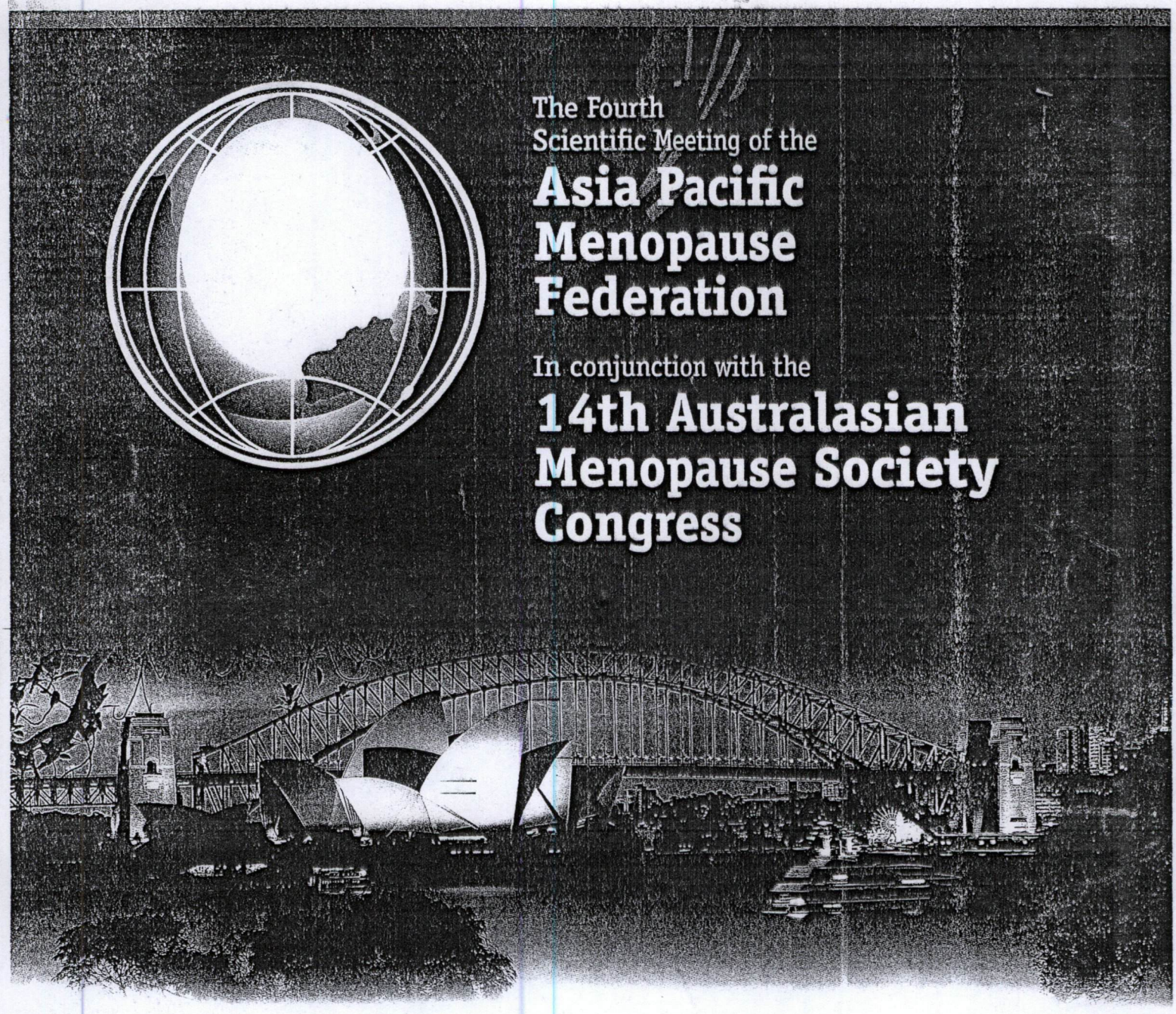
Meeting Program and Abstract Book



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ASIA PACIFIC MENOPAUSE FEDERATION

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Abstracts

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The Role of Leptin on Estradiol and Bone Mass Density of Post-Menopausal Women

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Background: Leptin is hormone with diverse range of local and systemic physiological functions produced in adipose tissues and secreted into the peripheral blood and also correlates well with body weight and adiposity. Estradiol has effects on food intake and body weight that are in the same direction as leptin. Serum estradiol also has positively correlation to bone density.

Objective: To evaluate whether leptin had role on estradiol and the bone mass density in postmenopausal women.

Methods: Serum leptin and estradiol of 17 non obese postmenopausal women and 17 non-obese nonmenopausal women as a control were evaluated using ELISA technique. Bone mass density value was evaluated using Dual energy X-ray absorptiometry (DEXA). All women had not taken any hormone, calcium and coticosteroid medication at least 6 months before the study. They had no established endocrinologic diseases (e.g. Hyperthyroidism, Cushing's disease, diabetes mellitus) or rheumatologic pathologies (e.g. rheumatoid arthritis, ankylosing spondylitis),

Results: Serum leptin concentration was higher in postmenopausal women (18,41±16,61) compared with nonmenopausal women (9,27±3,01) (p=0.02). BMD in postmenopausal women was lower (1,00±0,16) than nonmenopausal women (1.13± 0.12) (p=0.002). The median concentration of estradiol in postmenopausal women was lower (<20) than menopausal women (27,70) (p=0.0008). There were no significant correlations between leptin and estradiol concentration (r= 0.241, p = 0.352), and also between leptin concentration and bone mass density in postmenopausal women (r=0.625, p=0.004).

Conclusion: The increase concentration of serum leptin has no correlation on estradiol and bone mass density in postmenopausal women.

