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# Comparing the Effect of Cimifugol and Salvigol on Night Sweats in Postmenopausal Women: A Single-blind Clinical Trial

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**ABSTRACT**

***Background & aim:*** Hot flashes and night sweats are the most common consequences of menopause. This study aimed to compare the effects of Cimifugol and Salvigol capsules on night sweat in postmenopausal women.

***Methods:*** This randomized clinical trial was carried out on 80 postmenopausal women who were assigned to two groups of Cimifugol (n=40) and Salvigol (n=40). The participants of each group were requested to take Cimifugol (6.5 mg) and Salvigol (100 mg) three times a day for two months. Wiklund vasomotor symptom scale was used to record the intensity and frequency of night sweats. The two groups completed this questionnaire before the intervention and then every week until the end of the intervention period (8 weeks). The data were analyzed in SPSS software (version 20) using through independent t-test, Chi-square, analysis of covariance, repeated measure ANOVA and repeated measure ANCOVA tests.

***Results:*** The mean±SD values of the number of sweats as well as its duration in the Salvigol group were 8.93±6.350 and 6.15±4.394 before the intervention, respectively. However, the corresponding values were 2.53±1.132 and 195±1.108, respectively after the intervention (at the end of the eighth week). Salvigol reduced the frequency of night sweats in different weeks (P<0.001). No significant difference was observed before and after the intervention in the Cimifugol group regarding the frequency and duration of night sweat (P>0.05).

***Conclusion:*** Based on the results, it is recommended to use Salvigol in the treatment of menopausal sweating.

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## Introduction

Menopause is one of the most important stages in women's life. The definitive diagnosis of menopause which usually occurs at the age of 51 is accompanied by a reduction in estrogen and an increase in Follicle-stimulating hormone greater than 40 international units per liter (1). Reduction of estrogen level in the menopausal period leads to a wide range of symptoms the most common of which are vasomotor symptoms, including hot flashes and night sweats. Other symptoms of menopause may include dizziness, severe and irregular heartbeat, vaginal mucosal atrophy and bladder irritability, mood changes, sleep disorders,

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headache, aching muscles, joint pain, concentration disorder, and memory impairment (2).

Although menopause is accompanied by changes in the hypothalamic and pituitary hormones that regulate the menstrual cycle, it is not considered a central process rather a primary ovarian failure (3). At the surface of the ovary, ovarian follicles are evacuated most likely due to the planned cell death. Therefore, the ovary is no longer able to respond to pituitary hormones (e.g., Luteinizing hormone and Follicle-stimulating hormone) which stops the production of ovarian estrogen and progesterone. This course causes various complications and changes, such as the absence of menstruation, sleep disorders, mood changes, an increase in illnesses atrophy, night sweats, and hot flashes. Reduction in the size of the genitourinary system, cardiovascular system, and osteoporosis are among the side effects (4). Night sweats are characterized by intense sweating, which occurs during the night. It is worth mentioning that this kind of sweating is different from the one which is caused by the hot temperature of the environment or thickness of the sheet. Therefore, night sweats are defined as severe hot flashes occurring at nights that can drench sleepwear and sheets; moreover, it is not related to the temperature of the environment or the number of clothes. The physiology of hot flashes is not known yet (5); however, during the menopause period, the production of hormones stops, which results in a significant reduction in the level of estrogen in the bloodstream. The efficacy of estrogen therapy and the absence of hot flashes and night sweats in conditions lacking estrogen, such as gonadal dysgenesis, are clinically supported by the association of the hot flashes with night sweats and estrogen reduction (6).

Alternative treatments are divided into two categories of chemical and herbal medicines. Chemical medicines used to treat menopausal symptoms include adrenergic agonists (i.e., clonidine, methyldopa, and veraliprida), new antidepressants (i.e., fluoxetine, paroxetine, and venlafaxine), and anticonvulsants, such as gabapentin. Herbal treatments include soy combinations, fenugreek, red clover, Dong Quai, Wild Yam, Salvigol Officinalis, Oenothera, and Cimifugol (7).

The utilization of herbal medicines significantly prevents the symptoms and diseases caused by the reduction of estrogen hormones. Estrogen existed in plants is called phytoestrogen, which acts the same as estrogen in the human body. Herbal medicines containing phytoestrogens primarily reduce menopausal symptoms, and subsequently, regulate the release of hormones. Salvigol is a member of the mint family (Lamiaceae) and native to the Mediterranean region which is traditionally used for excessive sweating and menopausal sweating. Salvigol leaves contain 3%-8% tannins of catechin group (salivationen), phenolic acids, 1%-3% flavonoids, and volatile essential oils.

