



Original Research

Efficacy of Non-Soy Isoflavone (*Pueraria phaseoloides*) on The Symptoms Severity Scoring by Kupperman Index in Menopausal Women

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ABSTRACT

Introduction: Menopause is defined by a decline in estrogen levels, which causes various symptoms. Treatments based on foods or supplements enriched in phytoestrogens, notably isoflavones, plant-derived compounds with estrogenic effects, have recently become quite popular. This study aims to see how effective non-soy isoflavone supplementation is for menopausal symptoms in women.

Methods: 26 menopausal women were given 67.5 mg of non-soy isoflavone, and 25 menopausal women were given a placebo daily for 12 weeks in an analytical double-blind, randomized clinical trial (RCT). Inclusion criteria were (1) RCT, (2) perimenopausal or postmenopausal women experiencing menopausal symptoms, (3) intervention with an oral non-soy isoflavone. Symptoms Severity Score (SSS) based on the Kupperman index (KI) questionnaire was administered to the patients before starting and at the end of the study. The Statistical Package for Social Sciences (SPSS) software was used to analyze the responses.

Results: The difference in SSS scores between the treatment and control groups was significant ($p = 0.000$). Women receiving 67.5 mg of non-soy isoflavone daily, reduced myalgia, fatigue, and hot flushes by 92.3%, 77%, and 53.8%, respectively. For clinical significance rating, relative risk reduction (RRR) is used. A significant RRR value resulted from myalgia symptoms (76.6%), fatigue (55.7%), hot flushes (39.2%), and SSS (68.7%).

Conclusion: Isoflavones did not bring a significant change in Kupperman Index compared to placebo but provided significantly improved Symptoms Severity Scoring in menopausal women.

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INTRODUCTION

Menopause is the lack of follicular activity in the ovaries, which produces menstrual hormones, resulting in permanent cessation of menstruation. It affects women aged 50 to 10 and is diagnosed after a 12-month period of amenorrhea with no apparent physiological or pathological causes [1]. Hot flushes, night sweats, sleep disturbances, sexual discomfort, depression, changes in sex drive, vaginal dryness, dry skin, weight changes, hair loss, and urinary incontinence are all symptoms of menopause [2]. Those symptoms associated with

estrogen deprivation due to loss of follicular activity affected the quality of life and required therapeutic intervention. While hormone replacement treatment (HRT) substantially improves menopausal symptoms, it is linked to an increased risk of heart disease and breast cancer [3]. As a result, various treatments are needed to alleviate menopausal symptoms while minimizing side effects.

Phytoestrogens, specifically isoflavones, are plants considered chemoprotective, with estrogen-like properties compounds, due to their conformational similarity to β -estradiol, and can be used as an

alternative therapy for hormonal disorders [4,5]. Isoflavones are phenols that enable the activation of estrogen receptors (ER) and the regulation of gene expression in target tissue cell nuclei. [4]. Taking the isoflavones, dietary supplementation may reduce the frequency of hot flashes (10-20%) in menopausal women [6]. Isoflavones have already been isolated from *Pueraria* species which are not soy. The genus of *Pueraria* is a structural analog of estrogen 17 β -estradiol in the human body that is useful for alternative therapy to treat menopausal symptoms [4,7]. Tropical kudzu or Tunggak bean, *Pueraria phaseoloides* was used in Chinese herbal medicine that traced back to century-old.

However, no research on the effects of non-soy (*Pueraria phaseoloides*) isoflavone supplementation in menopausal women has been performed. Therefore, this study aimed to evaluate the effects of local non-soy (*Pueraria phaseoloides*) of isoflavone that improved menopausal symptoms.

MATERIAL AND METHODS

Study Design

This was an experimental study with a double-blind, randomized clinical trial (RCT) applied to menopausal women in Malang, where one sample was obtained in each area in each sub-district among Malang's ten sub-districts. This research was conducted for seven months, from April to November 2003.

Participants

Menopausal women from Malang were the subjects of this research. The inclusion criteria of this study were (1) RCT, (2) perimenopausal or postmenopausal women experiencing menopausal symptoms as measured by the Kupperman Index on Symptom Severity Score (SSS), and (4) intervention with an oral non-soy (*Pueraria phaseoloides*) isoflavone. Exclusion criteria for subjects in this study were women who received hormone replacement therapy (HRT), had chronic diseases, breast and/or endometrium cancer, and subjects suspected of being hypersensitive to estrogenic supplementation

Randomized and Interventions

A double-blind, randomized sample of menopausal women was divided into the control and treatment groups. Twenty-five people in the control group were given placebo milk every day for 12 weeks in the distribution. At the same time, the other 26 women in the treatment group were given skim milk with extract of non-soy (*Pueraria phaseoloides*) composed of 67.5 mg of isoflavone, once a day for 12 weeks. The Kupperman Index (KI) was used to grade all subjects for menopausal

symptoms using the Symptoms Severity Scoring (SSS) method.

Ethics

All techniques in this study were carried out in compliance with the appropriate manuals and regulations and were approved by the Health Research Ethics Committee, Faculty of Medicine, Brawijaya University, Malang, Indonesia.

Statistical analysis

We used SPSS Version 11.0 for Windows to conduct the statistical analysis. We used ANCOVA (Analysis of Covariant) to look at the differences between the two groups. Results were considered significant at a p-value <0.05.

