Original Article

Evaluation of Efficacy and Safety of EstroG-100® in Alleviating Menopausal Symptoms in Postmenopausal Women in India: A Prospective, Single-center, Single-arm, Interventional Study

Hepzibah Kirubamani, Prachi Ahire[1], Stalin C[1]

Department of Obstetrics and Gynecology, Saveetha Medical College and Hospital, [1]Medical Affairs, Shield Healthcare, Chennai, Tamil Nadu, India

Abstract

Background: Menopause is a natural stage in a woman's life marked by the cessation of menstrual periods. Common symptoms include hot flashes, mood swings, and vaginal discomfort, among others. These climacteric symptoms lead to a compromised quality of life affecting physical, biological, psychological, and social well-being. There are concerns with long-term clinical use of Hormone replacement therapy (HRT) and alternative therapies that are devoid of adverse risks are required. This study aimed to evaluate the safety and efficacy of EstroG-100®, containing a mixture of standardized extracts of *Cynanchum wilfordii*, *Phlomis umbrosa*, and *Angelica gigas*, on menopausal symptoms and its impact on quality of life. **Methodology:** This was a prospective, single-center, single-arm, interventional study. Sixty female subjects, with confirmed menopause and moderate-to-severe symptoms, were enrolled and treated with EstroG-100® twice daily, for 12 weeks. Improvement in the climacteric symptoms was evaluated using the Menopause Rating Scale-11 and Menopause Symptoms Treatment Satisfaction Questionnaire (MS-TSQ). All the results were evaluated by the SPSS software version 23.0. **Results:** A significant improvement was noticed in the somatic, urogenital, and psychological climacteric symptoms from baseline to 6 weeks ($P = 0.001$) and a highly significant improvement after 12 weeks ($P = 0.0001$) of treatment. 96.5% of patients were satisfied with the treatment outcome evaluated by the MS-TSQ. No changes in blood pressure and body mass index were reported. No side effects were reported during the study. **Conclusion:** The first study of EstroG-100® in Indian menopausal women demonstrated a statistically significant improvement in climacteric symptoms. A 12-week treatment proved safe and effective in enhancing postmenopausal women's quality of life. The remedy was well-tolerated and effectively alleviated menopausal symptoms.

Keywords: *EstroG-100, Menopause Rating Scale-11 and Menopause Symptoms Treatment Satisfaction Questionnaire, postmenopausal women*

Submitted: 07-Nov-2023 **Revised:** 08-Nov-2023
Accepted: 31-Jan-2024
Published: 23-Feb-2024

Introduction

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jomh

DOI: 10.4103/jmh.jmh_220_23

Address for correspondence: Dr. Hepzibah Kirubamani, Department of Obstetrics and Gynecology, Saveetha Medical College and Hospital, Chennai, Tamil Nadu, India. E-mail: hepsi1002@yahoo.co.in

How to cite this article: Kirubamani H, Ahire P, Stalin C. Evaluation of efficacy and safety of EstroG-100® in alleviating menopausal symptoms in postmenopausal women in India: A prospective, single-center, single-arm, interventional study. J Mid-life Health 2023;14:285-90.

Menopause-related symptoms and the available treatment modalities have been studied extensively in Western countries, but relatively less data are available from developing countries like India. India alone will host approximately more than 130 million menopausal women by 2025.[1,2]

Menopausal symptoms include hot flashes, urinary incontinence, vaginal atrophy, decreased sexual function, sleep problems, anxiety, irritability, depression,[3-10] and other conditions such as coronary heart disease and osteoporosis.[11-13] These menopausal symptoms lead to a compromised quality of life. Hormone replacement therapy (HRT) has been considered the standard treatment for menopausal symptoms.[14-16]

