The Effect of Melissa Officinalis on Postpartum Blues in Women Undergoing Cesarean Section

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A R T I C L E I N F O	**A B S T R A C T**
Article type: Original article	**Background & aim:** Postpartum blues is the most common postpartum mood disorder, which can turn into a chronic depression. Therefore, the prevention of this disorder is effective for the improvement of family mental health. The present study was conducted to investigate the effect of Melissa officinalis (Lemon balm) on the incidence of postpartum blues.
	Methods: The present triple blind placebo-controlled clinical trial was performed on 60 women with cesarean section (C- section) at teaching hospitals affiliated to Mashhad University of Medical Sciences, Mashhad, Iran, from 2016 to 2017. The participants were randomly divided into intervention and placebo groups. The interventiongroup was administered lemon balm capsules (500 mg) from the first day after cesarean section three times a day for 10 days. Edinburgh postnatal depression scale was completed by all subjects at three stages, namely on the 3rd-5th, 10th, and 14th days after C-section. The data were analyzed by SPSS software (version 16) using independent t-test, as well as Mann-Whitney U, Chi-square, Fisher's exact tests and Friedman test.
	Results: The Fisher's exact test showed that the incidence of postpartum blues on the 3rd-5th, 10th, and 14th days after C-section were 3.3% and 43.3% ($P<0.00$), 3.3% and 50% ($P<0.00$), and 0% and 33.3% ($P<0.00$) in the intervention and placebo groups, respectively. The results of the two-way ANOVA test revealed that the depression score increased with maternal age due to the intervention ($P=0.046$). **Conclusion:** The use of lemon balm could reduce the incidence of postpartum blues, which is one of the most common postpartum psychiatric disorders, without occurance of possible side effects. Therefore, it is recommended to be used, especially in susceptible women for postpartum blues after delivery.

Introduction

Postpartum blues is a transient condition during which maternal emotional responses are intensified and accompanied by symptoms, such as feeling sad or crying. This condition can be observed in half of the women almost in the first week of postpartum period. A mild mood disorder can threaten the mother and the infant if developed to postpartum depression (1).

Although there is disagreement on the precise outbreak of the postpartum blues, it generally has a high prevalence estimated as 50-80% and 26-84% by Kaplan in 2007 and by O'Hara in 2014, respectively (2, 3). Based on the evidence, the prevalence of the postpartum blues is 51.3% in Iran (4).

Postpartum blues usually begins 1-5 days

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after the delivery and resolves within 10 days. This complication can lead to an increased risk of maternal major depression in 10-15% of the intervention

(5). Continued postpartum blues results in depression; therefore, early diagnosis can be helpful for planning to prevent it (6). Pharmacological depression therapies in lactation include benzodiazepines and tricyclic antidepressants, which cause severe drowsiness and reduced maternal capacity in response to baby crying, altered sexual function by increasing fatigue, dizziness, hypotension, tachycardia, and relaxation effects on the infant through breast milk. Therefore, the consumption of these drugs is limited in breastfeeding due to their side effects.

The use of medicinal plants, such as Melissa officinalis (lemon balm), is known to be one of the practical and effective methods for the treatment of psychosocial disorder. In traditional medicine references, lemon balm is also known as a sedative in the treatment of disorders, such as stress, anxiety, and depression. The sedative effects of this plant are due to its effect on gamma-aminobutyric acid (GABA) and benzodiazepine receptors (7, 8).

In the traditional medicine, lemon balm has many applications, including the relaxation of nervous system. This plant is available in various forms, such as essential oil, oily extract, oil, ointment, compress, and herbal tea. In various studies, the essential oil of this plant is effective in softening neuropathic stomach pain, tight stomach, palpitations, unilateral headaches, dizziness, anger, insomnia, and vomiting during pregnancy. The leaves of lemon balm are also used to attenuate anxiety, nerve fatigue, and depression. In general, its antidepressant effects have been confirmed (9); therefore, given the potential properties of this plant, it can be applied as a unique medication substitute for some psychiatric disorders (10).

Postpartum blues is the most common postpartum mood disorder. If the symptoms of this disorder continue for more than two weeks, it can turn into a chronic depression. Consequently, the prevention of this mental state is effective in the protection of family mental health. The high prevalence of postpartum blues and the necessity of using complementary medicine based on the clinical guidelines urge the need for investigating different therapeutic options for this disorder. Regarding this, the present study aimed to investigate the effect of lemon balm on the incidence of postpartum blues.

