
HDL (mg/dL)	61.55 ± 17.84	64.28 ± 12.83	64.49 ± 15.34
LDL (mg/dL)	125.76 ± 27.89	128.50 ± 24.11	129.18 ± 25.79
Triglyceride (mg/dL)	127.59 ± 66.46	120.34 ± 61.44	118.03 ± 63.44
Weight (lb)	160.69 ± 37.61	160.31 ± 26.28	160.49 ± 31.89
Height (in)	63.72 ± 2.51	63.47 ± 2.72	63.59 ± 2.60
BMI (kg/m^2)	27.83 ± 5.79	27.94 ± 4.19	27.89 ± 4.97
Systolic pressure (mmHg)	112.48 ± 10.68	114.50 ± 11.60	113.50 ± 11.12
Diastolic pressure (mmHg)	75.76 ± 6.92	78.00 ± 7.41	76.93 ± 7.21

No significant difference observed between placebo and treatment groups ($p > 0.05$)

FSH, follicular stimulating hormone; E2, estradiol; hGH, human growth hormone; HDL, high density lipoprotein; LDL, low density lipoprotein; BMI, body mass index.

improvement of the individual symptoms was significant between the two groups at weeks 6 and 12 ($p < 0.01$). The mean scores of paresthesia and rheumatic pain were significantly lower in the EstroG-100 group at week 12 compared with baseline ($p < 0.01$) and between the treatment and placebo groups at week 12 ($p < 0.05$). Although the scores for headaches and palpitations were decreased significantly in both treatment and placebo groups, there were no statistically significant differences between treatment and placebo groups.

The mean formication score was reduced in the EstroG-100 group, 0.83 ± 0.85 at baseline to 0.14 ± 0.44 at week 6 and to 0.28 ± 0.45 at week 12, while it was lowered from 1.25 ± 1.05 at baseline to 0.88 ± 1.01 at week 6 after and to 0.72 ± 0.96 at week 12 in the placebo group. The decrease in the mean score at week 6 (0.69 ± 0.81 in the EstroG-100 group vs 0.38 ± 0.55 in the placebo group) was significant ($p < 0.05$), but the improvement at the completion of the study was not significant between the two groups (Table 2).

The mean score for vaginal dryness decreased in the study group from 1.45 ± 1.02 at baseline to 0.72 ± 0.88 at week 6 and to 0.59 ± 0.87 at week 12 ($p < 0.01$) compared with that of the placebo group that showed a reduction from 1.75 ± 1.11 at baseline to 1.28 ± 1.02 at week 12 ($p < 0.01$). This change was statistically significant between the treatment and placebo groups ($p < 0.05$) (Table 2).

Serum chemistry

No significant change in weight and the BMI was observed in either the EstroG-100 or the placebo groups after 12 weeks (Table 3). No statistically significant differences were observed between baseline and week 12 in each of the two groups, as well as between the two groups with regard to biochemical markers, serum estrogen (E2), growth hormone (hGH), osteocalcin, alkaline phosphatase, total cholesterol, LDL, HDL and triglyceride ($p > 0.05$) (Table 3). Although a statistically significant difference in mean serum FSH level was shown between the two groups ($p < 0.05$), the serum estradiol and FSH levels in the EstroG-100 group at week 12 were not changed significantly from that of the baseline. The change of FSH in the placebo group between baseline and week 12 was significant ($p < 0.05$) (Table 3).

Adverse events. No adverse events were observed or reported by participants who received EstroG-100 in this study.

DISCUSSION

This randomized, double-blind, placebo-controlled 12 week study showed that EstroG-100 effectively improves various climacteric symptoms. The mean Kupperman menopause index (KMI) score was significantly reduced in the EstroG-100 treatment group compared with that of the placebo group ($p < 0.01$). It is notable that vaginal dryness was also one of the symptoms significantly improved, along with most of the individual symptoms in the KMI questionnaire. While the exact mechanism of action is not clear, EstroG-100 significantly improved menopausal symptoms without affecting the female hormone levels in the human body. The effects of EstroG-100 are presumed to result from complex interactions of the diverse plant constituents.