Although HRT has been used in clinical practice for decades, it has been associated with a higher risk of breast cancer, endometrial cancer, thromboembolic events, and coronary heart disease.[4,17-20] The use of HRT has been reported to increase the risk of breast cancer, heart disease, and stroke by 26%, 29%, and 41%, respectively.[15] There is a need for a safe and effective remedy that can improve menopausal symptoms and subsequently the quality of life. EstroG-100® is a standardized extract of *Cynanchum wilfordii*, *Phlomis umbrosa*, and *Angelica gigas*. Multiple clinical, *in vitro*, and *in vivo* studies have confirmed the safety and efficacy of EstroG-100®. A clinical study conducted at Samsung Cheil Hospital, Sungkyunkwan University, South Korea, using the Kupperman Menopausal Index (KMI), proved that after 3 months of EstroG-100® use, various menopausal symptoms (such as hot flashes, sleep disturbances, fatigue, or joint pain) showed statistically significant improvement compared to the placebo group.[20] It showed a significant improvement in femur bone mineral density. In another clinical study conducted in California in the United States, EstroG-100® showed statistically significant improvement in the mean KMI scores, and in various menopausal symptoms individually.[21,22] The menopausal symptoms affect the physical, biological, psychological, and social well-being of women and compromise the quality of life. This clinical study was conducted to evaluate the efficacy and safety of EstroG-100® in Indian postmenopausal women, which contains a blend of standardized plant extracts of *C. wilfordii*, *P. umbrosa*, and *A. gigas*, on symptoms of menopause.

Methodology

This was a prospective single-center, single-arm,

interventional study with the primary objective to evaluate the improvement in climacteric symptoms using the Menopause Rating Scale (MRS-11) and Menopause Symptoms Treatment Satisfaction Questionnaire (MS-TSQ). The secondary objective was to assess any changes in body mass index (BMI) and hematological and biochemical blood parameters from baseline to 12 weeks.

Sixty female subjects with confirmed menopause (no menstrual cycle for consecutive 12 months) and with moderate-to-severe symptoms, controlled hypertension, and controlled blood glucose levels were included in the study. Exclusion criteria included subjects with the usage of estrogen- or progestin-containing products in the past 3 months, history of irregular vaginal bleeding, history of hormone-dependent cancer (breast, uterine, or endometrial), abnormal renal or liver function tests, abnormal thyroid function test, and abnormal breast ultrasound and women receiving menopause-related medicine or supplements in the past 3 months.

Demographic data (height, weight, BMI, and age), history pertaining to cardiovascular disease, medical history, vitals, and systemic examination were done at screening. The enrolled subjects received EstroG-100®, orally twice daily, for 12 weeks. The subjects were allowed on standard treatment for other comorbid conditions as per the standard guidelines.

The MRS consisted of a list of 11 items (symptoms or complaints). Each of the 11 symptoms was scored from 0 (no complaints), 1 (mild complaints), 2 (moderate), 3 (severe), and 4 points (very severe symptoms) depending on the severity of the complaints perceived by the women completing the scale.

Adverse event monitoring was done throughout the study period. The study was approved by the Ethics Committee of Saveetha Medical College, Chennai.

In this study, 75 subjects were screened and 60 were enrolled after fulfilling the eligibility criteria and getting informed consent. Considering the test reliability of 95%, power of 80%, and 10% lost to follow-up, the minimum sample size required was 60. All the results were evaluated and compared between various time points of the test group using an independent *t*-test and repeated measures ANOVA, by the SPSS software version 23.0.

Results

Of the subjects enrolled [Figure 1] 46% belonged to the age group of 40-50 years and 37% belonged to 50-60 years [Table 1]. The BMI of 25% subjects were normal, 36% of subjects were overweight and 32% were obese [Table 2]. In our study population 66% of women had

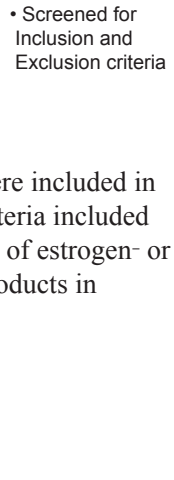


Figure 1: Flowchart of subjects' enrollment

confirmed menopause of less than five years duration and women with surgical menopause were also included.

The study results [Table 3] have shown a significant improvement in the mean scores of Menopause Rating Scale – 11 from baseline up to 6 weeks ($P = 0.001$) and a highly significant improvement after 12 weeks ($P = 0.0001$) of treatment with Estro G 100 [Figure 2]. There is also a significant improvement in the mean scores of Improvement in MS-TSQ [Table 4] from baseline up to 6 weeks ($P < 0.001$) and at 12 weeks ($P < 0.0001$) of treatment with Estro G 100. With respect to the percentage of satisfaction in improvement of menopausal symptoms post treatment, more than 96 % of patients were satisfied with the treatment [Table 5]. Table 6 depicts the assessment of blood parameters pre and post treatment. The complete hemogram was maintained within the normal range after completion of treatment duration of 12 weeks with Estro G 100. The blood counts, renal and hepatic parameters were maintained within the normal range. The haemoglobin showed a significant increase post treatment. The blood sugar levels were maintained within the normal range. The renal function was maintained within normal limits but reduction in Urea was noted posttreatment [Figure 3]. The liver enzymes and bilirubin showed significant reduction post treatment [Figure 4] and no significant changes observed in lipid profile. There were no serious adverse events observed during the entire treatment duration of 12 weeks.