Laboratory and clinical studies have proven the antimicrobial, antifungal, and antiviral effectiveness of Salvigol. This plant can effectively inhibit sweating and this effect is attributed to the tannins of cathicine group and phenolic acids, such as rosmarinic (8).

Cimifugol is an indigenous American plant that contains triterpene glycoside (i.e., actein, cimicifugoside, and deoxyactein), acidophilic, salicylic acid, tannins, and isoflavones. The E2 Commission in Germany has approved the use of Cimifugol for the treatment of dysmenorrhea, symptoms of premenstrual syndrome, and menopause (9). To date, many medicinal herbal remedies, such as Salvigol and Cimifugol, are effective in the treatment of sweating during menopause. However, insufficient information is available about their full effects on sweating during this period; accordingly, more research is required to be conducted in this regard.

One of the most important challenges for women during the menopause period is night sweats and its treatment. Considering the increasing frequency of postmenopausal women, it is of utmost importance to study the symptoms and therapeutic methods. Therefore, this study aimed to investigate the effect of Cimifugol and Salvigol on night sweats in postmenopausal women.

## Materials and Methods

This randomized clinical trial was conducted on 80 postmenopausal women who were admitted to Hamadan health centers in 2016.

According to Sadeghi et al. (2013), the sample size was determined at 40 cases in each group based on the following formula with the mean difference of 3, a standard deviation of 4, a significant level of 5%, and power test of 90% (10).

$$n = \frac{(\sigma_1^2 + \sigma_2^2)(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{(\mu_1 - \mu_2)^2}$$

The inclusion criteria were: 1) one-year interval from the last menstruation, 2) no acute and chronic disease[1] according to the approval of a physician, 3) no use of any herbal medicine since 3 months before the intervention, 4) lack of any sensitivity to the herbs, and 5) no symptoms of breast and genital cancers. On the other hand, the participants who were allergic to the medicine, and those with no acute or chronic illnesses during the study and lack of consuming the medicine were excluded from the study.

The participants were selected randomly from postmenopausal women. For this purpose, 32 healthcare centers in Hamadan, Iran, were divided into three districts of north, center, and south considering the socioeconomic condition. Subsequently, two clinics from each district (n=6) were randomly selected, and from each district, a healthcare center was randomly assigned to the Cimifugol (A) or Salvigol groups (B). In the next stage, 13 patients were selected from each center using the simple random method (Figure 1).

The researcher visited the centers and recorded the list of menopausal women. They were then contacted through phone calls, and if they were qualified and willing to participate in the study, a visit time was set in the clinic on a specific day. After visiting the participants and checking the inclusion criteria, they were referred to a physician to assess their general health status. If their health condition was confirmed, a written consent form was obtained from them after giving the necessary explanations. Each participant was interviewed and then entered the study according to the inclusion criteria. The women were randomly assigned into two groups of Cimifugol (A, n=40) and Salvigol (B, n=40), and they were then requested to complete a sweating questionnaire one week before the intervention, which included the number, severity, and duration of the sweating. They were also informed of the treatment with assigned medication for eight weeks. The Cimifugol group received Cimifugol (6.5mg) capsule made by the Goldaru pharmaceutical company once a day. On the other hand, group B was asked to consume Salvigol (100 mg) made by the Goldaru pharmaceutical company three times a day. It should be noted that to reduce the possibility of bias in this study, the assistant researcher was blinded to the sampling stage and distributed drugs to the participants of the two groups in this single-blind study.

The data were collected using a demographic characteristics form including such information as age, height, weight, marital status, economic status, occupational status, education level, type of residence, menopause, number of deliveries, and number of children. Moreover, the Wiklund vasomotor symptom scale was used in this study to collect the relevant data.

This scale that was developed based on the definition given in Harrison (2008) and U.S Food and Drug Administration measures the intensity, duration, as well as frequency of night and bedtime sweats per minute. The reliability of this checklist was estimated at 0.87 using Cronbach's alpha. The participants were then requested to complete this form one week before the intervention if they experienced night sweats. Following that, they were subjected to the treatment for 8 weeks. It should be noted that they were informed that Salvigol Officinalis might reduce blood glucose but without specific side effects. On the other hand, Cimifugol might be associated with nausea, vomiting, headache, and dizziness if used in excessive doses.