In the postmenopausal state, ovarian reserve is diminished resulting in lower serum estradiol levels. In the premenopausal state, lower serum estradiol levels result in the stimulation of the pituitary gland, which in turn produces more follicle stimulating hormone (FSH). Higher serum FSH levels then stimulate the ovary to produce more estradiol. In postmenopausal women, this negative feedback system is interrupted because the ovaries are unable to respond to this increased FSH level. This results in lower E2 levels and higher FSH levels (Messinis, 2006). In this study, the mean serum E2 levels in the EstroG-100 group did not increase, implying that EstroG-100 is not an active estrogenic compound. The mean serum FSH levels also remained unchanged, an indication that EstroG-100

Table 2. Mean change in scores of the each individual question of the Kupperman menopause index and vaginal dryness

	EstroG-100			Placebo		
	Week 0 (baseline)	Week 6	Week 12	Week 0 (baseline)	Week 6	Week 12
Hot flush or cold sweat (= vasomotor)	2.24 ± 0.69	1.03 ± 0.82[abc]	0.79 ± 0.73[abc]	2.22 ± 0.66	1.78 ± 0.75[c]	2.06 ± 0.76
Numbness and tingling (= paresthesia)	1.31 ± 0.85	0.59 ± 0.78[cd]	0.55 ± 0.74[cd]	1.41 ± 0.91	1.13 ± 0.94[e]	1.09 ± 0.96[c]
Trouble sleeping (= insomnia)	2.28 ± 0.84	1.28 ± 0.96[acd]	0.97 ± 0.82[abc]	2.03 ± 0.86	1.63 ± 1.01[e]	1.63 ± 0.87[e]
Nervousness	1.72 ± 0.88	0.76 ± 0.69[abc]	0.66 ± 0.67[abc]	1.56 ± 0.84	1.22 ± 0.83	1.34 ± 0.75
Feeling blue or depressed (= melancholia)	1.93 ± 0.88	1.03 ± 0.68[abc]	0.83 ± 0.71[abc]	1.59 ± 0.95	1.31 ± 0.93	1.31 ± 0.74
Dizzy spells (= vertigo)	0.97 ± 0.82	0.21 ± 0.49[abc]	0.21 ± 0.41[abc]	0.75 ± 0.72	0.72 ± 0.77	0.59 ± 0.80
Tired feelings (= fatigue)	2.21 ± 0.77	0.90 ± 0.77[abc]	0.72 ± 0.70[abc]	2.00 ± 0.88	1.69 ± 0.90[e]	1.59 ± 0.80[e]
Rheumatic pain (= arthralgia and myalgia)	1.59 ± 1.02	0.79 ± 0.94[acd]	0.55 ± 0.78[cd]	1.84 ± 0.95	1.63 ± 0.83	1.47 ± 0.88
Headaches	1.34 ± 1.04	0.69 ± 0.76[c]	0.66 ± 0.77[c]	1.53 ± 0.95	1.13 ± 0.91[e]	0.84 ± 0.72[c]
Pounding of the heart (= palpitation)	1.00 ± 0.96	0.48 ± 0.69[e]	0.55 ± 0.63[e]	1.31 ± 0.93	0.91 ± 0.82[c]	0.75 ± 0.84[c]
Sensation of crawling on the skin (= formication)	0.83 ± 0.85	0.14 ± 0.44[cd]	0.28 ± 0.45[c]	1.25 ± 1.05	0.88 ± 1.01[c]	0.72 ± 0.96[c]
Vaginal dryness	1.45 ± 1.02	0.72 ± 0.88[abc]	0.59 ± 0.87[cd]	1.75 ± 1.11	1.50 ± 1.11[e]	1.28 ± 1.02[c]

[a] $p < 0.01$ compared between groups by *t*-test.
[b] $p < 0.01$ compared between groups by Wilcoxon rank sum test.
[c] $p < 0.01$ compared with baseline by paired *t*-test.
[d] $p < 0.05$ compared between groups.
[e] $p < 0.05$ compared with baseline.

does not appear to exert its effect at the hormone receptor level. This is consistent with a previous receptor binding affinity test, which showed that EstroG-100 did not bind to either estrogen receptor-alpha or estrogen-receptor-beta (data not shown). The findings in the current study are also consistent with a prior randomized, double-blind, placebo-controlled clinical study that showed no statistically significant change in the E2 and FSH (Lee *et al*., 2005).