Materials and Methods

The present triple-blinded placebo-controlled clinical trial was carried out on women with C-section from 2016 to 2017. Regarding the novelty of the research idea and the lack of similar study, the sample size was estimated as 30 intervention in each group based on a pilot study performed on 10 subjects in each group and using the formula for comparing two sample proportions with 95% confidence interval, 80% test power, and 10% sample dropout. A total of 60 eligible women with C-section were selected through purposive sampling method.

The inclusion criteria were: 1) age of 18-35 years, 2) education level of primary school, 3) first marriage and monogamy, 4) C-section experience, 5) possession of a healthy baby, 6) physical and mental health, 7) residency in Mashhad, 8) score of 0-10 in the Beck test on the first day post-delivery, 9) singleton pregnancy, 10) gestational age of 37-42 weeks (based on 26th gestational ultrasonography, fundal height, and the first day of the last menstruation), 11) absence of abnormalities in the child, 12) no need for specific treatment interventions (e.g., need for drug prescription, serum injection, infant admission to the neonatal intensive care unit) during the study, 13) birth weight of < 2 kg, 14) no unintended pregnancy, 15) no history of stillbirth or infertility and two abortions and more, 16) no history of medical illness (e.g., diabetes, cardiovascular disease, thyroid, and gastric ulcer), 17) lack of midwifery problem during the current pregnancy (e.g., placenta previa, placental abruption, oligohydramnios, polyhydramnios), 18) no family history of mental disorders, 19) no physical disability, mental retardation, or chronic illness in the spouse or children, 20) no history of severe emotional excitement during the past six months, 21) no history of mental illness, 22) non-use of psychoactive medication (e.g., diazepam, morphine, pethidine, and phenobarbital), and 23) no smoking or drug addiction.

On the other hand, the exclusion criteria were: 1) postpartum complications (e.g., preeclampsia, eclampsia, postpartum haemorrhage, infection, breast problems, and anaemia), 2) non-consumption of the prescribed drug for one day, and 3) irregular use of medication (less than three times a day). Three and four cases in the intervention and placebo groups discontinued using the drug, respectively, due to the fear of complications.

The utilized tools in this study included the Beck depression inventory (BDI), Edinburgh postnatal depression scale (EPDS), and a researcher-made checklist. This checklist covered such data related to personal information (13 items), pregnancy and childbirth (22 items), and marital life (10 items). The content validity method was used to determine the validity of the research unit selection questionnaire, personal data, pregnancy- and childbirth-related information, post-delivery maternal and neonatal information, marital characteristics, exclusion criteria, satisfaction with the treatment method, and side effects during drug consumption.

Therefore, this checklist was set up after a thorough study of the latest books, as well as national and international scientific articles and journals, and then reviewed and approved by ten faculty members of the School of Nursing and Midwifery at Mashhad University of Medical Sciences. The checklist was finalized after necessary amendments.

Furthermore, the reliability of the research unit selection questionnaire, including such data as demographic information, pregnancy- and childbirth-related information, post-delivery maternal and neonatal information, marital characteristics, and exclusion criteria was confirmed owing to entailing clear questions repeatedly used in other studies.

The BDI-II measures the types of emotions and behaviors clinically shown by a depressed person to detect the level of depression. This scale consists of 21 self-report items, each of which containing four phrases rated on a four-point Likert scale ranging from 0 to 3. In this instrument, the subject should select at least one phrase in each item. If the respondent selected more than one phrase, the phrase with the higher score would be considered. Therefore,

the subjects were included in the study based on the maximum score they obtained (score of 0-10 from the Beck self-report test on the first day of postpartum), indicating no postpartum blues and depression.

The EPDS is a standard questionnaire for evaluating postpartum depression. Studies have shown that it can also be used to measure mood disorders in the first days of puerperium. This test consists of 10 four-option multiple-choice items. In this instrument, the respondent should mark the option that is closest to her feelings not only at the present, but also in the last seven days. This questionnaire has a score range of 5-20. Accordingly, scores of < 10, 10-15, and > 15 are considered as signifying healthy status, postpartum blues, and postpartum depression, respectively.