Differences Effects of Isoflavone and Placebo in Reducing Hot Flushes Menopausal Women In Palembang

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Background: Hot flushes is the most vasomotor symptoms suffered by most women at age of menopause. Around three quarters of menopausal women experience symptoms of hot flushes in her life. These symptoms usually appear 1 -2 years before menopause and will continue for six months until the next five years. Hot flushes in menopausal women will affect the ability to work, disrupt the social life, sleep pattern and daily activities. Effort to reduce symptoms for menopausal women is by giving hormone therapy; administration of estrogen with or without progestin, or selective estrogen receptor modulators (SERMs) such as raloxifene and tamoxifen. besides that, hormone therapy should also be done in the long term even for life so that it will cause the problems in compliance of drug using and higher costs. One of the most widely studied phytoestrogens are isoflavones, a 17 -oestradiol which are weak estrogens and SERMs natural. Isoflavones are widely used derived from soy isoflavone extract in capsules, tablets and liquids.

Objective: Study aims to know the differences effect of isoflavones and placebo in reducing hot flushes complaints of menopausal women. Overall benefits of the research is expected Isoflavones to be considered as alternative therapy in managements of menopausal complaints and can improve quality of life of women during this period with relatively affordable cost.

Design and method: This study is randomized clinical trial to isoflavon 2x40mg group and placebo group during 12 weeks. Was performed from September 2007 until June 2008 at Muhammad Hoesin Hospital Palembang, Dempo Public Health Centre , and Merdeka Public Health Centre Palembang. There were 90 sample in age 45-55 years old that meet the inclusion criteria and participated to this study.

Results: From the results, the mean age of subjects in the isoflavone group for 50,75±2,31 years old and 51,10±2,25 years old in placebo group. The mean menopausal age of isoflavone group for 48,12±1. 57 years old and 48.30±1.53 years old in placebo group. The majority of subject had a normal body mass index (BMI= 18,5-25), as many as 30 subject (75,0%) in isoflavon group and 28 subject (70%) in placebo group. The biggest subject distribution of isoflavon group is more than 2 parity as many as 29 subject (72,5%), likewise in placebo group 23 subject (67,5%). Overall, subject characteristics of both group before intervention was found on the entire body of 18 subjects (45,0%) in the isoflavon group and 16 subjects (40%) in placebo group.

Conclusions: Result showed there were significant differences in the effect of isoflavone and placebo in reducing hot flushes complaints of menopausal women. Frequency of hot flushes decrease significantly in the first two weeks up to two weeks of sixth. The mean frequency of hot flushes at two weeks of sixth is 9.60±4.18 times in two weeks (± once a day) in isoflavone group and 17.98±5.51 times in two weeks (±twice a day) in placebo group (P<0.05)

This is also followed by a decrease in the duration and severity of hot flushes in the group of isoflavone. In the two weeks of sixth, the average duration of hot flushes isoflavone group 2.20±1.01 minutes versus 5.70±3.03 minutes in group placebo and have proven statistically significant. Overall in isoflavone group, there were 32 subjects with mild degrees of hot flushes and 8 subjects with moderate hot flushes. While in the placebo group, there were 17 subjects with mild degrees of hot flushes and 23 subjects with moderate degrees of hot flushes.

DIFFERENCES EFFECT OF ISOFLAVON AND PLACEBO IN REDUCING HOT FLASHES MENOPAUSAL WOMEN IN PALEMBANG

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Background: The purpose of this study was to find the differences between the effect of isoflavon and placebo in reducing the hot flashes in menopausal women.

Settings: This study was conducted in Mohammad Hoesin Hospital Palembang, Dempo Public Health Service, and Merdeka Public Health Service Palembang.

Design: This a randomized control trial. The evaluation of hot flashes was based on the Hot Flashes Score from Sloan.

Methods : This study was conducted from September 2007 until June 2008. During this period total sample that matched with the inclusion criteria was 90 subjects, aged from 45-55 years. We also evaluated the FSH level.

We divided the subject using simple randomization with numbered random table. We found 44 subjects in isoflavon group, 43 subjects in placebo group. During the study period, there were 4 subjects from isoflavon group and 3 subjects from placebo group dropped out from the study because they did not take the medication or lost of follow up.

Results: Mean age of the study sample from isoflavon group was 50,75 ± 2,31 years, and placebo group was 51,10 ± 2,25 year. There are significant decreasing in the first two weeks until the sixth two weeks. Mean frequency in the sixth two weeks was 9,60 ±4,18 times in two weeks or ± 1 time daily in the isoflavon group, and 17,98 ±5,51 times in two weeks or ± 2 times daily in placebo group ($p<0,05$). This is followed by the decreasing of the hot flashes duration in isoflavon group. In the sixth two weeks, the mean duration of hot flashes in isoflavon group was 2,20 ± 1,01 minutes, and 5,70 ± 3,01 minutes in placebo group, and statistically significant ($p<0.05$).

Conclusion: It was statistically proven using the x^2 test that there are no differences in hot flashes duration between isoflavon and placebo group ($p=0.822$).

Keywords: Hot flashes, isoflavon, menopause.

Introduction

Menopause was defined as a period when the menstrual cycle was stop, followed by the lost follicle activity. [1-5]. Menopause derived from the Greece word "men" (month) and "pausis" (stop). Few years before the menopause happened, there are changes in normal ovarian cycle until the cycle was stop, this is called menopause transition, where the cycle is not normal.

The symptoms include changes in menstrual pattern, vasomotor symptoms (hot flashes, sweating), genital atrophy, and secondary problems that was caused by the lack of estrogen, such as osteoporosis and cardiovascular disease. [4,5]

Hot flashes are the main vasomotor symptoms in menopausal women. 1/3 of

menopausal women experiencing hot flashes during their menopausal period. This symptom happens 1-2 years before menopause and continued until 6 months – 5 years later.[6,7]

According to Kronenberg, in 20% of women, hot flashes will occur until 15 years after menopause. [8] This symptom will affect the ability to work, disturbed social life, and daily activity.