One of the most widely used herbs for menopausal symptoms is black cohosh. While the exact mechanism of black cohosh has not been established, one stipulation is that it plays a role as a selective estrogen receptor modulator (SERM) (Seidlova-Wuttke *et al*., 2003). The SERM are a class of compounds that act on the estrogen receptors. A characteristic that distinguishes these substances from pure receptor agonists and antagonists is that their action is different in various tissues, thereby granting the possibility to selectively inhibit or stimulate estrogen-like action in various tissues. Like black cohosh, the mechanism of action of EstroG-100 is not clear. It may be related to some form of estrogen agonist and/or antagonist actions that benefit bone metabolism and menopausal symptoms, while having no effect on E2 and FSH levels (Lee *et al*., 2005, 2008; Kim *et al*., 2008). Further studies will be needed to investigate the mechanism of action.

Some of the previous studies involving other popular dietary supplements for menopause have been disappointing. In some clinical trials, black cohosh was effective in the menopause rating scale (Wuttke *et al*., 2003; Osmers *et al*., 2005) and health related quality of life scale (Mollá *et al*., 2009) when compared with conjugated estrogen or the placebo group. In other studies the number of hot flashes, number of vasomotor symptoms or anxiety rating scale were not significantly improved in the black cohosh group compared with the placebo group (Jacobson *et al*., 2001; Geller *et al*., 2009; Amsterdam *et al*., 2009). Isoflavones, another popular product used in menopause, have yielded conflicting results in aiding women with menopausal symptoms. The study by Geller *et al*. (2009) showed no improvement with the exception of anxiety in the isoflavone treatment group, while some studies showed statistically significant improvements of the Kupperman index, the number of hot flashes and the menopausal symptom quality of life questionnaire (Welty *et al*., 2007; Drews *et al*., 2007).

The safety and efficacy of EstroG-100 have been demonstrated in previous studies involving rats as well as humans (Lee *et al*., 2005, 2008; Kim *et al*., 2008). In a non-reproductive tract target tissue response to measure estrogen-specific alkaline phosphatase (ALP) levels in women, *Cynanchum wilfordii*, *Phlomis umbrosa* and *Angelica gigas* in combination were found to promote the ALP level more than any of the individual herbal extracts alone to create a synergistic effect (Lee *et al*., 2005). In studies involving the reproductive tract response, EstroG-100 did not increase the uterus weight of ovariectomized rats while it did increase femoral bone mineral density (Lee *et al*., 2008; Kim *et al*., 2008). In the previous human clinical trial (Lee *et al*., 2005), EstroG-100 significantly improved menopausal symptoms without adverse events. While LDL and HDL levels were changed significantly with HRT after administration of E2 (Turgeon *et al*., 2006), EstroG-100 had no effect on weight or biochemical and metabolic markers such as liver enzymes, renal function and lipids in the current study. There were no adverse reactions or events reported with EstroG-100 including vaginal bleeding, while showing statistically significant improvement in most symptoms of menopause, including vaginal dryness.

The current study measured the scores of KMI symptoms that may not represent all the menopausal symptoms. However, the KMI is a widely accepted instrument for evaluating menopause symptoms. Vaginal dryness was added to the primary outcome measures as it is a common symptom experienced by postmenopausal women.