Beck et al. in 1996 confirmed the validity and reliability of BDI-II. According to Zealley and Aitken, this questionnaire is the best instrument to determine depression. The implementation and scoring of this test is simple and does not require any special training. Moreover, this scale is standard and has the necessary reliability. Rajabi confirmed the validity and reliability of this questionnaire in Iran using internal consistency (12). In addition, Mosallanegad et al. in 2005 affirmed the validity and reliability of the EPDS in Iran (4). Dolatian (2006) also endorsed the reliability of this scale in Iran by content validity using ten research units (11). The content validity of the EPDS was confirmed by ten faculty members of the School of Nursing and Midwifery at Mashhad University of Medical Sciences.

The lemon balm was purchased dry and used after the verification of herbarium experts at Mashhad University of Medical Sciences. In the present study, the lemon balm was applied as a capsule prepared by a pharmaceutical expert in the pharmacy laboratory of the Faculty of Traditional Medicine of Mashhad University of Medical Sciences. The researcher, sampler, research units, and analyst of the statistical information were unaware of the capsule contents. The pharmacist informed the research group about the content of the capsules after completing the statistical analysis. The medication dose was selected according to the studies performed by Zarghami et al. (2010) and

Heidari et al. (2015) (13, 14).

In order to observe the ethical considera-tions, written informed consent was obtained from all the participants. Furthermore, the subjects were informed about the research objectives and methodology. They were also assured about the possibility of study withdrawal without any adverse effect on their treatment process. After receiving a formal presentation from the School of Nursing and Midwifery, the researcher identified the mothers under C-section and conducted an initial assessment if they wished to participate in the study. Subsequently, those meeting the eligibility criteria were entered into the study.

The demographic form was completed for the subjects who had a score of 10 or less in the BDI-II on the first day of postpartum period. Then, the samples were randomly divided into two groups of intervention and placebo (30 cases in each group). The EPDS and drug usage checklist were completed. The intervention group received training on how to complete the forms; furthermore, they were informed about the time limitation of filling out the instruments. The intervention group used lemon balm as a 500-mg capsule three times a day for 10 days. The placebo group was also prescribed to use capsules containing placebo under the same condition. Routine care was performed in both groups. The checklist for the daily intake of capsules was completed. In addition, EPDS was filled out at three stages, namely on the 3rd-5th, 10th, and 14th days after C-section.

In the next step, the severity of postpartum blues was measured through the Edinburgh Self-Rating Scale on the 3rd-5th, 10th, and 14th days after delivery. Eventually, the researcher attended the subjects' houses after making telephone contacts and coordination with mothers, to take the forms from the research units. Two cases in the placebo group were not responsive despite the frequent visits and follow-ups, and therefore were excluded.

The data were analysed in SPSS software (version 16). First, the data related to personal information, marital life, pregnancy and delivery, and maternal and neonatal status in the two groups were analyzed by the independent t-test (for the quantitative variables) and Mann-Whitney U test (for the quantitative variables)

with non-normal distribution or categorical scale. In addition, the Chi-square test was utilized to evaluate the homogeneity of qualitative variables with a nominal scale. If the Chi-square test assumptions were not established, Fisher's exact test would be used by integrating the lateral levels.

Friedman test was applied for the intragroup comparison of the Edinburgh score on 3rd-5th, 10th, and 14th days. According to the normal or non-normal distribution of variables, the independent t-test and Mann-Whitney U tests were employed for intergroup comparisons. P-value less than 0.05 was considered statistically significant.

Results

The gestational age at delivery was 38-42 weeks in the two groups. The mean ages of the patients were 28.5±4.6 and 29.2±4.3 years in the intervention and placebo groups, respectively, which were not significantly different (P=0.564).

At first, the normality of the variables was examined by Kolmogorov-Smirnov and Shapiro-Wilk tests to decide on the appropriate test for comparing the demographic and the underlying variables between the two groups. According to the results, age and duration of marriage had a normal distribution, and other variables had non-normal distribution. Therefore, the two groups were homogeneous regarding variables, such as age, frequency of pregnancies, delivery, family size, and duration of marriage (Table 1).

According to Table 2, the two groups were homogeneous in terms of education level, occupation, and spousal occupation.

Comparison of the incidence of postpartum blues in women giving birth on the 3rd-5th, 10th, and 14th days after delivery in the intervention and placebo groups using Fisher's exact test showed that the difference in the incidence of postpartum blues was significant (P<0.001) in the two groups on these days (Table 3).

The intragroup comparison of mean EPDS score by means of the Friedman test showed that the intervention group obtained a significantly different blues score after theintervention, compared to that before the intervention (P<0.001). Additionally, the post hoc test revealed a significant

difference in this regard in the stage between the　　　pre- and post-intervention stages (P<0.001).