There were several ways to reduce this symptom, include hormonal therapy, estrogen therapy with or without progestin or selective estrogen receptor modulators (SERMs) such as raloxifene and tamoxifene.[9,10] But this hormone replacing therapy were also associated with the increased risk for breast cancer, coronary heart disease, cerebrovascular disease, and lung embolism. Another problem in hormone replacing therapy is that before we begin the therapy, we have to perform the screening test, and this therapy needs long terms follow up. This therapy is should be given in long term. This therapy is also need the adherence and high cost therapy. [11]

One of the efforts to solve this problem is to develop the preparat such as natural estrogen therapy like fitoestrogen. [12-14] One of the fitoestrogen that have been studied is isoflavon, 17β-oestradiol which is the week estrogen and natural SERM. Isoflavon that have been used recently derived from soya, in the shape of capsul, tablet, and liquid. [15] Research from Kyung K, Han and Jose M. Soarces from Brazil in 80 menopausal women with hot flashes symptom, showed that 100 mg isoflavon administration will reduce this symptom significantly ($p < 0,01$) after 12 weeks.[16] Another research showed a different result, Kronenberg and Fugh-Berman make a study to 29 randomized clinical trial about alternative therapy in menopausal symptom, showed that there is no consistent prove about the benefit of alternative therapy although 6 from 11 randomized control trial using isoflavon showed changes in hot flashes symptom and menopausal symptom.[8] This study was a meta analysis study which is different from Kyung K, Han and Jose, so this study showed a different result.

There differences between this result makes us interested to performed the clinical trial on the effect of isoflavon in reducing hot flashes symptom in menopausal women in Palembang.

Material and methods

This is a randomized control trial to the group that was given 2x40 mg isoflavon and placebo for 12 weeks. All of the participants were given daily journal about the degree of hot flashes that were evaluated in 4th, 8th, and 12th weeks. The evaluation of hot flashes was based on the Hot Flashes Score from Sloan.

Study population

Study population are the menopausal women in Palembang that matched the inclusion criteria. Material of the study are women in Mohammad Hoesin Hospital, Merdeka Public Health Service, Dempo Public Health Service who were matched the inclusion criteria.

Study Sample

Sample were collected from September 2007. Sample size had 95% confidence interval, and power test 80%. The result that was expected 12 weeks after the isoflavon treatment is 80%. Sample size in this study were based on the formula:

$$\mathbf{n} = \frac{\mathbf{Pt(1-Pt)+Pc(1-Pc)}}{\mathbf{(Pt-Pc)^2}} \times \mathbf{f}_{(\alpha,\beta)}$$

where:

n = number of sample

Pt = proportion that was expected 80%

Pc = placebo proportion 50%

f = coefficient from the table with α 95%, β 80% is 7,9

α = confident interval 95%

β = power test 80%

$$\mathbf{n} = \frac{0,8(1-0,8)+0,5(1-0,5)}{(0,8-0,5)^2} \times 7,9$$

= 35,9 sample → 36 sampel.

Minimum sample size from each group were 36 sample, in this study we found 40 sample that participate until the study finished.

Inclusion criteria

a. Menopausal women who did not had menstruation in 12 weeks.
b. Hot flashes symptom.
c. FSH serum more than 40 mIU/ml.
d. Agree to participate and sign the informed consent form.

Exclusion criteria

a. Using the hormonal drug or other therapy for systemic disease (DM, hypertension, hormone replacing therapy)
b. History of hysterectomy and or salphingooforectomy
c. Withdrawl from the study.

Study variable

Study variable include:

1. Demography characteristics
2. Frequency of hot flashes
3. Duration of hot flashes
4. Degree of hot flashes

Tools and materials

Tools and material in this study consist of:

a. Isoflavon capsule isoflavon 40 mg (Promeno®)
b. Placebo capsule contained glycerin
c. Dispossible syringe 3 cc
d. Double oxalat tube
e Daily form

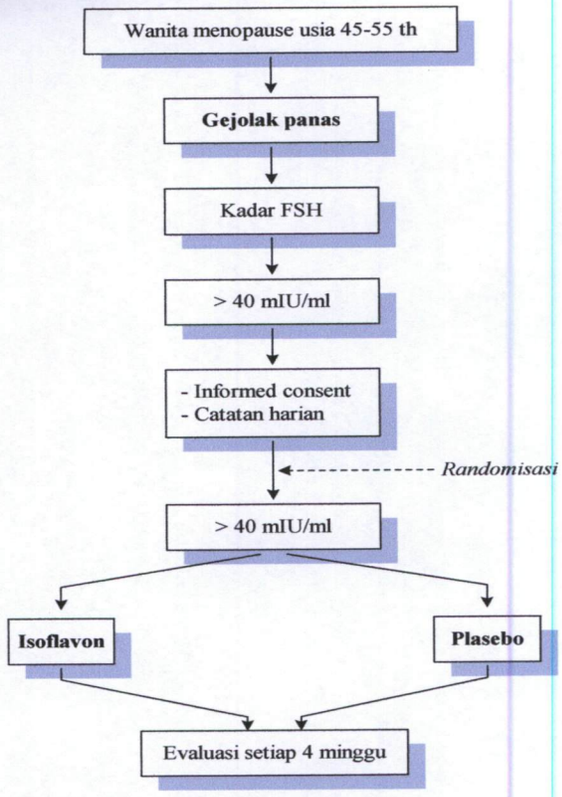
Working procedure

Women who were matched the inclusion criteria, were given the number based on the alphabet. Performed the simple randomization using the numbered random table, then we performed the anamnese to the responden. If the responden agree to participate in the study then they sign the informed consent.

After that we check the FSH serum by collecting 5 cc of blood sample from vein. Then the blood samples were collect in the tube and given the label name and send to the Prodia Laboratory in Palembang. Then the respondents were given the information about how to fill the questioner for daily forms that were given to the respondent. The respondents will be given the placebo or isoflavon for 4 weeks and every day they took the medication at 07.00 AM and 07.00 PM. And the medication was continued for the next 8 weeks.

The capsule usage was controlled by called the respondents, visited the respondents house, and confirmed at the second and third week of capsule administration. During the confirmation, we performed the evaluation of daily journal, and the respondents were remain about the procedure of the medication and to fill the daily journal every day.

