Research Journal of Pharmacognosy (RJP) 4(4), 2017: 33-39
Received: 21 June 2017
Accepted: 5 Sep 2017

Original article

Effect of "*Gol-e-ghand"*, a mixture of rose petals and honey, on migraine attacks: a before-after pilot study

A. Maddahian[1], M. Togha[2], S. Sahranavard[3], S.M. Riahi[4], S. Dehghan[1], M. Movahhed[1*]

[1]*Department of Traditional Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
[2]*Headache Department, Iranian Center of Neurological Research, Neurosciences Institute, Tehran University of Medical Sciences, Tehran, Iran.*
[3]*Department of Traditional Pharmacy, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
[4]*Department of Public Health, Faculty of Health, Birjand University of Medical Sciences, Birjand, Iran.*
[5]*Department of Epidemiology, Faculty of Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

Abstract

Background and objectives: Migraine is the seventh most common cause of disability among all ailments according to the World Health Organization. Despite the availability of some medicines for prevention of migraine, their complications are a cause for concern. Traditional system of medicine and use of medicinal herbs can be beneficial in management of migraine. "*Gol-e-ghand"* is one of the most commonly prescribed products for the management of headaches in the Iranian traditional medicine. The present study was designed to evaluate the effect of "*Ghol-e-ghand"* on decreasing the frequency of migraine attacks. **Methods:** Nineteen migraine patients, who met the eligibility criteria, according to the International Headache Society diagnostic criteria were assigned to the intervention. The study was conducted as a before-after clinical trial and included two phases of drug administration. Propranolol was given during the first phase, while "*Ghol-e-ghand*" was administered along with propranolol in the second phase. The severity, duration, and frequency of headaches were measured before and after the intervention. **Results:** The analysis showed that "*Ghol-e-ghand"* decreased the frequency of migraine (20%, p=0.04), but it was not effective in decreasing the duration and severity of the attacks. **Conclusion**: "*Ghol-e-ghand"* can be suggested in migraine patients for reducing frequency of attacks.

Keywords: *Ghol-e-ghand*, Iranian traditional medicine, *Rosa damascena*, migraine

Introduction

Migraine is debilitating neurological ailment with chronic nature. Migraine headache is the third most common disorder, the seventh most peculiar reason for disability throughout the world, and the third most common cause of headache [1]. The prevalence of migraine has been stated to be

Available at: http://rjpharmacognosy.ir
*Corresponding author: minamovahhed@sbmu.ac.ir, Tel: +9821-88773521, Fax: +9821-88773521

various in different studies [2] and has been estimated between 10% to 33% in women and 6% to 15% in men [2-4]. It is a chronic disorder without definite treatment [5], and complications of modern medications are unavoidable. Finding new drugs for migraine is a necessity which has urged the World Health Organization to encourage the use of alternative medicine in various countries [6-8].

Numerous preventive measures are used to employ the traditional medicine in complicated diseases [8]. Recent studies have shown the efficacy of some traditional herbs in the management of headaches [9,10]; moreover, there is a surge in the use of herbal medicine in chronic ailments [11]. Iranian traditional medicine (ITM) or Persian medicine is a type of traditional medicine in the Middle East with a history of more than thousand years [10]. It was the leading medical paradigm in most parts of the world from the medieval time until the renaissance era [12].

In ITM, the treatment of headache is described in detail and various medicinal plants have been suggested [13,14]. For example, aromatic herbs have been used to treat a type of headache that raised from weakness of the brain (called "*Zaa'f-e-demagh*"). Weakness of the brain is an important cause of chronic and recurrent headaches in ITM text [14,15]. New pharmacological studies have shown that herbs such as *Rosa damascena*, Mill. may play a major role in the treatment of various ailments [16-18]. *Rosa damascena* (known as*''Gol-e-mohammadi'')* belongs to the Rosaceae family and is cultivated throughout the world mostly as a decorative plant. It is also a well-known medicinal herb [19].

Rosa damascena has shown several pharmacological characteristics, such as anti-anxiety, antioxidant and antibacterial effects along with potentially anti-tumor properties [20-23].

