Hypotheses of Traditional Medicine

Camel milk could be helpful in the treatment of asthma

Mohammad Ravaghi [1], Mahdi Yousefi [1], Seyed Mousalreza Hosseini [2], Saeed Zibaee [3], Zohreh Feyzabadi [1], Roshanak Salari [4]*

[1]Department of Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [2]School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [3]Department of Veterinary Research and Biotechnology, Razi Vaccine and Serum Research Institute, Mashhad, Iran. [4]Department of Pharmaceutical Sciences in Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

[*]**Correspondence to:** Roshanak Salari, Department of Pharmaceutical Sciences in Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. E-mail: Salarir@mums.ac.ir.

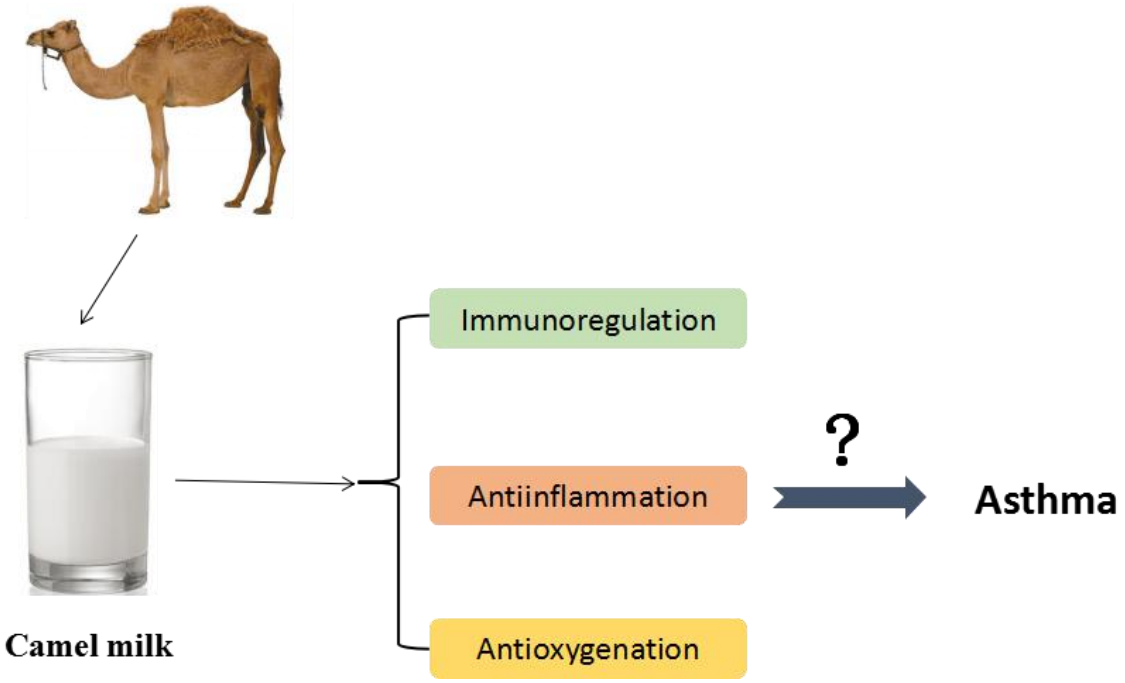
Highlights

This paper proposed a hypothesis that camel milk could be helpful in the treatment of asthma.

Editor's Summary

Food is a double-edged sword of health. On the one hand, cow milk could lead to the occurence of asthma. On the other hand, camel milk could be used to treat asthma via its effects of immunoregulation, antiinflammation and antioxygenation.

.



Citation: Ravaghi M, Yousefi M, Hosseini SM, *et al*. Camel milk could be helpful in the treatment of asthma. Traditional Medicine Research 2018, 3(6): 307-312.
DOI: 10.12032/TMR201814090
Submitted: 10 August 2018, **Accepted:** 20 October 2018, **Online:** 25 October 2018.