Evaluation of the side effects and the problems that were happened during the study, such as if the respondents were sick, the usage of other medication and antibiotic during the study should be written in special card and should be reported to the researcher for further evaluation.



Statistical Analyses

Study data were collected in a form that were analyse using the softwere SPSS version 11 Windows. Statistical analysis were conducted using the Mann-Whitney test for both group, and we performed the Wilcoxon test to analyse the differences of median data for isoflavon group in the observation 0 (P0), 4th weeks (P1), 8th weeks (P2), and 12th weeks (P3). The significancy was based on the *p* value < 0,05.

Results

Subjects Characteristics

The mean age for isoflavon subjects were 50,75 ± 2,31 years, in placebo group 51,10 ± 2,25 years. The subjects were mostly in the age of 51–55 years that were consist of 23 isoflavon subjects (57,5%), and 27 subjects (67,5%) in placebo group. The educational degree in most of the subjects were university/ diploma 20 subjects (50,0%), and 23 subjects (57,5%) in placebo group. 5 isoflavon subjects were elementary school (12,5%), and 4 placebo group. Both the majority of group sample were a working women, which is consist of 23 subjects (57,5%) and 27 subjects (67,5%).

Most of the subjects in isoflavon group (30 subjects/ 75,0%) had the body mass index (BMI) 18,5 – 25 (normal), and 28 subjects (70,0%) in the placebo group. Only 4 subjects (10,0%) in isoflavon group and 1 subjects (2,5%) in placebo group had BMI < 18,5. There are 6 subjects (13,4%) in isoflavon group and 11 subjects (27,5%) in placebo group had the BMI > 25.

Most of the isoflavon subjects had 3 parity (18 subjects/45,0%), and in placebo group most of the subjects had 2 parity (13 subjects/ 32,5%). In isoflavon group there are 1 subject (2,5%) that had 7 parity, and 2 subjects (5,0%) in placebo group. The characteristics of the subjects are shows in table 4.

Table 4. Distribution of the subjects based on the age, education, BMI, parity.

Characteristics	Isoflavon		Placebo	
	n	%	n	%
Age (years)				
45-50	17	42,5	13	32,5
51-55	23	57,5	27	67,5
Education				
Elementary	5	12,5	4	10,0
Junior High	6	15,0	6	15,0
Senior High	9	22,5	7	17,5
Diploma/ Graduate	20	50,0	23	57,5
Occupation				
Housewife	17	42,5	13	32,5
Pedagang	1	5,0	4	10,0
Trader	1	5,0	-	-
Private	-	-	1	2,5
Civil Servant	9	22,5	9	22,5
Midwife	10	25,0	13	32,5
Nurse	2	5,0	-	-
Body Mass Index (BMI)				
< 18,5	4	10,0	1	2,5
18,5 – 25	30	75,0	28	70,0
> 25	6	15,0	11	27,5
Parity				
2	11	27,5	13	32,5
3	18	45,0	7	17,5
4	4	10,0	4	10,0
5	3	7,5	10	25,0
6	3	7,5	4	10,0
7	1	2,5	2	5,0
Total	40	100,0	40	100,0

Comparison Analysis

Subjects General Characteristis

Analysis of the subject characteristics is to find the homogeneity in both group. According to the age, we found the analysis result using the x^2, there are no significant differences between both group (p=0.356). The result of this analysis is shows in Table 5.

Table 5. Comparison analysis of subjects' age

Age (year)	Isoflavon		Plasebo	
	n	%	n	%
45-50	17	42,5	13	32,5
51-55	23	57,5	27	67,5
Total	40	100,0	40	100,0

x^2 test; p=0,356

The education of the subjects were divided into low education (below senior high) and high education (above senior high). The analysis using x^2 test shows that there are no significant differences between both group (p=0.501). Result from this analysis is shows in Table 6.

Table 6. Comparison analysis of the subject's education

Education	Isoflavon		Plasebo	
	n	%	n	%
≤ High School	20	50,0	17	42,5
> High School	20	50,0	23	57,5
Total	40	100,0	40	100,0

x^2 test; p=0,501

The occupation of the subjects in both group were divided into house wife and working women. From the analysis using x^2, there are no significant differences between both group (p=0,356), shows in table 7.

Table 7. Comparison analysis of subjects occupation

Occupation	Isoflavon		Plasebo	
	n	%	n	%
Housewife	17	42,5	13	32,5
Working	23	57,5	27	67,5
Total	40	100,0	40	100,0

x^2 test; p=0,356

There are no significant differences in body mass index in both group (p=0.188), shows in table 8.

Table 8. Comparison analysis for BMI

BMI	Isoflavon		Placebo	
	n	%	n	%
< 18,5	4	10,0	1	2,5
18,5 – 25	30	75,0	28	70,0
> 25	6	15,0	11	27,5
Total	40	100,0	40	100,0

x^2 test; p = 0.188

Comparison of the parity based on percentile 50, the subjects were divided into two group, which is parity less than 2 and parity more than 2. The Pearson X^2 test, shows there is no significant differences between both group (p=0.626). The analysis results shows in table 9.

Table 9. Comparison analysis for the parity

Parity (number of child)	Isoflavon		Plasebo	
	n	%	n	%
≤ 2	11	27,5	13	32,5
> 2	29	72,5	27	67,5
Total	40	100,0	40	100,0

x^2 test; p=0,626

Menstrual characteristics analysis

In this study we performed the analysis for the menstrual history, consist of menarche, menopause, menstrual duration in one cycle, and the duration when the patient stop menstrual. We found the mean menarche age 13,03±1,34 years in isoflavon group, and 12,88±1,45 years in placebo group. Mean menopause age for isoflavon group 48,12±1,57 years, and 48,30±1,53 years in placebo group. Mean menstrual duration in isoflavon group 5,08±1,24 days, and 5,30±1,20 in placebo group. The mean duration for non menstrual period was 31,5±15,53 months and 33,6±16,3 months in placebo group.

Overall using the t test, we found there are no significant differences in menarche age, menopause age, menstrual duration, non menstrual period between both group. (p>0.05). The analysis result for the menstruation history shown in table 10.