Discussion

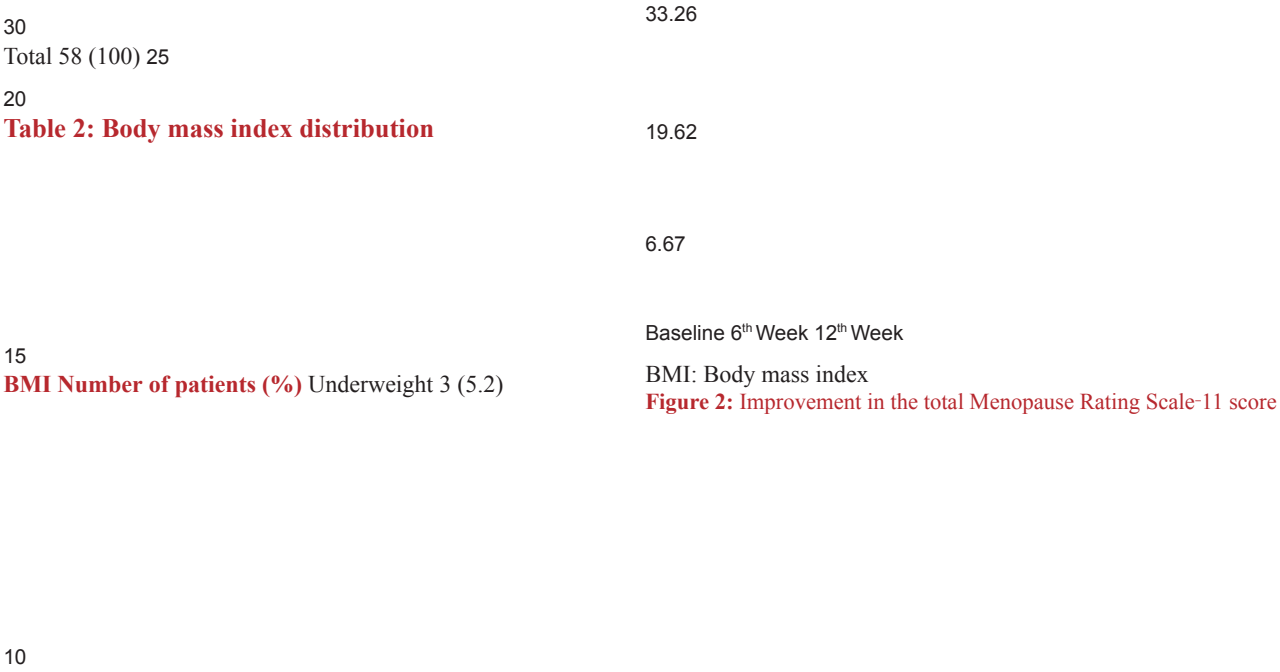
This was the first study of EstroG-100® in Indian women showing significant improvement in climacteric symptoms evaluated by MRS-11 and significant treatment satisfaction evaluated by the MS-TSQ. The patients were enrolled on various inclusion and exclusion criteria [Figure 1]. Of the total subjects enrolled, 46% belonged to the age group of 40–50 years and 37% belonged to 50–60 years [Table 1]. The BMI of 25% of subjects was normal, 36% of subjects were overweight, and 32% were obese [Table 2]. In our study population, 66% of women had confirmed menopause of <5 years duration, and women with surgical menopause were

Table 1: Age distribution of subjects

Age	Number of patients (%)
40–50	27 (46.6)
51–60	22 (37.9)
61–70	9 (15.5)
Total	58 (100)

Table 2: Body mass index distribution

BMI	Number of patients (%)
Underweight	3 (5.2)
Normal	15 (25.9)
Overweight	21 (36.2)
Obesity	19 (32.8)
Total	58 (100)