Abstract

Asthma is a chronic inflammatory disease with excessive irritability and airway narrowing and inflammation plays an important role in it. There are 300 million asthmatic people in the world currently. Main treatments for asthma include two groups of bronchodilators and inflammation controllers. Researches was continued in order to reach new treatments to reduce drug side effects and treatment-resistant cases or the types associated with weak treatment response. Today, World Health Organization recommends the application of traditional medicine especially in underdeveloped countries because of insufficient health resources and spread of diseases. Iranian traditional medicine (ITM) or Persian medicine is one of the oldest comprehensive traditional medicines with thousands years history which could help us to manage different diseases. The aim of this hypothesis is to investigate the camel milk as a complementary treatment of asthma because this chronic disease is sometimes resistant or response weakly to the treatment. In this article, the administration of camel milk in lung inflammatory diseases was studied by searching the PubMed and Scopus scientific databases. The results of this study indicated that camel milk due to having anti-inflammatory, immunomodulatory and anti-oxidant effects could decrease the levels of inflammatory factors such as tumor necrosis factor α, interleukin-17 (IL-17), IL-6, IL-1B and transforming growth factor-β1 in a human and animal samples with inflammatory diseases. Besides, based on ITM, camel milk was used in treatment patients with asthma. But, clinical studies are needed to validate the effectiveness of camel milk in asthma and its mechanisms.

Keywords: Camel milk, Asthma, Iranian traditional medicine, Camel whey protein

摘要

哮喘是一种慢性炎症性疾病，伴有过度的烦躁和气道狭窄，炎症在其中发挥着重要作用。目前世界上有 3 亿名哮喘患者。目前哮喘的主要治疗方法包括扩张支气管和控制炎症。寻找新的治疗方法的研究还在继续，旨在减少药物的副作用和耐药性的发生以及增强患者对治疗的应答。因为卫生资源不足和疾病的传播，现在世界卫生组织推荐传统医学的应用尤其是在不发达国家。伊朗传统医学（ITM）或波斯医学是最古老的综合性传统医学之一，具有几千年的历史，可以用来治疗不同的疾病。因为有时候哮喘患者对现有的治疗方法耐受或者不应答，本假设旨在探讨骆驼乳作为哮喘的辅助治疗方式。通过检索 PubMed 和 Scopus 数据库来研究骆驼乳对肺部炎症性疾病的疗效。结果表明，骆驼乳具有抗炎、免疫调节和抗氧化的作用，能降低患有炎症性疾病的人和动物体内的炎症因子的水平，例如 TNF-α、IL-17、IL-6，IL-1β和 TGF-β1。此外还发现骆驼乳可以治疗哮喘，但是还需要进一步的临床研究来验证骆驼乳在哮喘中的治疗作用及其机制。

关键词：骆驼乳，哮喘，伊朗传统药物，骆驼乳清蛋白

Abbreviations: ITM, Iranian traditional medicine; TNF-α, Tumor necrosis factor α; TGF-β, Transforming growth factor-β; IL, Interleukin.

Funding: This study was supported by Mashhad University of Medical Sciences Research Council, Mashhad, Iran.
Competing interests: The authors have no conflicts of interest.

Executive Editor: Cui-Hong Zhu.

Background

Asthma is a chronic inflammatory disease with excessive irritability and the airways narrowing that inflammation plays a basic role in its pathophysiology. Currently there are about 300 million asthmatic people around the world and are expected to reach 400 million by 2025. The prevalence of asthma in children is 15% and in adults is 10-12%. This amount is fixed in rich countries, while in developing countries is increasing. The prevalence of treatment-resistant asthma is 5%. Several environmental factors such as air pollution, smoking and infectious factors can lead to lung injury. With the reaction of various kinds of immune cells and mediators, bronchial inflammation and airway obstruction will occur which can lead to clinical demonstrations such as coughing, wheezing and breath shortness. This obstruction is usually reversible, but in some chronic forms of asthma, some part of the obstruction is irreversible. In asthma, as a heterogeneous disorder, cells such as TH1, TH2, TH17, T regulators, neutrophils, macrophages, dendritic cells, epithelial cells and smooth muscle cells of airways, produce cytokines related to the disease, which their increasing level in the asthma clinical samples is recognized [1, 2].