Table 10. Comparison analysis for menstruation history

Variable	Isoflavon (mean ± SD)		Placebo (mean ± SD)		*p*
Menarche age (year)	13,03 ±	1,34	12,88 ±	1,45	0,634
Menopause age (year)	48,12 ±	1,57	48,30 ±	1,53	0,616
Menstruation duration (day)	5,08 ±	1,24	5,30 ±	1,20	0,414
Non menstrual duration (month)	31,5 ±	15,53	33,6 ±	16,3	0,558

t test ; SD: standard deviation

Analysis of the history and location of hot flashes

1. Duration of hot flashes

The duration of hot flashes before the treatment were divided into two group, ≤ 2 years, and > 2 years. Most of the subjects felt the hot flashes for more than two years, 22 subject in isoflavon group (55%) dan 23 subject (57,5%) in placebo group. The proportion of the hot flashes duration, shown in table 11.

Table 11. Comparison analysis of hot flashes

Hot flashes duration (year)	Isoflavon		Placebo	
	n	%	n	%
≤ 2	18	45,0	17	42,5
> 2	22	55,0	23	57,5
Total	40	100,0	40	100,0

duration

x^2 test; p=0,822

It was statistically proven using the x^2 test that there are no differences in hot flashes duration between both group (p=0.822).

2. Location of hot flashes

Characteristics of hot flashes location in this study divided into three groups in the face, neck, and the whole body. Before the intervention the location of hot flashes mostly in the whole body, 18 subjects (45,0%) in isoflavon group and 16 subjects (40%) in placebo group. Location of hot flashes for both group shown in table 12.

Table 12. Comparison analysis for hot flashes location

Hot flashes location	Isoflavon		Placebo	
	n	%	n	%
Face	9	22,5	10	23,8
Neck	13	32,5	14	33,8
Whole body	18	45,0	16	42,4
Total	40	100,0	40	100,0

x^2 test; p=0,902.

Using x^2 test, there are no differences in hot flashes location in both group (p=0.902).

The effect of isoflavon and placebo in reducing the hot flashes in menopausal women

1. Hot flashes frequency

The evaluation for the frequency of hot flashes was based on Hot Flashes Score from Sloan, and evaluate for two weeks. Mean hot flashes frequency before the intervention in isoflavon group were 18,92±5,92 times in two weeks or ± 2 times daily, and 16,10±5,59 times in two weeks or ± 2 times daily in placebo group.

In the first two weeks after the intervention there are decreasing of the hot flashes intervention in isoflavon group 16,05±5,18 times in two weeks or ± 1,5 times daily, and in placebo group there are increasing of frequency become 20,60±6,25 times in two weeks, or ± 2 times daily. Frequency of hot flashes shows in table 13.

Table 13. Frequency of hot flashes

Hot flashes frequency per 2 weeks (14 days)	Isoflavon (mean ± SD)	Placebo (mean ± SD)	*p*
2 weeks before	18,12 ± 5,92	16,10 ±5,59	0,120
I 2 weeks	16,05 ± 5,18	20,60 ± 6,25	0,001
II 2 weeks	15,00 ± 5,09	21,43 ± 6,07	0,0001
III 2 weeks	13,48 ± 5,08	20,88 ± 6,10	0,0001
IV 2 weeks	11,50 ± 4,70	18,63 ± 5,95	0,0001
V 2 weeks	9,75 ± 4,63	18,55 ± 5,96	0,0001
VI 2 weeks	9,60 ± 4,18	17,98 ± 5,51	0,0001

t test ; SD = standard deviation

Within 2 weeks before the intervention we performed the t test, and we found there is no significant differences in hot flashes frequency between both group (p=0.120). Within the first two weeks until the sixth two weeks after the intervention, we found significant differences in hot flashes frequency between two groups (p<0.05).

The distribution of hot flashes frequency in this study shown in table 6. At the beginning of the study we found the frequency of hot flashes is higher in isoflavon group compared with placebo group. In the first two weeks there are decreasing of hot flashes frequency in isoflavon group, and increased in placebo group. In the second two weeks after the

intervention, there decreasing in hot flashes frequency in isoflavon group, but remains still in placebo group.

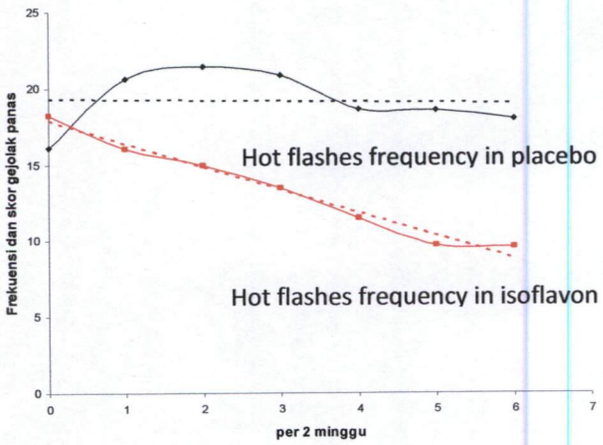


Figure 6. Frequency of hot flashes

2. Hot flashes duration

From this study we found the mean hot flashes duration before the intervention is 5,13±3,45 minutes in isoflavon group, and 5,28±3,22 minutes in placebo group. Duration of hot flashes in the first two weeks after the intervention, mean duration of hot flashes in isoflavon group is shorter 3,63±2,57 minutes, and 5,08±2,28 minutes in placebo group.

In the next two weeks, the duration in isoflavon group is shorter than the placebo group. Mean duration within the sixth two weeks is 2,20±1,01 minutes in isoflavon group and 5,70±3,01 minutes in placebo group.

There are no significant differences in the duration of hot flashes before the intervention between both group, but in the first two weeks untik the sixth two weeks we found the significant t test ($p<0.05$). Duration of hot flashes shown in table 14.