Golghand is one of the most popular remedies prescribed for the management of headache in ITM texts [24,25]. It has been used to treat headaches which occurred along with other conditions such as stomach diseases and anxiety. "*Ghol-e-ghand"* is composed of honey and petals of *Rosa damascena*, which has been used as a brain and heart tonic and has laxative properties as well [14,26]. *Rhazes*, in "*Al-havi"* (Liber continent), and other traditional scholars have indicated that even in the absence of complaints related to constipation, using laxatives and stool softeners can lead to more successful management of headaches such as participatory headache. That is why most drugs used for headache management in ITM have some laxative components. Participatory headache, is one type of headache which can occur due to participation and dysfunction of organs except brain and has several subtypes such as headaches of gastrointestinal origin, which may be caused due to constipation [13,26,27,28].

Some earlier studies have discussed headache in ITM [27-31], but there is no clinical evidence regarding the effect of "*Ghol-e-ghand*". Therefore, this study was designed to evaluate the effect of "*Ghol-e-ghand"* on migraine.

Experimental

Herbal product

"Ghol-e-ghand", an ITM product composed of the petals of *Rosa damascena* and honey, was used in the study.

Study design

The subjects were educated about the purpose of the study, and the informed consent was obtained. The subjects were free to withdraw from the study at any time during the study. The study was approved by the Ethical Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.REC.1394.156).

The patients attended the Headache Clinic of Sina Hospital, Tehran, Iran. The details of the individual selection process have been presented in figure 1. In the initial examination, 25 participants were eligible for enrollment. During the first and second phases of study, six participants were excluded due to having less than three migraine headache per month (n=2), onset of cancer (1), Loss to flow-up (n=2) and treatment noncompliance (n=1), and finally 19 participants were enrolled in the analysis (figure 1). Adults aged 18-55 years old who had migraine according to the international classification of headache disorders [ICHD-III], suffering from at least three attacks per month, were included in the study.