Table 1. Mean quantitative and demographic variables in mothers studied in the intervention and placebo groups

Variables	intervention group	Placebo group	Test results
	Mean±standard deviation	Mean±standard deviation	
Frequency of pregnancy	2.6±0.9	2.3±0.9	U=364.5 P=0.182 Mann-Whitney
Frequency of delivery	2.3±0.6	2.1±0.9	U=396.0 P=0.385 Mann-Whitney
Family size	4.3±0.7	4.2±1.1	U=390.0 P=0.338 Mann-Whitney
Birth weight (g)	3231.0±341.4	3324.0±351.1	U=377.5 P=0.382 Mann-Whitney
Duration of marriage (year)	9.3±4.8	8.3±5.1	t=0.7, df=58 P=0.461 Independent t-test

Table 2. Frequency distribution of mothers according to their educational level, occupation, and spouse's occupation in in the drug group and placebo group

Variables		intervention group	Placebo group	Test results
		Frequency (percentage)	Frequency (percentage)	
Education level	Primary school	4 (13.3)	5 (16.7)	U=442.5 P=0.905 Mann-Whitney
	Junior high school	7 (23.3)	7 (23.3)	
	High school	16 (53.3)	14 (46.7)	
	Academic	3 (10.0)	4 (13.3)	
	Total	30 (100.0)	30 (100.0)	
Maternal occupation	Housekeeper	29 (96.7)	28 (96.6)	Chi=0.0, df=1 P=1.000 Exact Chi-square
	Employee	1 (3.3)	1 (3.4)	
	Total	30 (100.0)	30 (100.0)	
Spousal occupation	Employee	2 (6.7)	1 (3.3)	Chi=2.0, df=3 P=0.604 Exact Chi-square
	Worker	10 (33.3)	8 (26.7)	
	Self-employed	17 (56.7)	21 (70.0)	
	Unemployed	1 (3.3)	0 (0.0)	
	Total	30 (100.0)	30 (100.0)	

Table 3. Frequency distribution of mothers according to the incidence of postpartum blues on days 3-5, 10, and 14 after delivery in the intervention and placebo groups

Variables		intervention group	Placebo group	Fisher's exact test results
		Frequency (percentage)	Frequency (percentage)	
Incidence of blues on days 3-5	Yes	1 (3.3)	13 (43.3)	P<0.001
	No	29 (96.7)	17 (56.7)	
	Total	30 (100.0)	30 (1000.0)	
Incidence of blues on day 10	Yes	1 (3.3)	15 (50.0)	P<0.001
	No	29 (96.7)	15 (50.0)	
	Total	30 (100.0)	30 (100.0)	
Incidence of blues on day 14	Yes	0 (0.0)	10 (33.3)	P<0.001
	No	30 (100.0)	20 (66.7)	
	Total	30 (100.0)	30 (100.0)	

Table 4. Mean postpartum blues scores in mothers in the intervention and placebo groups

Incidence of blues	intervention group Mean±standard deviation	Placebo group Mean±standard deviation	Test results
Before intervention	1.8±1.3	2.3±1.1	t=1.6, df=58 P=0.110 Independent t-test
Days 3-5	4.9±2.5	9.2±5.6	t=3.8, df=58 P<0.001 Independent t-test
Day 10	4.3±3.1	9.2±6.0	t=4.0, df=58 P<0.001 Independent t-test
Day 14	3.7±2.9	8.6±7.2	U=224.5 P=0.001 Mann-Whitney
Difference between day 14 and pre-intervention	1.9±3.3	6.2±7.2	t=3.0, df=58 P=0.004 Independent t-test
Intragroup test result	Chi=38.5, df =3 P<0.001 Friedman test	Chi=18.7, df =3 P<0.001 Friedman test	

Regarding the placebo group, the results of the Friedman test indicated a significant difference in the blues scores obtained after the intervention, compared to those gained before the treatment (P<0.001). The post hoc test also demonstrated a significant difference between the pre- and post-intervention stages in this respect (P<0.001) (Table 4).

Discussion

The present study examined the effect of lemon balm on postpartum blues. The findings of the present study revealed that postpartum depression scores were significantly lower on the 3rd-5th, 10th, and 14th days after delivery in the intervention group, compared to those in the placebo group. These findings are indicative of the effectiveness of lemon balm in treating postpartum blues.