Table 14. Analysis of hot flashes duration

Duration of hot flashes (minute)	Isoflavon (mean ± SD)	Placebo (mean ± SD)	*p*
0 2 weeks	5,13±3,45	5,28±3,22	0,842
I 2 weeks	3,63±2,57	5,08±2,28	0,005
II 2 weeks	3,88±2,35	5,35±2,40	0,007
III 2 weeks	3,28±1,58	6,35±3,22	0,0001
IV 2 weeks	2,83±1,76	5,80±3,09	0,0001
V 2 weeks	2,63±1,59	6,15±3,10	0,0001
VI 2 weeks	2,20±1,01	5,70±3,01	0,0001

t test ; SD = standard deviation

Distribution of hot flashes duration in both group shown in figure 7. At the beginning of the study, the hot flashes duration in isoflavon group is lower than placebo group, but not statistically significant ($p=0.842$). In the first two weeks after the intervention, there are decreasing of hot flashes duration in isoflavon group, but not stable in placebo group. Within the next weeks we found there is decreasing of hot flashes in isoflavon group and increased in placebo group.

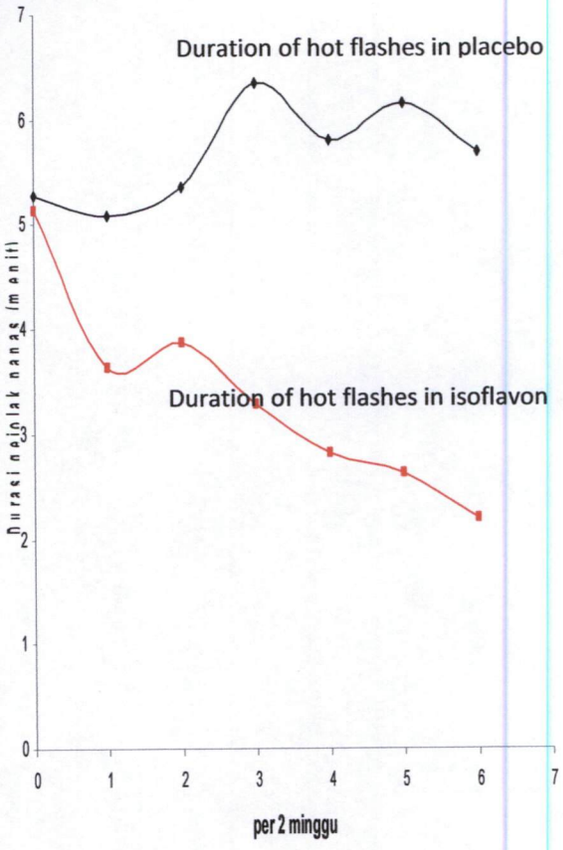


Figure 7. Duration of hot flashes

3. Hot flashes level

The evaluation of hot flashes in this study was based on the Hot Flashes Score from Sloan, and were divided into 4 category, consist of mild (1-14), moderate (15-28), severe (29-42), very heavy (43-56), shown in table 3. Table 15 shows the effect of the administration of isoflavon in reducing the hot flashes in menopausal women. Within two weeks before the administration of isoflavon and placebo, we found 17 subjects (42,5%) from isoflavon subjects with mild hot flashes, and 23 subjects (57,5%) with moderate hot flashes, mean while in placebo group we found 14 subject (35.0%) with mild hot flashes, and 26 subjects (65.0%) with moderate hot flashes.

In the first two weeks, in isoflavon group we found one subject that having changes in the level of hot flashes from moderate become mild, and in placebo group we found 5 subject from mild hot flashes become moderate. Overall there are 18 subjects (45%) with mild hot flashes and 22 subjects (55%) with moderate hot flashes. In placebo group, there are 9 subjects (22.5%) with mild hot flashes and 31 subjects (77.5%) with moderate hot flashes. Within two weeks after the administration, there are additional 2 subjects with moderate hot flashes become mild hot flashes, but remain the same in the placebo group.

In the third two weeks, the number of subjects in the isoflavon group, 8 subjects from moderate hot flashes become mild hot flashes, and in placebo group there are two subjects from moderate hot flashes become mild hot flashes. Overall, there are 25 subjects (62,5%) with mild hot flashes, and 15 subjects (37,5%) with moderate hot flashes in isoflavon group. But in placebo group there are 11 subjects (27,5%) with mild hot flashes and 29 subjects (72,5%) with moderate hot flashes.

It shows the same result in the fifth two weeks, there are decreasing in the subject with mild hot flashes in isoflavon group. In the fifth two weeks, in the isoflavon group there are 31 subjects (77,5%) with mild hot flashes, and 9 subjects (22,5%) with moderate hot flashes. But in placebo group, there are 15 subjects (37,5%) with mild hot flashes, and 25 subjects (62,5%) with moderate hot flashes.

From the beginning until the end of the study, in isoflavon group there are 15 subjects with moderate hot flashes become mild hot flashes, and in placebo group there are 3 subjects with moderate hot flashes become mild hot flashes. Overall in isoflavon group there are 32 subjects (80.0%) with mild hot flashes, and 8 subjects (20%) with moderate hot flashes. And in

placebo group, there are 17 subjects (42,5%) with mild hot flashes and 23 subjects (57,5%) with moderate hot flashes.

The result of the statistic analysis using t test shows, at two weeks before intervension there are no significant differences in the level of hot flashes between two group (p=0.001). Mean while at the first two weeks until the sixth two weeks, we found significant differences between two group (p<0,05). Level of hot flashes shown in Table 15.