BMI: Body mass index

Figure 2: Improvement in the total Menopause Rating Scale-11 score

Table 3: Improvement in the Menopause Rating Scale-11 (mean±standard deviation)

MRS-11 parameters	Baseline	Week 6	*P*	Week 12	*P*
Somatic subscale					
Joint muscular discomfort	2.84±0.55	1.67±0.63	0.001	0.71±0.53	0.0001
Sleep problems	3.76±0.43	2.45±0.59	0.001	0.88±0.42	0.0001
Heart discomfort	3.45±0.56	2.12±0.77	0.001	0.67±0.47	0.0001
Hot flashes	3.22±0.77	2.0±0.87	0.001	0.60±0.52	0.0001
Urogenital subscale					
Dryness of the vagina	2.16±0.64	1.03±0.70	0.001	0.34±0.51	0.0001
Bladder problems	2.21±0.61	1.12±0.70	0.001	0.40±0.52	0.0001
Sexual problems	1.98±0.98	1.03±0.67	0.001	0.33±0.50	0.0001
Psychological subscale					
Physical and mental exhaustion	3.19±0.63	1.60±0.77	0.001	0.50±0.53	0.0001
Anxiety	3.53±0.56	2.05±0.84	0.001	0.71±0.59	0.0001
Irritability	3.6±0.56	2.29±0.72	0.001	0.74±0.57	0.0001
Depressive mood	3.47±0.62	2.28±0.76	0.001	0.81±0.57	0.0001

MRS: Menopause Rating Scale, SD: Standard deviation

Table 4: Improvement in the Menopause Symptoms Treatment Satisfaction Questionnaire

MS-TSQ parameters	Baseline	Week 6	*P*	Week 12	*P*
Hot flashes during the day	3.86±0.34	2.07±0.67	0.001	0.62±0.52	0.0001
Hot flashes during the night	3.62±0.61	1.84±0.67	0.001	0.64±0.48	0.0001
Quality of sleep	3.6±0.52	2.1±0.76	0.001	0.67±0.47	0.0001
Mood or emotions	3.22±0.79	1.66±0.69	0.001	0.57±0.59	0.0001
Interest in sex	3.52±0.59	1.84±0.74	0.001	0.40±0.56	0.0001
Tolerability	3.38±0.69	1.81±0.54	0.001	0.26±0.48	0.0001
Overall satisfaction	3.45±0.65	1.84±0.55	0.001	0.24±0.43	0.0001

MS-TSQ: Menopause Symptoms Treatment Satisfaction Questionnaire

Table 5: Percentage of satisfaction with respect to the Menopause Symptoms Treatment Satisfaction Questionnaire

Parameter	Extremely dissatisfied		Dissatisfied		Neutral		Satisfied		Extremely satisfied	
	Prestudy (%)	Poststudy (%)	Prestudy (%)	Poststudy (%)	Prestudy (%)	Poststudy (%)	Prestudy (%)	Poststudy (%)	Prestudy (%)	Poststudy (%)

Hot flashes during the day 86.21 0.00 13.79 0.00 0.00 3.45 0.00 46.55 0.00 50 Hot flashes during the night 50 0 34.48 0 15.52 3.45 0 46.55 0 50 Quality of sleep 72.41 0 22.41 0 5.17 0 0 60.34 0 39.66 Mood or emotions 63.79 0 31.03 0 5.17 0 0 65.51 0 34.48 Interest in sex 48.28 0 34.48 0 17.24 0 0 46.55 0 53.45 Ability to concentrate 58.62 0 36.21 0 5.17 3.45 0 34.48 0 62.07 Tolerability 53.45 0 36.21 0 10.34 0 0 24.14 0 75.86 Overall satisfaction 58.62 0 34.48 0 6.90 0 0 24.14 0 75.86

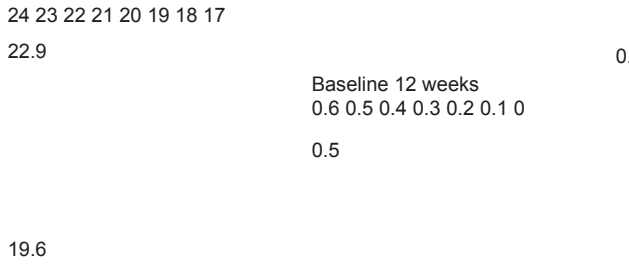


Figure 3: Comparison of blood urea levels – pre- and posttreatment. Significant reduction ($P = 0.003$) in blood urea from baseline to 12 weeks