Today, World Health Organization recommends the application of traditional medicine especially in underdeveloped countries because of insufficient health resources and spread of diseases [3]. Iranian traditional medicine (ITM) or Persian medicine is one of the oldest comprehensive traditional medicines with thousands years history which has been founded by many great scientists from countries like Greece, Egypt, India, and China [4-6]. ITM is also called temperamental medicine. Temperament was meant the dominant quality of the composite objects and it was made of the interaction of four basic elements (hot, cold, wet, and dry). Temperament was an important factor to maintain the body health of individuals [7]. ITM have different theoretical and practical solutions in diagnosis, prevention, and treatment of diseases which is provided by Persian physicians, such as Avicenna (980 A.D.-1037 A.D.), Zakariya al-Razi (864 A.D.-930 A.D.), Seyed Esmail Jorjani (1042 A.D.-1137 A.D.), and others [8]. Nutrition and diet is one of the major principles of this approaches [9]. Generally in ITM, every milk has three components; water, fat and cheese components. Compared to other milks, camel milk has the most water component and the lowest fat and cheese components. The mechanisms of the effect of camel milk on asthma treatment are mentioned only in some Iranian traditional texts while in most references, only the usefulness of camel milk, without its mechanisms of action, is mentioned in the treatment of asthma. In ITM, Avicenna believed that camel milk is more compatible than other milk for humans [10].

Main treatments for asthma include two groups of drugs, bronchodilators and inflammation controllers. Bronchodilators include β2 agonists, anticholinergics, and theophylline as well as inflammation controllers include inhalation, edible corticosteroids, anti-leukotrienes, chromones and anti-IgE antibodies, which help to quickly improve the disease symptoms and control inflammation. From new approaches, treatment with antibodies which block interleukin (IL) 9, 4, and 5 can decrease the call of inflammatory cells to airways [11]. Based on the need to use long-term and high-dose corticosteroids in the disease, which may lead to these drugs' side effects. It seems that the use of camel milk could be helpful. In this regard, anti-inflammatory effects of camel milk were searched by the words "Camel milk (CM)", "Asthma", "Iranian traditional medicine (ITM)" and "Camel whey proteins (CWP)" in the PubMed and Scopus scientific databases.

The facts based on study

Many human and animal studies have verified the anti-inflammatory, immunomodulatory and antioxidant properties of camel milk. We will study the available documentation regarding the complementary administration of camel milk in the asthma treatment.

1. In a study by Mohamed WA, *et al.* on hepatitis C patients, camel milk raised the total antioxidant capacity and vitamin D, while reducing tumor necrosis factor α (TNF-α) and transforming growth factor-β (TGF-β) [12].
2. Also it was effective in the treatment of autism as a nutritional supplement with anti-oxidant features [13].
3. Tereza, *et al.,* reported the importance of camel milk in severe cough treatment. The camel milk has anti-inflammatory and anti-oxidant features and is effective in controlling diabetes, liver and colon damages [14].
4. In a study by Arab HH, *et al*., on mice which suffer from colitis, camel milk decreased the levels of TNF-α cytokines. On the other hand, it decreased the leukocytes influx into colon tissues and restrained colon cells' apoptosis in colon cells and then led to decrease oxidative stress [14].
5. Zhu WW, *et al*., stated that camel milk in mice by acute respiratory distress syndrome led to decrease TNF-α and IL-1B and oxidative stress markers (with anti-inflammatory and anti-oxidant properties) [15].
6. In another similar study, camel milk peptide had a strong antioxidant potential that reduced the effect of free oxygen radicals, so it is useful in wound healing [16].
7. In the animal study done by Soleiman MM, *et al*., on pathogenicity made by Escherichia coli and Staphylococcus aureus, the camel milk decreased the increased levels of IL-6 and TGF-β and controlled the inflammation and apoptosis [17].
8. In mice treated with gentamicin, the anti-oxidant, hepatoprotective and nephroprotective effects of camel milk have been diagnosed [18].
9. In addition, in the past, camel milk has also been used in the Asian and African continents to treat dyspnea and asthma [19].
10. Traditionally, camel milk was used in dyspnea [20], asthma [8, 21, 22] and tuberculosis [6]. It also could increase appetite and sexual desire [20, 21, 23]. It was nutritious [20, 21, 22] and diuretic [20, 21] and had

positive effects on skin beauty [20], teeth growth facilitating [22], maintaining the health of the elderly individuals [24], improving the renal and eye vision weakness [8-20], hepatitis [13] and obstruction of the liver [6], seizure [25], leprosy [26] and hemorrhoids [21], swelling and obstruction of the spleen, gastric ulcer and swelling, uterine and gastrointestinal cancers, stiff swollen uterus, bladder ulcers and cystitis, eczema, depression and phobia [6]. It was recommended to drink approximately 70 cc to 2400 cc daily, which should be slowly increase the amount of drink [20, 27]. It was contraindicated in fever and may have complications like diarrhea, constipation, stomach illness and thirst [22].