Table 15. Level of hot flashes

Level of hot flashes	Isoflavon		Plasebo		*p**
	n	%	n	%	
2 week 0					
Mild	17	42,5	14	35,0	0,491
Moderate	23	57,5	26	65,0	
2 week I					
Mild	18	45,0	9	22,5	0,033
Moderate	22	55,0	31	77,5	
2 week II					
Mild	20	50,0	9	22,5	0,011
Moderate	20	50,0	31	77,5	
2 week III					
Mild	25	62,5	11	27,5	0,002
Moderate	15	37,5	29	72,5	
2 week IV					
Mild	28	70,0	11	27,5	0,000
Moderate	12	30,0	29	72,5	
2 week V					
Mild	31	77,5	15	37,5	0,000
Moderate	9	22,5	25	62,5	
2 week VI					
Mild	32	80,0	17	42,5	0,001
Moderate	8	20,0	23	57,5	
Total	40	100,0	40	100,0	

* x^2 test

Conclusion

Mean age of the subjects was 50,75 ± 2,31 years in isoflavon and 51,10 ± 2,25 years in placebo group. Mean menopause age was 48,12±1,57 years in isoflavon and 48,30±1,53 years in placebo group. BMI in most subjects (30 subjects/ 75.0%) was 18,5–25 (normal), and 28 subjects (70.0%) in placebo group. Most of the isoflavon subjects had 2 parity, which is 29 subjects (72.5%), and in placebo group was 27 subjects (67.5%). Overall, there are no significant differences in the subjects characteristics between two groups (p>0.05). The location of hot flashes between intervention mostly in the whole body, and we found it in 18 isoflavon subjects (45.0%) and 16 placebo subjects (40%).

Results of this study show that there are significant differences for the effect of isoflavon and placebo in reducing the hot flashes in menopausal women. There are significant decreasing in the first two weeks until the sixth two weeks. Mean frequency in the sixth two weeks was 9,60 ±4,18 times in two weeks or ± 1 time daily in the isoflavon group, and 17,98 ±5,51 times in two weeks or ± 2 times daily in placebo group (p<0,05). This is followed by the decreasing of the hot flashes duration in isoflavon group. In the sixth two weeks, the mean duration of hot flashes in isoflavon group was 2,20±1,01 minutes, and 5,70±3,01 minutes in placebo group, and statistically significant (p<0.05). Overall in isoflavon group there are 32 subjects (80.0%) with mild hot flashes and 8 subjects (20%) with moderate hot flashes. Mean while in placebo group there are 17 subjects (42.5%) with mild hot flashes and 23 subjects (57.5%) with moderate hot flashes.

The conclusion of this study is that, the administrasion of isoflavon could reduce the hot flashes, and this could be an alternative in symptomatic therapy in menopausal women.

Recommendation

Isoflavon administrations were considered as the alternative therapy for the treatment of hot flashes in menopausal women, in order to increased the quality of life with the low cost therapy.

Reference

1. Baziad A. Menopause dan Andropause. Edisi Pertama, Jakarta: Yayasan Bina Pustaka Sarwono Prawirohardjo, 2003;1-6.
2. Speroff L. The Perimenopause definitions, demography, and physiology. Obstet Gynecol Clin N Am. 2002;29:397-410.
3. Speroff L, Glass RH, Kasse NG. Regulation of menstrual cycle. dalam: Speroff L. Clinical Gynecologic Endocrinology and Infertility. 7th ed Baltimore Maryland: Williams & Wilkins, 2005:183-230.
4. Speroff L, Glass RH, Kasse NG. Menopause and the perimenopausal transtition. dalam: Speroff L. Clinical Gynecologic Endocrinology and Infertility. 7th ed Baltimore Maryland: Williams & Wilkins, 2005:621-88.
5. Lobo RA. Menopause and aging. dalam: Strauss JF, Barbieri RL. Yen and Jaffe's Reproductive Endocrinology, 5th ed.,Philadelphia:Elsevier Inc,2004;421-45.
6. Wise LA, Krieger N, Zierler S. Lifetime socioeconomic position in relation to onset of perimenopause. J Epid Comm Health. 2002;56:851-60.
7. Miquel J, Bosca AR, Boska JVR, Alperi JD. Monoupause: Areview on the role of oxygen strees and favorable effects of diatary antioxidant. Archives of Gerontology and Geriatrics. 2006; 42 : 289-306.
8. Kurzer S. Phytoestrogen supplement use by women. J. Nutr. 2003;133:1983S-6S.
9. Kronenberg F, Fugh-Berman, A complementary and alternative medicine for menopausal symptoms: a review of randomized, controlled trials. Ann Intern Med. 2002;137:805–13
10. Wylie-Rosett. Menopause, micronutrients, and hormone therapy. Am J Clin Nutr. 2005;81:1223S-31S.
11. Gallicchio. L, Whiteman MK, Tomic D, Miller PK, Langenberg P, Flaws JA. Type of menopause, patterns of hormone therapy use and hot flashes. Fertility and Sterility. 2006; 85: 5.
12. Vered Stearns, Daniel F. Hayes. Cooling off hot flashes. J Clin Oncol. 2002;20: 1436-8.
13. Philp HA. Hot Flashes: A Review of the literature on alternative and complementary treatment approaches. Altr Med Rev. 2003;8:284-302.
14. Kass-annese B. Alternative therapies for menopause. Clin Obstet Gynecol. 2000;43:162-83.
15. Chiechi LM, Micheli L. Utility of dietary phytoestrogens in preventing postmenopausal osteoporosis. Current Topics in Nutraceutical Research. 2005; 3: 1:15-28.
16. Fugate SE. Nonestrogen treatment modalities for vasomotor symptoms associated with menopause. The Annals of Pharmacotherapy. 2004;38:1482-99.
17. Dalal S, Zhukovsky DS. Pathophysiology and management of hot flashes. J. Support Oncol. 2006;4:315-20.
18. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD. Factor associated with age at natural menopause in a multiethnic sample of midlife women. Am J. Epidemiol. 2001;153:865-74.
19. Newton KM, Reed SD, LaCroix. AZ, Grothaus, LC, Ehrlich K, Gultinan J. Treatmen of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placeo. Ann Intern Med.2006;145:869-879.
20. Kyung K. Han, Jose M. Soares, Mauro A. Haidar. Benefits of soy isoflavone therapeutic regimen on menopausal symptoms Obstet Gynecol. 2002;99:389-94.
21. Melby MK, Lock M, Kaufert P, Culture and symptom reforting at menopause. Human Reproduction Update. 2005; 11:5: 495-512.
22. Fan MD, Maslow BS, Santoro N, Schoenbaum E. HIV and the menopause. Menopause Internasional. 2008;14:163-8.
23. Schouw YT, Pijpe A, Lebrun CEI, Bots' ML, Peeters PHM, Staveren WA, Lamberts SJW, Grobbee DE. Higher usual dietary intake of phytoestrogens is associated with lower aortic stiffness in postmenopausal women. Arterioscler Thormb Vasc Biol. 2002;22:1316-22.
24. Mackey R, Eden J. Phytoestrogens and the menopause. Climacteric. 1998;1:302-8.
25. Geller SE, Studee L. Soy and red clover for mid-life and aging. Climacteric. 2006; 9: 245-63.
26. Williams RE, Kalilani L, DiBenedetti DB, Zhou X, Granger AL, Fehnel SE, Levine KB, Jordan J, Clark RV. Frequency and severity of vasomotor symptoms among peri-and postmenopausal women in the United States. Climacteric. 2008;11:32-43.
27. Freeman EW, Sherif K. Prevalence of hot flushes and night sweats around the world:a systematic review. Climacteric. 2007;10:197-214.
28. Freedmand RR. Hot flashes : behavioral treatments, mechanisms, and relations to sleep. The Am J of Medicine. 2005; vol 118(12B):124S-30S.
29. Mold JW, Robert M, Aboshady HM. Prevalence and predictors of night sweats, day sweats and hot flashes in older primary care patiens: An OKPRN Study. Ann Fam Med. 2004; 2:391-7.