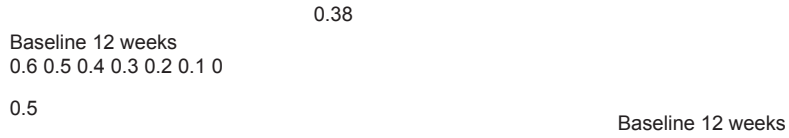


Figure 4: Comparison of bilirubin – pre- and posttreatment. Significant reduction ($P = 0.009$) in total bilirubin from baseline to 12 weeks

also included. There was a significant improvement in postmenopausal symptoms as per the MRS [Table 3]. Significant improvement in the quality of life with respect to MS-TSQ was reported [Tables 4 and 5]. The complete hemogram was maintained within the normal range after completion of treatment for 12 weeks with EstroG-100 [Table 6]. The blood counts and renal and hepatic parameters were maintained within the normal range. The hemoglobin showed a significant increase posttreatment. The blood sugar levels were maintained within the normal range. The renal function was maintained within normal limits, but reduction in urea was noted posttreatment. The liver enzymes and bilirubin showed significant reduction posttreatment, and no significant changes were observed in the lipid profile [Figures 3 and 4]. The subjects were extremely satisfied, and no serious adverse events were reported during the 12 weeks of treatment.

The results correspond to the earlier studies conducted in Korea and US/Canada.[20-22] EstroG-100® showed a statistically significant improvement ($P < 0.001$) in all the climacteric symptoms measured by the MRS-11, such as hot flash, heart discomfort, sleep problems, anxiety, depressed moods, irritability, vaginal dryness, bladder problems, sexual problems, joint and muscular discomforts, and physical and mental exhaustion compared to the baseline. There was a significant improvement in the vasomotor, urogenital, and psychological symptoms as early as 6 weeks as well as at 12 weeks ($P \leq 0.0001$) of treatment with EstroG-100®. EstroG-100® has been reported to improve bladder

Table 6: Assessment of blood parameters

Variables	Pre (mean±SD)	Post (mean±SD)	*P*
Hb (g/dL)	11.852±1.4027	12.83±1.675	0.002
Urea (mg/dL)	22.87±6.84	19.611±5.6904	0.003
Creatinine (mg/dL)	0.6±0.144	0.632±0.12916	0.158
Total cholesterol (mg/dL)	193.49±36.965	203.009±37.5496	0.206
Triglycerides (mg/dL)	161.89±78.14	172.038±83.2645	0.499
HDL (mg/dL)	43.533±9.0149	47.05±11.985	0.088
LDL (mg/dL)	126.88±45.281	113.265±32.1009	0.064
Total bilirubin (mg/dL)	0.5056±0.22932	0.3806±0.23719	0.009
Direct bilirubin (mg/dL)	0.1898±0.11606	0.44±1.344	0.184
SGOT (U/L)	24.226±8.0448	24.444±12.2465	0.908
SGPT (U/L)	22.443±22.2324	25.007±12.0336	0.47
Alkaline phosphatase (U/L)	95.228±31.7884	82.211±41.4934	0.016

Hb: Hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase, SD: Standard deviation

observed during the treatment duration of 12 weeks. The blood sugar levels were maintained within the normal range; hence, patients with controlled diabetes can take this drug safely. A significant reduction in blood urea was noted poststudy and other renal parameters were maintained within normal limits. The liver enzymes and bilirubin showed significant reduction posttreatment.

With respect to lipid profile, there was an increase in high-density lipoprotein levels and a decrease in low-density lipoprotein levels; the drug can be taken safely by hyperlipidemic patients too.