Lemon balm is an aromatic and herbaceous plant from the Lamiaceae family and a sedative plant that affects the nervous system and causes relaxation (15). However, the sedative and antidepressant effects of this plant have not been sufficiently investigated. Similar to this research, some studies have examined the effects of lemon balm on mood and mood disorders. In this regard, Zarghami et al. studied the effect of lemon balm at a daily dose of 1200 mg, compared with daily administration of 30-mg fluoxetine in patients with major depression. They demonstrated that lemon balm and fluoxetine were equally efficient (13).

Emamghoreishi et al. investigated the antidepressant effect of aqueous extract and essential oil of lemon balm in mice during immobility, climbing, and swimming behaviors in a forced swimming test. In general, the results of the mentioned study revealed that lemon balm had an anti-depressant effect similar to imipramine, which is used to treat depression (16).

Martins et al. confirmed the antioxidant properties of Melissa officinalis aqueous extract and its effectiveness in oxidative stress reduction (17). In another study, Chehroudi et al. revealed the positive effects of lemon balm on serum antioxidant levels and mood quality in burn patients. Their results demonstrated that the frequency of anxiety and depression in the intervention group was significantly lower than that in the placebo group after the intervention.

Therefore, lemon balm can significantly reduce anxiety and depression and improve sleep quality (18). Ernst et al. (2007) expressed that lemon balm affects GABA receptors, thereby playing a positive role in the treatment of mild to moderate depression and anxiety (8). Cases et

al. (2010) examined the effect of lemon balm extract on the treatment of patients with mild to moderate anxiety disorders and sleep difficulties. They exhibited that lemon balm consumption reduced the effects of stress, anxiety, and insomnia and improved the clinical symptoms (19).

In addition, Sarris et al. (2011) confirmed the effectiveness of lemon balm on anxiety, insomnia, and depression by inhibiting GABA and cytokine receptors (20). Cases et al. studied the effectiveness of lemon balm extract in patients with mild to moderate anxiety disorders and sleep difficulties. Their findings revealed that 95% of the cases showed a positive responses to treatment, 70% and 85% of which had a complete recovery for anxiety and insomnia, respectively (19).

Postpartum blues is directly associated with low mood, and anxiety is one of the major factors affecting mood level (19). The findings of the aforementioned studies are partly in line with those of the present study. Other similar studies also verified the positive effect of lemon balm on sleep quality, anxiety, depression (21, 22), physical and psychological symptoms of menopause (23), and Alzheimer's disease (24, 25).

Postpartum blues is a prevalent condition that can eventually lead to postpartum depression, which may result in suicide or infanticide by the mother. Regarding this, the determination of the factors that can help prevent this complication is important and can be considered as an effective step to promote maternal health. Some of the strengths of the present study are the use of a triple-blinded design, homogeneous medication, and placebo group. One of the weaknesses of this study was reliance on the responses of the subjects with underlying mental disorder and individual and personality differences.

Conclusion

The present study revealed that the use of lemon balm could reduce the incidence rate of postpartum blues, which is one of the most common postpartum psychiatric disorders, without the development of possible side effects. Given the importance of natural childbirth, it is recommended to perform a similar study on women with vaginal delivery.

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Conflicts of interest

The authors declare no conflicts of interest.

References
1. Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. Williams obstetrics. 24th ed. New York: McGraw-Hill; 2014.
2. O'Hara MW, Wisner KL. Perinatal mental illness: definition, description and aetiology. Best Practice & Research Clinical Obstetrics & Gynaecology. 2014; 28(1):3-12.
3. Sadock BJ, Kaplan HI, Sadock VA. Kaplan & Sadock's synopsis of psychiatry: behavioral sciences/clinical psychiatry. Philadelphia: Lippincott Williams & Wilkins; 2007.
4. Mosallanegad L, Gahanmiri LH, Ashkani H. Assessing post partum blue in women referring to maternity clinic in Shiraz-2003. Jahrom Medical Journal. 2005; 2(2):22-7.
5. O'hara MW, McCabe JE. Postpartum depression: current status and future directions. Annual Review of Clinical Psychology. 2013; 9:379-407.
6. Field T. Postpartum depression effects on early interactions, parenting, and safety practices: a review. Infant Behavior and Development. 2010; 33(1):1-6.
7. Akman C, Uguz F, Kaya N. Postpartum-onset major depression is associated with personality disorders. Comprehensive Psychiatry. 2007; 48(4): 343-347.
8. Ernst E. Herbal remedies for depression and anxiety. Advances in Psychiatric Treatment. 2007; 13(4):312-316.
9. López V, Martín S, Gómez-Serranillos MP, Carretero ME, Jäger AK, Calvo MI. Neuroprotective and neurological properties of Melissa officinalis. Neurochemical Research. 2009; 34(11):1955-1961.
10. Taiwo AE, Leite FB, Lucena GM, Barros M, Silveira