30. Rapkin. AJ. Vasomotor symptoms in menopause:physiologic condition and central nervous system approaches to treatment. Am J Obstet Gynecol. 2007;196:97-106.
31. Kronenberg F. Hot flashes: Phenomenology, quality of life, and search for treatment options. Experimental Gerontology. 1994; 29:319-36.
32. Freedmand RR. Bichemical, metabolic, and vascular mechanisms in menopause hot flases. Fertility and Sterility. 1998;70: 332-7.
33. Sloan JA, Loprinzi CL, Novotny PJ, Barton DL, Labasseur BI, Windschitl H. Methodologic Lessons Learned From Hot Flas Studies. Journal of Clinical Oncology. 2001; 19 : 23 : 4280-90.
34. Thurston RC, Blumenthal JA, Babyak JA, Sherwood A. Emotional antecendent of hot flashes during daily life. Psychosomatic Medicine. 2005;67:137-46.
35. Aktan E, Kaleli B, Sungurtekin H. Do menopausal hot flashes have any signifivant effects on arterial blood gas measuraments?. Maturitas. 1998;29:225-7.
36. Freedman RR, Norton D, Woodward S, Cornelissen G. Core body temperature and circadian rhythm of hot flashes on menopausal women. Journal of Clinical Endocrinology and Metabolism. 1995;80:2354-8.
37. Gold EB, Block G, Crawford S, Lachance L, FitGerald G, Miracle H, Sherman S. Lifestyle and demographic factor in relation to vasomotor symptoms:baseline result from the study of women's health across the nations. Am. J of Epidemiol. 2004;159:1189-99.
38. Nelson HD, Vesco KK, Haney E, Fu R, Nedrow A, Miller J, Nicolaidis C, Walker M, Humphrey L. Nonhormal therapies for menopausal hot flashes : systematic review and meta-analysis. Jama. 2006; 17:2057
39. Sloan JA, Loprinzi CL. Methodologic lessons learned from hot flashes studies. J Clin Oncol. 2001;19:4280-90
40. Wiklund I. Methods of assessing the impact of climacteric complains on quality of life. J Clim Postm 1998;43:41-50
41. Atkinson C, Compston JE, Day EN, Dowsett M, Bingham SA. The effects of phytoestrogen isoflavones on bone density in Women: a double-blind, randomized, placebo-controlled trial. Am J Clin Nuts 2004;79:326-33.
42. Weijer PHM, Barentsen R. Isoflavones from red cover (promensil) significantly reduce menopausal hot flush symptoms compared with placebo. Maturitas. 2002 ; 42:187-93.
43. Howes LG, Howes JB, Kight DC. Isoflavone therapy for menopausal flushes: A systematic review and Meta-analysis. Maturitas. 2006; 55: 203-11.
44. Tice JA., Ettinger B, Ensrud K. Phttoestrogen supplements for the treatment of hot flashes: The Isoflavone clover extract (ICE) Study: A Randomized controlled trial. Jama. 2003 ; 290(2):207-14.
45. Chisato Nagata, Naoyoshi Takatsuka, Norito Kawakami. Soy product intake and hot flashes in japanese women: results from a community-based prospective study. Am J Clin Nutr. 2001;153:790-3.
46. Speroff L, Glass RH, Kase NG. Hormone biosynthesis, metabolism and mechanism action. dalam: Speroff L. Clinical Gynecologic Endocrinology and Infertility. 6th ed Baltimore Maryland: Williams & Wilkins, 1999:37-43.
47. Joanne M. Murabito, Qiong Yang, Caroline Fox. Heritability of age at natural menopause in the framingham heart study. J Clin Endocrin Metab. 2005;90:3427-30.
48. Julie R. Palmer, Lynn Rosenberg, Lauren A. Wise. Onset of natural menopause in african american women. Am J Publ Health. 2003;93:299-306.
49. Heather B. Patisaul, Marietta Dindo, Patricia L. Whitte. Soy isoflavone supplements antagonize reproductive behavior and estrogen receptor- and ß-dependent gene expression in the brain. Endocrinology. 2001;142:2946-52.
50. Kreijkamp SK, Kok L, Grobbee DE. Effect of soy protein containing isoflavones on cognitive function, bone mineral density, and plasma lipids in postmenopausal women: A Randomized controlled trial. Jama. 2004;292(1);65-74.
51. Baber RJ, Templemen C, Morton T, Kelly GE, West L. Randomized placebo-controlled trial of an isoflavone supplement and menopausal symptoms in women's. Climacteric. 1999;2:2:85-92.