[1] Cardiovascular, kidney disease, and diabetes

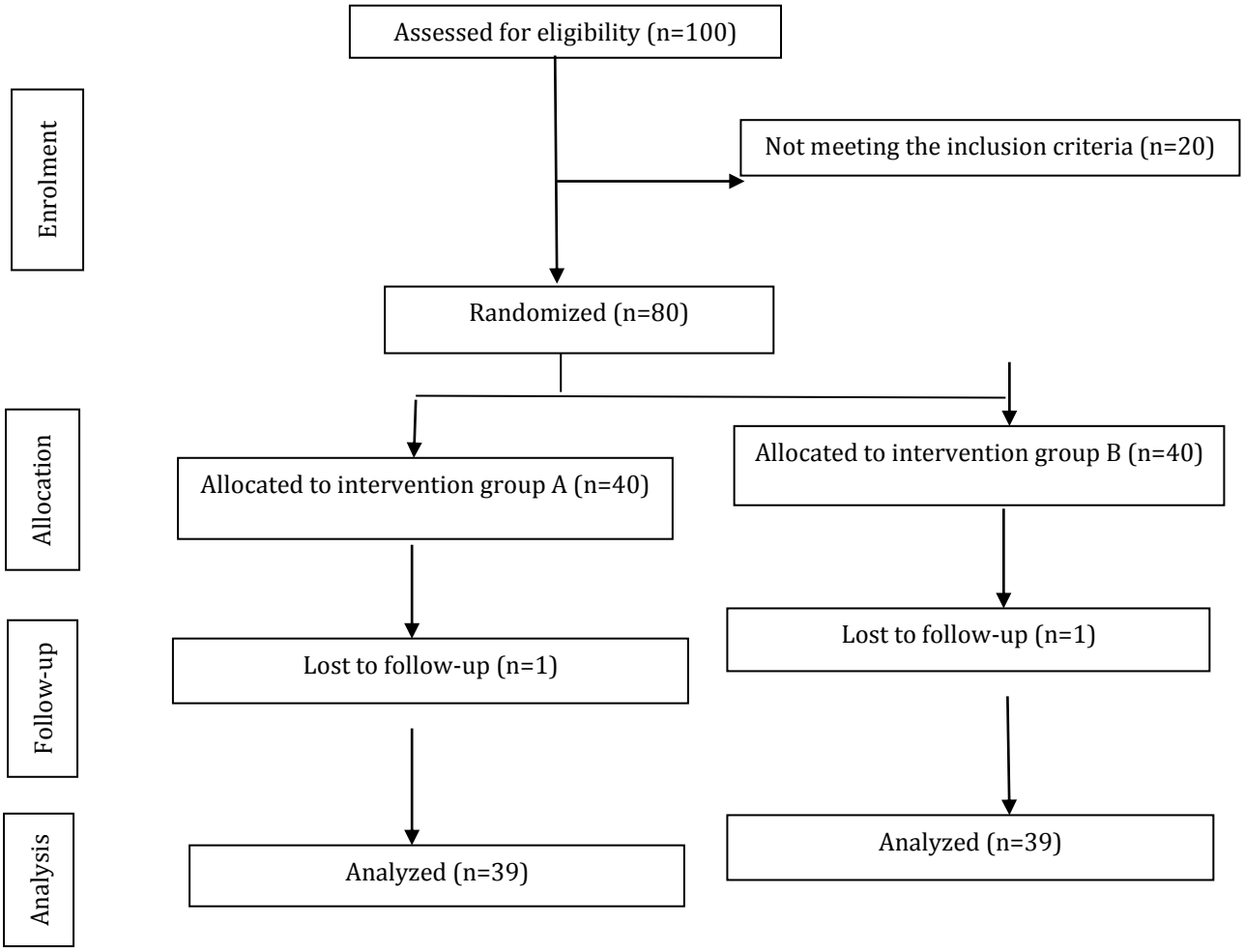


**Figure 1.** Sample selection process

The prescribed daily dose was one Cimifugol capsule and three Salvigol capsules. The proper and regular use of the medicines was followed up weekly by phone call. In addition, the participants were provided with the researcher's contact number to have access in case of any complications. The results were compared and analyzed at the end of each week and continued until the end of the intervention these issues by following them up, as well as providing complete training.