Study population

Participants with history of unknown abdominal

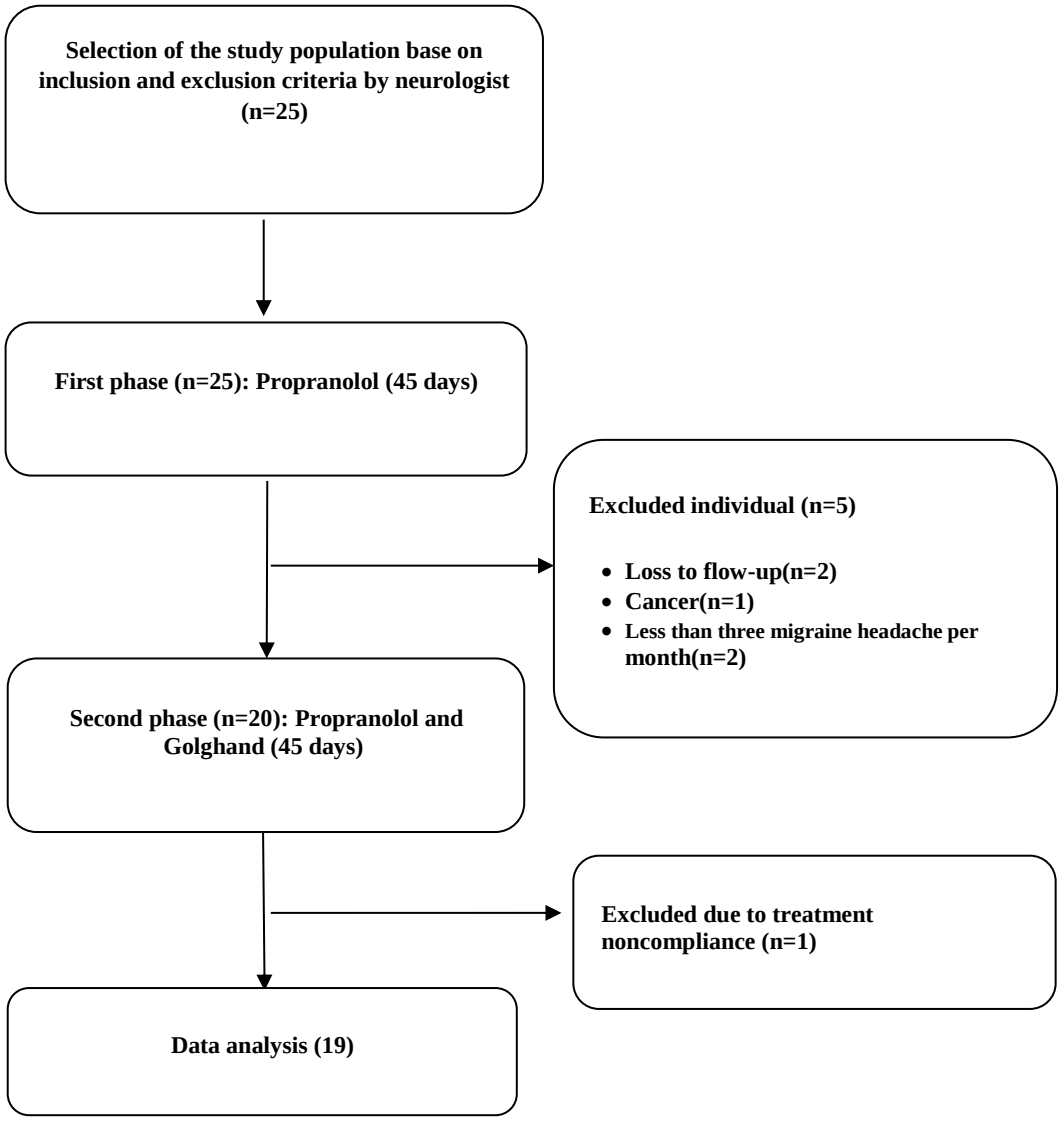

Figure 1. Diagram for the individual selection process through the different phases of study

pain, acute abdomen surgery, renal and hepatic diseases, obstructive gastrointestinal disease, malignancy, presence of warning signs such as GI bleeding, weight loss and anemia, diabetes mellitus (fasting blood sugar test above 110 mg/dL), HTN, addiction to opioids and stimulants and alcohol consumption were excluded. In addition, patients who did not want to continue the research; or those who were non-compliant about taking the prescribed drug correctly or using laxatives including those of traditional medicine and those experiencing unpredictable complications leading to drug intolerance such as idiosyncratic complications; or those experiencing significant change in the lifestyle effecting the headache during the intervention, were excluded. In the present study, no special side effect was noticed.

To calculatee the sample size, the mean and standard deviation of the headache frequency were considered 7 and 3.7, respectively according to a previous study [28]. The expected effect size was considered on average 1.5 headaches per month. The correlation coefficient before and after the intervention was considered 0.8, and type I and type II errors were considered 0.05 and 0.2, respectively. The overall sample size was calculated 17 individuals. Finally, taking into account an attrition of 10%, 19 individuals were selected for the study. The Gpower software was used for calculating the sample size.

Intervention
All patients received propranolol 20 mg twice daily during the whole study period. The study had two phases. In the 1st phase, the participants received propranolol for a period of 45 day. In the second phase, (from the 46th day), the intervention was started with "*Ghol-e-ghand"* as a supplement and subjects received it in addition to propranolol. "*Ghol-e-ghand"* was taken twice daily, 5 g in the morning, 30 min before breakfast and10 g at night, 30 min before sleep. It was mixed with 150 mL lukewarm water and consumed.

Outcome measurement
Initially, the baseline and demographic characteristics were recorded for each patient. Also, the patients were asked to record duration, frequency and intensity of each pain during the entire study [32].

Statistical analysis
In the present study, for assessing the effect of the intervention on the duration, severity, and frequency of migraine headrace attacks, paired t-test was used for comparing before and after parameters of the intervention. The One-Sample Kolmogorov-Smirnov test was also used for checking the normality assumption.
The SPSS software version 22.0 was used for data analysis and *p* values less than 0.05 were considered significant.

Result and Discussion
In the present study, no special side effect was noticed; among the 19 subjects, 14 (73.68%) were female. The mean age of participants was 40.94±7.56 years and their mean BMI was 26.71±4.11. Also, the finding showed there were several stimulating factors in each patient (table 1).
Major components of *Rosa demascena* include phenyl ethyl alcohol, citrenellol, nonadecane, and flavonoids [23,33-35]. *R. damascena* also contains vitamin C which has antioxidant and anti-inflammatory properties [23]. Since inflammation is one of the several mechanisms hypothesized to be involved in migraine [36,37], these compounds might have some roles in the analgesic and hypnotic effects of the plant [33,35, 38].