Hypothesis

Regarding the anti-inflammatory, anti-oxidant and ITM features of camel milk, can it be used as complementary treatment of asthma?

Evaluation of the hypothesis

Inflammation plays an important role in the asthma pathophysiology. Inflammation is associated with various immune cells' reaction and different mediators, which finally leads to asthma pathophysiology. Types of cytokines play a role in asthma, pathogenesis of which are lymphokines, pre-inflammatory cytokines, growth factors and chemokines [1]. On the other hand, the balance between free radicals and antioxidants is an important factor in maintaining health. There is strong evidence that this balance is disrupted in some diseases, including asthma. It is specified that kinds of reactive oxygen play an important role in airways inflammation and determining the severity of asthma. In addition, the antioxidant defense system is decreased in asthma and strong oxidative stress is made in asthma due to increased oxidant forces and decreased antioxidant capacity [28].

In general, lung tissue is in constant contact with high levels of oxygen and blood, which put it at risk of tissue damage by oxidants. Oxidative stress can be due to inhalation oxidants from the outside or increase of the production of reactive oxygen species (ROS) level inside the body. For example, various environmental factors such as air pollution, smoking and infectious factors can lead to the production of free radicals and inflammatory cells such as eosinophils, neutrophils, monocytes and active macrophage, which further lead to cellular damage and lung injury via oxygen metabolism pathway. The resident cells such as smooth muscle cells and epithelial cells can produce ROS inside the body. These reactive oxygen can attack proteins and fats and lead to oxidation of proteins, DNA and lipids, and tissue damage and change of their structure. Tissue damage, in turn, can also produce other active oxygen species. Thus, the complicated reaction between cells and mediators leads to ROS increased production which is accompanied with severity of airways increased response [28].

Camel milk has some differences compared to other mammal's milk. It contains low cholesterol and sugar and many minerals such as potassium, sodium, iron, copper, zinc and magnesium, as well as high levels of vitamin C, on the other hand, it has natural antioxidants [19]. Compared with cow's milk, camel milk has more protein and V-protein (lactoferrin and immunoglobulin). In some inflammatory diseases, such as hepatitis, allergies, lactose intolerance and liver damages induced by alcohol, the benefits of camel milk can be related to important immunological components such as lysozyme, lactoferrin, lactoperoxidase, and etc. Besides this, antibodies of camel milk have a specific structure and function which may result in therapeutic benefits with the mechanism of immune system regulation [29]. Camels unlike other mammals, produce specific antibodies that don't have any light chain and can be fully bonded to the antigen. Antibodies with heavy chain are in microorganisms and have high stability and solubility. These camel milk's IgGs are very suitable to produce larger molecules [30]. These immunoglobulins have the ability to easily flux in to cells and tissues, while human immunoglobulins are not so. These antibodies due to small size, which is one tenth of the size of human antibodies, can easily flux in to the camel milk and brain blood barrier and can also be easily absorbed in the digestive system to the general circulation system. In addition, the immunoglobulin G level in camel milk is 1.6 mg / ml, which is higher than other mammals and even humans. On the other hand, the correlation between the deficiency of immunoglobulin G and asthma and food allergy has been diagnosed. Regarding this, it seems that the presence of these antibodies and other important biological components and their derivatives in the camel milk, has made it unique treatment choice [31].