Table 3. Change of the variables for 12 weeks of treatment with EstroG-100

	EstroG-100			Placebo			Total		
	Pre-treatment	Post-treatment	Mean difference (%)	Pre-treatment	Post-treatment	Mean difference (%)	Pre-treatment	Post-treatment	Mean difference (%)
FSH (mIU/mL)	50.95 ± 36.48	52.43 ± 35.30	2.90	71.97 ± 40.52	59.93 ± 30.44[a]	−16.73	68.10 ± 39.77	59.78 ± 32.82[b]	−12.22
E2 (pg/mL)	55.26 ± 51.78	40.60 ± 26.62	−26.54	40.83 ± 38.27	45.40 ± 32.47	11.20	46.39 ± 45.40	42.91 ± 29.63	−7.51
Fasting glucose (mg/dL)	88.90 ± 9.65	90.24 ± 8.77	1.51	91.97 ± 6.72	89.39 ± 9.07	−2.81	90.51 ± 8.32	89.80 ± 8.86	−0.78
Osteocalcin (ng/mL)	20.2 ± 9.12	20.7 ± 9.29	2.30	18.6 ± 8.01	19.5 ± 7.40	4.76	20.2 ± 8.58	20.9 ± 8.38	3.37
Alkaline phosphatase (IU/L)	79.5 ± 29.5	81.5 ± 24.7	2.62	73.9 ± 15.9	78.1 ± 19.5	5.64	78.8 ± 24.0	81.8 ± 22.2	3.77
hGh (ng/mL)	0.56 ± 0.66	1.17 ± 1.54	108.4	1.16 ± 2.26	1.92 ± 2.70[a]	64.9	0.63 ± 1.64	1.61 ± 2.20	154.5
Cholesterol (mg/dL)	217.2 ± 25.5	211.8 ± 35.1	−2.49	212.6 ± 30.9	209.8 ± 31.4	−1.31	217.6 ± 28.1	212.7 ± 33.1	−2.28
HDL (mg/dL)	64.3 ± 12.8	60.6 ± 14.3	−5.66	61.6 ± 17.8	59.6 ± 15.9[a]	−3.25	64.5 ± 15.3	61.3 ± 15.0	−4.88
LDL (mg/dL)	128.5 ± 24.11	127.8 ± 28.8	−0.54	125.8 ± 27.9	127.4 ± 28.0	1.34	129.2 ± 25.8	127.3 ± 28.2	−1.42
Triglyceride (mg/dL)	120.3 ± 61.4	114.8 ± 83.9	−4.57	127.6 ± 66.5	112.0 ± 50.3	−12.2	123.8 ± 63.4	113.5 ± 68.5	−8.32
Weight (lb)	160.69 ± 37.61	159.66 ± 37.35[a]	−0.64	160.31 ± 26.28	160.25 ± 27.43	−0.04	160.49 ± 31.89	159.78 ± 32.49	−0.44
BMI (kg/m^2)	27.83 ± 5.79	27.66 ± 5.73	−0.62	27.94 ± 4.19	28.00 ± 4.27	0.34	27.89 ± 4.97	27.85 ± 5.01	−0.13

[a]Significantly different from baseline, $p < 0.05$, paired t-test.

[b]Significantly different between groups, $p < 0.05$, t-test.

FSH, follicular stimulating hormone; E2, 17ß-estradiol; BMI, body mass index; hGH, human growth hormone; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

CONCLUSIONS

A 12 week treatment with EstroG-100 showed a statistically significant improvement in the various menopausal symptoms such as hot flash, night sweats, paresthesia, insomnia, nervousness, melancholia, vertigo, fatigue, rheumatic pain and vaginal dryness, compared with the placebo group. No adverse effects were reported with EstroG-100. There were no significant changes in body weight, BMI, serum E2 levels, serum FSH levels, or liver enzymes, all of which have previously been observed with hormone replacement therapy. In this clinical trial, EstroG-100 appears to be an effective and safe dietary supplement for use in pre-, peri- and post-menopausal women.

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Conflict of Interest

The authors have no conflict of interest to declare.

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