Table 1. Distribution of stimulating factors in the study population

Factors	Number of patients (%)
Food	8 (42.11)
Light	14 (73.68)
Noise	14 (73.68)
Sleep disorders	17(89.47)
Hunger	16 (84.2)
Odors	14 (73.68)
Menstruation	13 (92.68)
Fatigue	14 (73.68)
Stress	16 (84.2)

There are a few clinical trials on migraine in the field of ITM [28,39]; however, Gharabaghi conducted a study on the effect of *Rosa damascena* on elective C-section post-surgical pain and reported that the intensity of pain was lower in the *Rosa* group, which had a significant association with time [40]. Moreover, Hajhashemi indicated the anti-inflammatory and analgesic effects of *Rosa damascena* hydroalcoholic extract against inflammatory diseases in animal model. In another study Kim *et al.* reported the positive effect of aromatherapy of *R. damascena* on management of menstrual pain [21,22,41,42].
In a meta-analysis review study, propranolol caused, on average, an approximately 45% reduction in the migraine activity when the patients' daily headache recordings were used to assess the effectiveness of the treatment. On the other hand, placebo yielded, on average, only about a 14% reduction in the migraine activity outcome [43].
To our knowledge, no previous study has evaluated the effect of "*Ghol-e-ghand* "on migraine. The results of the present study showed that headache frequency was 20% lower (compared to first phase) after intervention with *"Ghol-e-ghand"* (second phase) but the intensity and duration did not change significantly (table 2). Nevertheless, there were limitations in our study. The brain temperament of the target

population was one limitation of our study. Based on ITM, headache can be categorized into two types: warm and cold headache. The warm type can be managed with remedies which have a cold nature, and the cold type of headache responds to remedies with a warm nature; therefore the warm temperament of "*Ghol-e-ghand "* may be more effective in the management of headache in individuals with cold temperament of the brain.

Table 2. Comparison of mean headache frequency, intensity, and duration

Variable	Status	Mean	(SD)	Mean difference	*p* value
Headache frequency*	Before	6.57	4.08	-1.32	0.04
	After	5.39	3.72		
Headache intensity**	Before	5.52	1.82	- 0.05	0.87
	After	5.45	1.94		
Headache duration***	Before	7.96	5.45	- 0.56	0.42
	After	7.40	5.11		

*: number of attacks per month; **: Visual Analogue Scale (Rank 1-10); ***: duration of each attack (h)

Moreover, the subjects received "*Ghol-e-ghand"* for a limited period of time; therefore, these results could not be generalized to long-term efficacy of *Ghol-e-ghand*. The follow-up period would identify the durability of the drug effects but the patients were not followed up after finishing the study.

Long-term studies on special populations which focus on patients suffering from participatory headache with relevant temperament are recommended and a follow-up period would be helpful.

Overall, according to the findings of this investigation, it can be concluded that the combination of "*Ghol-e-ghand"* and propranolol has short-term effects on migraine, and is efficient in the reduction of the frequency of migraine attacks in a period of 45 days. Therefore, the use of "*Ghol-e-ghand"* may be justified as a supplement in the prevention of migraine attacks.

Acknowledgments

This article was established on the Ph.D. thesis of Dr. Alimohamad Maddahian (No.174), Department of Traditional Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. We would like to thank Dr. Ehsan Sharifipour, Dr. Abbas Tafakhori, Barij Essence Company, Kashan, Iran for their consultation and all the study participants for their cooperation.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the content of the paper.

References

[1] Steiner TJ, Birbeck GL, Jensen RH, Katsarava Z, Stovner LJ, Martelletti P. Headache disorders are third cause of disability worldwide. *J Headache Pain*. 2015; 16(1): 1-3.

[2] Stewart WF, Shechter A, Rasmussen B. Migraine prevalence. A review of population-based studies. *Neurology*. 1994; 44(64): 17-23.

[3] Waters W, O'connor P. Prevalence of migraine. *J Neurol Neurosurg Psychiatry*. 1975; 38(6): 613-616.

[4] Launer LJ, Terwindt GM, Ferrari MD. The prevalence and characteristics of migraine in a population-based cohort The GEM Study. *Neurology*. 1999; 53(3): 537-539.

[5] Ayatollahi SMT, Sahebi L, Borhani Haghighi A. Epidemiologic and clinical characteristics of migraine and tensiontype headaches among hospitals staffs of Shiraz (Iran). *Acta Med Iran*. 2009; 47(2): 115-120.