The data were analyzed in SPSS software (version 20) through independent t-test, Chi-square, analysis of covariance (ANCOVA), repeated measure ANOVA, and repeated measure ANCOVA (covariate: baseline). A p-

(8 weeks). Due to the possible side effects of Cimifugol on the liver, the physician first examined the participants to be assured of their health and then assigned them into group A. If any side effects were observed, medicine administration would be stopped. From the beginning of the study, through predicting cases, such as delayed medicine administration and using other drugs, it was attempted to control value less than 0.05 was considered statistically significant.

## Results

The participants in this study were homogeneous in terms of the effect of environmental factors, such as education level, economic status, community support,

characteristics, and special habits of life in different women along with their impact on the effect of herbal medicines. The mean±SD ages of the Salvigol and Cimifugol groups were 52.25±4.79 and 54.52±5.66 years, respectively.

**Table 1.** Comparison of the Cimifugol and Salvigol effects on Night Sweats in Postmenopausal Women: A Single-Blind Clinical Trial Study

| Variable | Group | Mean (SD) | P-value* |
|---|---|---|---|
| **Age** | Salvigol | 52.25(4.792) | 0.09 |
| | Cimifugol | 54.25(5.664) | |
| **Age of menopause** | Salvigol | 48.73(4.857) | 0.94 |
| | Cimifugol | 48.81(4.214) | |
| **Body mass index** | Salvigol | 26.58(4.468) | 0.41 |
| | Cimifugol | 27.48(5.208) | |
| **Duration of menopause** | Salvigol | 3.53(2.000) | 0.017 |
| | Cimifugol | 5.44(4.545) | |
| **Number of deliveries** | Salvigol | 4.13(1.911) | 0.092 |
| | Cimifugol | 4.97(2.408) | |

* independent t-test

In group A, 86.1% and 35% of the participants were married and illiterate, respectively. Moreover, 52.5% of the cases had a good social and economic status. On the other hand, 82.5% and 44.4% of the participants in group B were married and illiterate, respectively, and 55.65% of them had good social and economic status. The results of the Chi-square test showed no significant difference between the two groups in terms of marital status, education level, and economic status (P>0.05). Furthermore, the independent t-test revealed no significant difference between Salvigol and Cimifugol groups regarding the mean age, menopause age, body mass index, and number of deliveries (P>0.05). However, a significant difference was observed between the two groups in terms of the mean menopause time (P=0.017, Table 1).

The frequency of night sweating at different times was evaluated in the two groups.

According to the results of the t-test, there was a significant difference between the two groups before the intervention regarding the frequency of night sweating. Since the differences between the two groups before the study were significant, the effect of this difference was adjusted using the analysis of covariance (covariate: baseline).

**Table 2.** Comparison of the frequency of night sweats before and after the intervention in the Cimifugol and Salvigol groups

| Time | Group | | P-value* |
|---|---|---|---|
| | Cimifugol | Salvigol | |
| | Mean(SD) | Mean(SD) | |
| Before intervention | 5.28(3.997) | 8.93(6.350) | 0.004 |
| First week | 7.58(4.919) | 9.65(6.971) | 0.144 |
| Second week | 7.36 (3.424) | 9.00(5.796) | 0.143 |
| Third week | 8.22(4.517) | 8.08(5.846) | 0.903 |
| Fourth week | 8.69(4.522 ) | 7.58(5.168) | 0.321 |
| Fifth week | 7.86(4.310) | 7.00(5.074) | 0.430 |
| Sixth week | 8.83 ( 4.16) | 7.30(5.689) | 0.188 |
| Seventh week | 7.72(4.165) | 6.08(4.747) | 0.114 |
| Eight week | 6.81(3.756) | 6.15(4.394) | 0.489 |
| **P-value | P=0.071 | P<0.001 | |

* T-test and ANCOVA
** Repeated Measure ANOVA

The results showed that, at other times, the differences between the two groups were the same. Repeated measure ANOVA was used to check the frequency of night sweating at

different times (before and 8 weeks after the medication use) in each group according to the order of the desired variable. Due to its significance, it has been effective in the Salvigol group (P<0.05, Table 2)

Furthermore, the two groups were evaluated in terms of the mean duration of sweating at different times. According to the results, here was a significant difference between the two groups before and first weak after the intervention in terms of sweating duration. However, at other times, the differences between the two groups were the same. Repeated measure ANOVA was utilized to check the mean number of sweating at different times (before and 8 weeks after the medication consumption) in each group according to the order of the desired variable. Due to its significance, it has been effective in group B (Salvigol) (P<0.05, Table 3).