Limitations of the study

The study has a few limitations too, including a single-arm, open-label study without a comparator arm. Single-arm design was planned because the objective of problems and increase urinary frequency, urgency, and nocturia which are common problems in menopausal

women. There was no change in the blood pressure and BMI when compared with the baseline values, which was also evident in the previous studies.[21-25]

The most common adverse effects of HRT are bleeding, spotting, nausea, and malaise, resulting in many women discontinuing treatment within the first 3 months. Unopposed estrogen-based HRT carries several inherent risks, such as breast cancer, endometrial cancer, venous thromboembolism, and stroke;[26-29] these effects of HRT are primarily mediated by ER-α. The estrogenic activity of EstroG-100® was evaluated using estrogen ligand-binding affinity assays in the HeLa-9903 cell line. EstroG-100® showed negligible binding affinities for ERα, ERβ, and nonselective ER compared to estradiol which showed strong affinities in the ER binding assay. These results suggest that EstroG-100® does not have significant effects on ER signaling and the associated adverse effects.[30,31] In addition, EstroG-100® showed no proliferation of human breast cancer (MCF-7) cells or increase in the uterus weight of ovariectomized rats.[31]

EstroG-100® has also been shown to improve femoral BMD and bone health.[32] The exact mechanism of action of EstroG-100® is not clear, but it provides benefits for menopausal symptoms and bone metabolism while having no effect on estrogen and FSH levels. The safety and efficacy of EstroG-100® have been demonstrated in previous studies and confirmed in this study.[20-22]

All the blood parameters were maintained within the normal range on posttreatment with EstroG-100®. There were no serious adverse events observed. No nonserious adverse events related to EstroG-100® were

the study was to obtain evidence of treatment efficacy and collect additional safety data. All patients served as their own control, as we compared the improvement in the scores from baseline to 12 weeks.

Conclusion

To conclude, EstroG-100® stands out as a safe and highly effective treatment for alleviating a range of climacteric and postmenopausal symptoms, significantly enhancing the quality of life for Indian postmenopausal women.

Acknowledgment

The authors would like to acknowledge the Ki3 CRO support for data analysis and study report.

Financial support and sponsorship

This study was funded by Shield Healthcare Pvt. Ltd.

Conflicts of interest

There are no conflicts of interest.

References

1. Singh A, Pradhan SK. Menopausal symptoms of postmenopausal women in a rural community of Delhi, India: A cross-sectional study. J Midlife Health 2014;5:62-7.
2. Ahuja M. Age of menopause and determinants of menopause age: A PAN India survey by IMS. J Midlife Health 2016;7:126-31. 3. Beyene Y. Cultural significance and physiological manifestations of menopause. A biocultural analysis. Cult Med Psychiatry 1986;10:47-71.
4. Milsom I, Ekelund P, Molander U, Arvidsson L, Areskoug B. The influence of age, parity, oral contraception, hysterectomy and menopause on the prevalence of urinary incontinence in women. J Urol 1993;149:1459-62.
5. Hilton P, Tweddell AL, Mayne C. Oral and intravaginal estrogens alone and in combination with alpha-adrenergic stimulation in genuine stress incontinence. Int Urogynecol J 1990;1:80-6.
6. Stone SC, Mickal A, Rye PH. Postmenopausal symptomatology, maturation index, and plasma estrogen levels. Obstet Gynecol 1975;45:625-7.

7. Greendale GA, Hogan P, Shumaker S. Sexual functioning in postmenopausal women: The postmenopausal estrogen/ progestin interventions (PEPI) trial. J Womens Health 1996;5:445-58.
8. Diokno AC, Brown MB, Herzog AR. Sexual function in the elderly. Arch Intern Med 1990;150:197-200.
9. Pearlstein T, Rosen K, Stone AB. Mood disorders and menopause. Endocrinol Metab Clin North Am 1997;26:279-94. 10. Vivian-Taylor J, Hickey M. Menopause and depression: Is there a link? Maturitas 2014;79:142-6.
11. Gordon T, Kannel WB, Hjortland MC, McNamara PM. Menopause and coronary heart disease. The Framingham study. Ann Intern Med 1978;89:157-61.
12. Rosano GM, Vitale C, Marazzi G, Volterrani M. Menopause and cardiovascular disease: The evidence. Climacteric 2007;10 Suppl 1:19-24.
13. Ahlborg HG, Johnell O, Turner CH, Rannevik G, Karlsson MK. Bone loss and bone size after menopause. N Engl J Med 2003;349:327-34.
14. Grady D, Rubin SM, Petitti DB, Fox CS, Black D, Ettinger B, *et al.* Hormone therapy to prevent disease and prolong life in postmenopausal women. Ann Intern Med 1992;117:1016-37.
15. Shah SH, Alexander KP. Hormone replacement therapy for primary and secondary prevention of heart disease. Curr Treat Options Cardiovasc Med 2003;5:25-33.
16. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, *et al.* Trends in alternative medicine use in the United States, 1990-1997: Results of a follow-up national survey. JAMA 1998;280:1569-75.
17. Seidl MM, Stewart DE. Alternative treatments for menopausal symptoms. Systematic review of scientific and lay literature. Can Fam Physician 1998;44:1299-308.
18. Dailey RK, Neale AV, Northrup J, West P, Schwartz KL. Herbal product use and menopause symptom relief in primary care patients: A MetroNet study. J Womens Health (Larchmt) 2003;12:633-41.
19. Huntley AL, Ernst E. A systematic review of herbal medicinal products for the treatment of menopausal symptoms. Menopause 2003;10:465-76.
20. Lee KH, Lee DJ, Kim SM, Je SH, Kim EK, Han HS, *et al.* Evaluation of effectiveness and safety of natural plants extract (Estromon®) on perimenopausal women for 1 year. J Menopausal Med 2005;11:16-26.
21. Chang A, Kwak BY, Yi K, Kim JS. The effect of herbal