[6] Steiner TJ. Headache in the world: public health and research priorities. *Expert Rev Pharmacoecon Outcomes Res*. 2013; 13(1): 51-57.

[7] World Health Organization. *Atlas of headache disorders and resources in the world 2011*. Geneva: World Health Organisation, 2011.

[8] Pal SK, Shukla Y. Herbal medicine: current status and the future. *Asian Pac J Cancer Prev*. 2003; 4(4): 281-288.

[9] Borhani Haghighi A, Motazedian S, Rezaii R, Mohammadi F, Salarian L, Pourmokhtari M, Khodaei S, Vossoughi M, Miri R. Cutaneous application of menthol 10% solution as an abortive treatment of migraine without aura: a randomised, double-blind, placebo-controlled, crossed-over study. *Int J Clin Pract*. 2010; 64(4): 451-456.

[10] Wang L, Zhang J, Hong Y, Feng Y, Chen M, Wang Y. Phytochemical and pharmacological review of da chuanxiong formula: a famous herb pair composed of chuanxiong rhizoma and gastrodiae rhizoma for headache. *Evid Based Complement Altern Med*. 2013; Article ID 425369.

[11] Kamali SH, Khalaj AR, Hasani-Ranjbar S, Esfehani MM, Kamalinejad M, Soheil O, Kamali SA. Efficacy of 'Itrifal Saghir', a combination of three medicinal plants in the treatment of obesity; a randomized controlled trial. *Daru J Pharm Sci*. 2012; Article ID 3559014.

[12] Zargaran A, Zarshenas MM, Mehdizadeh A, Mohagheghzadeh A. Management of tremor in medieval Persia. *J Hist Neurosci*. 2013; 22(1): 53-61.

[13] Jorjani S. *Zakhire-ye-Kharazmshahi*. Tehran: Iranian Medical Science Culture Publication, 2003.

[14] Avicenna. *The Canon of medicine.* Tehran: Soroush press, 1997.

[15] Arzani MA. *Tebb-e-Akbari*. QOM: Jalaleddin, 2008.

[16] Zaidi SF, Muhammad JS, Shahryar S, Usmanghani K, Gilani AH, Jafri W, Sugiyama T. Anti-inflammatory and cytoprotective effects of selected Pakistani medicinal plants in *Helicobacter pylori*-infected gastric epithelial cells. *J Ethnopharmacol*. 2012; 141(1): 403-410.

[17] Sadraei H, Asghari G, Emami S. Inhibitory effect of *Rosa damascena* Mill. flower essential oil, geraniol and citronellol on rat ileum contraction. *Res Pharm Sci*. 2013; 8(1): 17-23.

[18] Joukar S, Askarzadeh M, Shahouzehi B, Najafipour H, Fathpour H. Assessment of safety and therapeutic efficacy of *Rosa damascena* L. and *Quercus infectoria* on cardiovascular performance of normal and hyperlipidemic rabbits: physiologically based approach. *J Toxicol*. 2013; Article ID 769143.

[19] Loghmani-Khouzani H, Sabzi Fini O, Safari J. Essential oil composition of *Rosa damascena* Mill. cultivated in central Iran. *Sci Iran*. 2007; 14(4): 316-319.

[20] Zargaran A, Borhani-Haghighi A, Faridi P, Daneshamouz S, Kordafshari G, Mohagheghzadeh A. Potential effect and mechanism of action of topical chamomile (*Matricaria chammomila* L.) oil on migraine headache: a medical hypothesis. *Med Hypotheses*. 2014; 83(5): 566-569.

[21] Moein S, Moein M, Khoshnoud MJ, Kalanteri T. *In vitro* antioxidant properties evaluation of 10 Iranian medicinal plants by different methods. *Red Crescent Med J*. 2012; 14(12): 771-775.

[22] Jazayeri SB, Amanlou A, Ghanadian N, Pasalar P, Amanlou M. A preliminary investigation of anticholinesterase activity of some Iranian medicinal plants commonly used in traditional medicine. *Daru J Pharm Sci*. 2014; Article ID 3896674.

[23] Yassa N, Masoomi F, Rankouhi SR, Hadjiakhoondi A. Chemical composition and antioxidant activity of the extract and essential oil of *Rosa damascena* from Iran, population of Guilan. *Daru J Pharm Sci*. 2015; 17(3): 175-180.

[24] Aghili Khorasani MH. *Makhzan-al-advia*. Tehran: Rahe kamal, 2009.