D, Silva MV, et al. Anxiolytic and antidepressant-like effects of Melissa officinalis (lemon balm) extract in rats: influence of administration and gender. Indian Journal of Pharmacology. 2012; 44(2):189.

11. Dolatian M, Maziar P, Majd HA, Yazdjerdi M. The relationship between mode of delivery and postpartum depression. Journal of Reproduction & Infertility. 2006; 7(3):260-268.

12. Rajabi G, Kasmaei S. The suitability of psychometric indices persian version of the beck-second depression inventory (BDI-II). Educational Measurement. 2012; 3(10):139-157.

13. Eudes Filho J, Silveira D, Soares AI, Carneiro FP, de Assis MS, Leite FB, et al. Effects of lemon balm (Melissa officinalis) on behavioral deficits and memory impairment of rats surviving sepsis. Journal of Medicinal Plants Research. 2017; 11(8):153-160.

14. Heidari M, Soltanpour A, Naseri M, Kazemnezhad A. The effect of Lemon Balm (Melissa Officinalis) on depression in patients after coronary artery bypass graft. Cardiovascular Nursing Journal. 2015; 4(2):36-43.

15. Schultz V, Hänsel R, Tyler VE. Rational phytotherapy: a physician's guide to herbal medicine. London: Psychology Press; 2001.

16. Emamghoreishi M, Talebianpour MS. Antidepressant effect of Melissa officinalis in the forced swimming test. DARU Journal of Pharmaceutical Sciences. 2015; 17(1):42-47.

17. Martins EN, Pessano NT, Leal L, Roos DH, Folmer V, Puntel GO, et al. Protective effect of Melissa officinalis aqueous extract against Mn-induced oxidative stress in chronically exposed mice. Brain Research Bulletin. 2012; 87(1):74-79.

18. Chehroudi S, Fatemi MJ, Saberi MS, Salehi SH, Akbari H, Samimi R. Effects of Melissa officinalis L. on reducing stress, alleviating anxiety disorders, depression, and insomnia, and increasing total antioxidants in burn patients. Trauma Monthly. 2016; 22(4):e33630.

19. Cases J, Ibarra A, Feuillere N, Roller M, Sukkar SG. Pilot trial of Melissa officinalis L. leaf extract in the treatment of volunteers suffering from mild-to-moderate anxiety disorders and sleep disturbances. Mediterranean Journal of Nutrition and Metabolism. 2011; 4(3):211-218.

20. Sarris J, Panossian A, Schweitzer I, Stough C, Scholey A. Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence. European Neuropsycho-pharmacology. 2011; 21(12):841-860.

21. Heidari M, Soltanpour A, Naseri M, Kazemnezhad A. The effect of Lemon Balm (Melissa Officinalis) on depression in patients after coronary artery bypass graft. Cardiovascular Cardiovascular Nursing Journal. 2015; 4(2):36-43.

22. Taavoni S, Nazem Ekbatani N, Haghani H. The effect of lemon Balm on sleep disorder in menopausal women 60-50 years old. Complementary Medicine Journal of Faculty of Nursing & Midwifery. 2013; 2(4):344-534.

23. Taavoni S, Nazem EN, Izadjoo M, Haghani H. Effect of Lemon Balm supplementation on menopausal symptoms. Complementary Medicine Journal of Faculty of Nursing & Midwifery. 2016; 5(4):1324-1336.

24. Akhondzadeh S, Noroozian M, Mohammadi MR, Ohadinia S, Jamshidi A, Khani M. Melissa officinalis L. extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomized and placebo-controlled trial. Journal of Medicinal Plants. 2002; 4(4):47-57.

25. Dastmalchi K, Ollilainen V, Lackman P, af Gennäs GB, Dorman HD, Järvinen PP, et al. Acetylcholinesterase inhibitory guided fractionation of Melissa officinalis L. Bioorganic & Medicinal Chemistry. 2009; 17(2):867-871.