**Table 3.** Comparison of the duration of night sweats per minute before and after the intervention in the Cimifugol and Salvigol groups

| Time | Group | | P-value* |
|---|---|---|---|
| | Cimifugol | Salvigol | |
| | Mean(SD) | Mean(SD) | |
| Before intervention | 1.81(.980) | 2.53(1.132 ) | 0.004 |
| First week | 1.75(.806) | 2.50(1.109) | 0.001 |
| Second week | 1.86(.683) | 2.33(.997) | 0.022 |
| Third week | 1.83(.737) | 2.18(1.059) | 0.111 |
| Fourth week | 1.75(.770) | 2.13(1.042) | 0.081 |
| Fifth week | 1.92(.692) | 2.08 (1.047) | 0.445 |
| Sixth week | 2.03(.696) | 2.40(1.081) | 0.082 |
| Seventh week | 1.97(.810) | 2.03(1.097) | 0.814 |
| Eight week | 1.87(.806) | 1.95(1.108) | 0.882 |
| P-value ** | P=0.245 | P<0.001 | |

* T-test and ANCOVA
** Repeated Measure ANOVA

In other words, the trend of the night sweat duration of per minute during the follow-up period was significant in the group that consumed Salvigol.

## Discussion

The present study was carried out to evaluate the effect of Cimifugol and Salvigol on night sweats in postmenopausal women who were admitted to Hamadan health centers in 2016. The results showed that Salvigol was effective in reducing the intensity of night sweats; however, no significant change was observed over time in the Cimifugol group. Regarding the comparison of the two medications, the severity and number of night sweats were less in the Cimifugol group, compared to the Salvigol group. In a study conducted by Shahnazi et al. in 2013, the efficacy of Black Cohosh (Cimicifuga Racemosa) was investigated on vasomotor symptoms in postmenopausal women. They concluded that Cimifugol was effective in reducing vasomotor symptoms (11). The results of the aforementioned study are not in line with the findings of the present study. This discrepancy may the result of comparing the two medications in terms of reducing vasomotor symptoms.

Kiani Rad et al. performed a double-blind randomized clinical trial on 100 postmenopausal women suffering from night sweats and hot flashes admitted to Shiraz health care center in 2016. The results showed that Salvigol capsule could be effective in reducing the frequency and duration of hot flashes and decreasing the intensity of night sweats, which is consistent with the results of the present study. Both studies indicate the beneficial effects of the Salvigol capsule in reducing the intensity of sweating in postmenopausal women (12).

In the same vein, Rahte et al. showed that Salvigol was effective in improving vasomotor disorders and hot flashes; moreover, due to its ubiquitous estrogenic flavonoids effects, it has been effective in reducing the symptoms (13).

The results of a study carried out by Leach (2012) showed insufficient certainty and

evidence for a reduction in night sweats and other signs of vasomotor in menopausal women by Cimifugol (14). Furthermore, in a study conducted by Tanmahasamut (2014), Cimifugol was no better at controlling vasomotor symptoms than placebo (15). However, in other studies, Cimifugol has been shown to be effective in the treatment of vasomotor disorders (16, 17). The results of this study indicate that the use of these two herbal medicines, especially Salvigol, can be effective in reducing night sweats, which can be used as a non-invasive method since no special side effect has been reported in this regard.

Regarding the limitations in this study, one can name the lack of any control group as the third group to receive routine treatment and long-term follow-up of more than two months after the treatment. Psychological problems and stresses in everyday life can exacerbate the menopause symptoms, and since this study was a randomized one, this problem has roughly been solved. However, further studies are recommended to obtain a definitive conclusion from the treatment of night sweats using Cimifugol and Salvigol.

## Conclusion

The results of this study showed the improvement of duration and frequency of night sweats in the Salvigol group, compared to the Cimifugol group. If later extensive studies confirm these results, the use of this effective plant can be recommended for the treatment of night sweats in the menopause process.

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## Conflicts of interest

Authors declared no conflicts of interest.

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