[25] Aghili Khorasani MH. *Kholase-ol-hekma*. Qom: Ismailian, 2006.

[26] Rhazes. *Al havi [liber continent]*. Tehran: Academy of medical sciences publication, 2005.

[27] Zarshenas MM, Petramfar P, Firoozabadi A, Moein MR, Mohagheghzadeh A. Types of headache and those remedies in traditional persian medicine. *Pharmacogn Rev*. 2013;

7(13): 17-26.
[28] Kasmaei HD, Ghorbanifar Z, Zayeri F, Minaei B, Kamali SH, Rezaeizadeh H, Amin G, Ghobadi A, Mirzaei Z. Effects of *Coriandrum sativum* syrup on migraine: a randomized, triple-blind, placebo-controlled trial. *Red Crescent Med J*. 2016; Aticle ID 4752800.
[29] Noghani MT, Rezaeizadeh H, Fazljoo SMB, Yousefifard M, Keshavarz M. Gastrointestinal headache; a narrative review. *Emerg*. 2015; 4(4): 171-183.
[30] Gorji A. Pharmacological treatment of headache using traditional Persian medicine. *Trends Pharmacol Sci*. 2003; 24(7): 331-334.
[31] Abokrysha N. Ibn Sina (Avicenna) on pathogenesis of migraine compared with the recent theories. *Headache*. 2009; 49(6): 923-927.
[32] Lucas C, Romatet S, Mekiès C, Allaf B, Lantéri-Minet M. Stability, responsiveness, and reproducibility of a visual analog scale for treatment satisfaction in migraine. *Headache*. 2012; 52(6): 1005-1018.
[33] Shafei MN, Saberi Z, Amini S. Pharmacological effects of *Rosa damascena*. *Iran J Basic Med Sci*. 2011; 14(4): 295-307.
[34] Schieber A, Mihalev K, Berardini N, Mollov P, Carle R. Flavonol glycosides from distilled petals of *Rosa damascena* Mill. *Z Naturforsch C Biosci*. 2005; 60(5-6): 379-384.
[35] Zargaran A, Borhani-Haghighi A, Faridi P, Daneshamouz S, Mohagheghzadeh A. A review on the management of migraine in the Avicenna's Canon of Medicine. *Neurol Sci*. 2016; 37(3): 471-478.
[36] Benemei S, De Cesaris F, Fusi C, Rossi E, Lupi C, Geppetti P. TRPA1 and other TRP channels in migraine. *J Headache Pain*. 2013; Article ID 3844362.
[37] Bernstein C, Burstein R. Sensitization of the trigeminovascular pathway: perspective and implications to migraine pathophysiology. *J Clin Neurol*. 2012; 8(2): 89-99.
[38] Rakhshandah H, Hosseini M, Dolati K. Hypnotic effect of *Rosa damascena* in mice. *Iran J Pharm Res*. 2010; 3(3): 181-185.
[39] Jafarpour M, Yousefi G, Hamedi A, Shariat A, Salehi A, Heydari M. Effect of a traditional syrup from *Citrus medica* L. fruit juice on migraine headache: A randomized double blind placebo controlled clinical trial. *J Ethnopharmacol*. 2016; 179: 170-176.
[40] Gharabaghi PM, Tabatabei F, Fard SA, Sayyah-Melli M, Del Azar EOA, Khoei SA, Gharabaghi MM, Ghojazadeh M, Mashrabi O. Evaluation of the effect of preemptive administration of *Rosa damascena* extract on post-operative pain in elective cesarean sections. *Iran J Nurs Midwifery Res.* 2011; 5(16): 1950-1955.
[41] Hajhashemi V, Ghannadi A, Hajiloo M. Analgesic and anti-inflammatory effects of *Rosa damascena* hydroalcoholic extract and its essential oil in animal models. *Iran J Pharm Res*. 2010; 9(2): 163-168.
[42] Kim YJ, Lee MS, Yang YS, Hur MH. Self-aromatherapy massage of the abdomen for the reduction of menstrual pain and anxiety during menstruation in nurses: a placebo-controlled clinical trial. *Eur J Integr Med.* 2011; 3(3): 165-168.
[43] Holroyd KA, Penzien DB, Cordingley GE. Propranolol in the management of recurrent migraine: a meta-analytic review. *Headache*. 1991; 31(5): 333-340.