RESULTS

A total of 51 samples were collected in this study. Based on the results of this study, it was found that after treatment of non-soy isoflavones, symptoms of sweating hot flushes, arthralgia and myalgia, fatigue, and headache have been reduced by 53.8%, 92.3%, 77%, and 50%, respectively, compared with before treatment (Table 1). Relative risk reduction (RRR) is used for clinical significant scoring. A significant RRR value resulted from myalgia symptoms (76.6%), fatigue (55.7%), hot flushes (39.2%), and SSS (68.7%). There was significantly differentiation in SSS scoring between the treatment (n = 26) and control group (n = 25) with p-value 0.000 (Table 2).

DISCUSSION

Isoflavones are being used for the alternative 'natural' management of menopausal symptoms, which are analogs of 17 β -estradiol and can bind both estrogen receptors α (ER α) and β (ER β) [7]. One of the plant-derived isoflavones was isolated from non-soy Tropical kudzu or Tunggak bean, *Pueraria phaseoloides* which compounds estrogenic properties, such as miroestrol, puerarin, deoxymiroestrol, kwakhurin, and among coumestrol class [5]. This study evaluated the effects of local non-soy (*Pueraria phaseoloides*) of isoflavone that improved menopausal symptoms.

The Kupperman Index's Symptoms Severity Scoring (SSS) was used to establish a composite score that multiplied the number of menopause symptoms by their severity at baseline and after 12 weeks of treatment with a non-soy extract (*Pueraria phaseoloides*) containing 67.5 mg of isoflavone daily. The SSS differed significantly between the treatment and placebo groups (p = 0.000) in this research. In women receiving 67.5 mg non-soy

Table 1. The Change in the Kupperman Index of Menopausal Women

Symptoms	Treatment (%)	Placebo (%)
Sweating hot flushes	-53.8	72
Insomnia	57.7	64
Nervousness	88.5	84
Paraesthesia	73.1	+56
Arthralgia, myalgia	-92.3	-64
Fatigue	-77	-48
Headache	-50	-40
Heart palpitation	61.5	76
Melancholia	76.9	+72
Vertigo	73.1	60

*) – (Decreasing score compared with before treatment); + (Increasing score compared with before treatment)

Table 2. Comparison of Kupperman Index and Symptoms Severity Scoring in Menopausal Women on Non-Soy Isoflavones

Variable	Treatment group (n=26)		Placebo group (n=25)		p-value
	Min	Max	Min	Max	
KI (before the study)	6	13	6	14	0.270
KI (after study)	0	5	1	12	
SSS (before the study)	2	3	2	3	0.000
SSS (after study)	0	2	1	3	

*) KI (Kupperman Index); SSS (Symptoms Severity Scoring): 0 (none), 1 (minimum), 2 (mild), 3 (moderate)

(*Pueraria phaseoloides*) isoflavone daily, sweating hot flushes has been reduced by 53.8%, arthralgia, and myalgia; 92.3%, fatigue; 77%, and headache; 50% compared with before treatment of non-soy isoflavones. Clinically meaningful rating is done using relative risk reduction (RRR) scoring. A significant RRR value resulted from myalgia symptoms (76.6%), fatigue (55.7%), hot flushes (39.2%), and SSS (68.7%).

The condition of the relative decrease in circulating estrogen in menopausal women causes dysfunction of the thermoregulatory nucleus due to the symptom of sweating hot flashes. In this study, hot flashes in the treatment group were reduced by 53.8% after receiving 67.5 mg of non-soy (*Pueraria phaseoloides*) isoflavone daily for 12 weeks. It was related to a meta-analysis study of 17 trials that revealed that respondents receiving 54 mg of isoflavones for six weeks to 12 months has significantly reduced the frequency of hot flashes (20.6%) [8]. Furthermore, isoflavone effectively reduced hot flashes and the Kupperman Index at 6 and 12 weeks compared to baseline in randomized, double-blind research [9]. The other trial found no difference in the frequency or intensity of hot flashes between the treatment group receiving 90 mg of isoflavone daily for 12 weeks and the placebo group [10].

In this study, the symptoms of arthralgia, myalgia, and fatigue were reduced. Isoflavones have been shown to improve bone health in several trials. Improvement of

bone-specific alkaline phosphatase (BALP) and levels of osteocalcin (OC) has been significantly increased by 20.3% when used isoflavone 75 mg daily for 12 weeks [8]. Those indicate that estradiol as the isoflavone compound increases bone formation, involves recruitment and differentiation of osteoblastic precursors, and stimulates osteoblastic activity by activating estrogen receptors [9].

The Kupperman Index (KI) did not differ significantly ($p=0.270$) in this study, but KI providing Symptoms Severity Scoring (SSS) has been significantly improved between the treatment group and placebo group ($p\text{-value} = 0.000$) with RRR scoring 68.7%. After 4 and 6 months of treatment, a previous RCT study found that isoflavone significantly reduced menopause symptoms on the Kupperman Index ($p = 0.0265$) in the treatment group compared to placebo [11].

There are some limitations to this study that should be taken into account. There was a lack of standardization in the dosages utilized and data on treatment adverse effects.

CONCLUSION

When compared to placebo, phytoestrogen, namely isoflavones, did not result in a significant change in the

Kupperman Index, but did result in a substantial improvement in Symptom Severity Scoring in menopausal women. While isoflavones help alleviate all menopausal symptoms, they also help reduce sweating, hot flashes, arthralgia and myalgia, fatigue, and headache. Isoflavones should be studied further to alleviate menopausal symptoms as well as their potential long-term side effects.

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CONFLICT OF INTEREST

There are no conflicts of interest declared by the authors.

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