extract (EstroG-100) on pre-, peri- and post-menopausal women: A randomized double-blind, placebo-controlled study. Phytother Res 2012;26:510-6.

22. Kim T, Ryu KJ, Lee S, Lee DJ, Seo SK. A 12-week, multi-center, doubleblind, randomized, placebo-controlled clinical trial for the evaluation of the efficacy and safety of the herbal extract (EstroG-100®) on menopausal symptoms. J Reprod Med Gynecol Obstet 2022;7:106.
23. Kim SJ, Kang SM, Ko KH, Nam SH. Physiological activities and inhibitory effect of extracts of *Cynanchi wilfordii* radix and *Perilla sikokiana* against cell differentiation in 3T3-L1 adipocytes. J Korean Soc Food Sci Nutr 2016;45:642-50.
24. Ma YF, Jung JY, Jung YJ, Choi JH, Jeong WS, Song YS, *et al*. Anti-inflammatory activities of coumarins isolated from *Angelica gigas* nakai on LPS-stimulated RAW 264.7 cells. Prev Nutr Food Sci 2009;14:179-87.
25. Kim J, Yang S, Choi CY. The evaluation of the effect of herbal extract on osteoarthritis: *In vitro* and *in vivo* study. Prev Nutr Food Sci 2016;21:310-6.
26. Oh KN, Oh DR, Jung MA, Kim Y, Choi EJ, Hong J, *et al*. Antidepressant effects of *Cynanchum wilfordii* hemsley, *Phlomis umbrosa* turcz, and *Angelica gigas* nakai via inhibition of 5-HT6 receptor-mediated cyclic AMP activity. J Physiol Pathol Korean Me 2018;32:247-54.
27. Lee G, Kim J, Kang H, Park S, Hong J, Oh J, *et al*. Effects of herbal mixture extract on menopausal hot flashes and pharmacokinetics in ovariectomized rat models. J Food Nutr Res 2018;6:116-23.
28. Mattsson LA, Skouby S, Rees M, Heikkinen J, Kudela M, Stadnicki-Kolendo A, *et al*. Efficacy and tolerability of continuous combined hormone replacement therapy in early postmenopausal women. Menopause Int 2007;13:124-31.
29. Cagnacci A, Venier M. The controversial history of hormone replacement therapy. Medicina (Kaunas) 2019;55:602. 30. Vollmer G, Papke A, Zierau O. Treatment of menopausal symptoms by an extract from the roots of rhapontic rhubarb: The role of estrogen receptors. Chin Med 2010;5:7.
31. Kim SJ, Jin SW, Lee GH, Kim YA, Jeong HG. Evaluation of estrogenic activity of extract from the herbal mixture *Cynanchum wilfordii* hemsley, *Phlomis umbrosa* turczaninow, and *Angelica gigas* nakai. Toxicol Res 2017;33:71-7.
32. Kim SN, Li YC, Xu HD, Yi DG, Kim MS, Lee SP, *et al*. Phytoestrogenic effects of combined plant extracts on the change of bone metabolism of OVX rats. Korean J Food Sci Technol 2008;40:316-20.