ITM was based on humoral theory or in the other name "khelty" theory. In this theory, four humors consists of phlegm "balgham" (with cold and wet qualities), blood "dam" (with hot and wet qualities), yellow bile "safra" (with hot and dry qualities), and black bile "soda" (with cold and dry qualities) play important roles in providing the human health. The humor is a substance which is produced by the digestive system [32, 33]. Maintaining health is dependent on the balance of these humors and abnormality in humors can lead to sickness or dystemperament which called "soo-e-mizaj" [34]. Jorjani (1042 A.D.-1137 A.D.) described etiology of asthma or "Rabv" in "Zakhireh-ye Khwarazm shahi" text. He believed that asthma etiologies were congenital and non-congenital or acquired. In congenital mode, the lung and thorax are created tight congenitally. In acquired condition asthma occurs because of sticky phlegm in respiratory airways, inflammation of the lungs, swelling of other organs like stomach and liver that prevent proper expansion of diaphragm, presence of ascites that cause shortness of breath, improper temperament such as dryness or cold temper of the lungs, rise of harmful substances towards the lungs in hot dystemperments and presence of smoke or concentrated "reeh" (current flow in the body, which acts like ''wind") in the lung [24, 35].

In ITM, camel milk has the following properties:

1. Polishing effect "Jala": It means that camel milk

separates and cleans the sticky moisture (like phlegm, etc.) from the member surface [22, 22, 24].
2. Washing effect "Ghasl": It means that camel milk rinses the surface of the organ with liquid moisture [24].
3. Strengthen effect "Taghviat": It means that camel milk reinforces the organs and prevents substances entry into the organs [20-22, 25].
4. Opening effect "Mofatteh": It means that camel milk open the closed ducts and cavities [20, 21, 25].

Therefore, according to ITM or Persian medicine, the camel milk can remove the sticky phlegm in the respiratory airways, prevent harmful substances entry into the lungs and improve the airways stenosis.

Regarding the above-mentioned cases, this study can be performed as a random clinical trial with control and intervention groups. In the control group, common treatments (corticosteroid and inhalation beta-agonist) and cow milk as a placebo and in the intervention group, pasteurized camel milk should be prescribed in addition to the common treatments. The spirometric indices (FEV1, FVC, and FEV1 to FVC ratio) and the questionnaire of asthma control test should be completed before and after the intervention and the results be compared using statistical tests.

Conclusion

As stated above, asthma is an inflammatory disease in which inflammation plays a key role. On the other hand, it is specified that ROS also play a key role in airways inflammation and asthma severity determination. Different studies reported anti-inflammatory, anti-oxidant and immunomodulatory effects of camel milk and its proteins in reduction of the inflammatory cytokines such as TNF-a, vascular endothelial growth factor, IL-17, IL-6, IL-1B and TGF-β1 in diverse inflammatory diseases in human and animal samples [12, 15, 17, 36]. Due to the natural nature of camel milk and its properties, and based on traditional properties of camel milk, it seems to be effective in asthma treatment, although this claim needs more extensive clinical studies in this field.

References

1. Ye Q, He XO, D'Urzo A. A Review on the safety and efficacy of inhaled corticosteroids in the management of ssthma. Pulm Ther 2017, 3: 1-18.
2. Bahrami Mahne S, Mahdaviani SA, Rezaei N. Role of the immune cells, mediators and cytokines in pathogrnrsis of asthma: a review article. TUMJ. 2017, 72: 273-285.
3. World Health Organization. WHO traditional Medicine Strategy: 2014-2023. Geneva: World Health Organization; 2013.
4. Gorji A, Khaleghi Ghadiri M. History of epilepsy in Medieval Iranian medicine. Neurosci Biobehav Rev 2001, 25: 455-461.
5. Brown E. Islamic Medicine. 5th ed. Tehran: Scientific and Cultural Publication; 1992.
6. Emtiazy M, Keshavarz M, Khodadoost M, *et al*. Relation between body humors and hypercholesterolemia: An Iranian traditional medicine perspective based on the teaching of Avicenna. Iranian Red Crescent Med J 2012, 14: 133.
7. Moradi H, Minaii B, Nikbakht Nasrabadi A, *et al*. Avicenna viewpoint about health preservation through healthy nutrition principles. Iran J Public Health 2013, 42: 220-221.
8. Hosseini SM, Zibaee S, Yousefi M, *et al*. Camel's milk: nutrition and health perspectives of Iranian traditional medicine. Int J Pediatr 2015, 3: 915-920.
9. Borhani M, Khoshzaban F, Jodeiri B, *et al*. Diet and food in Iranian traditional medicine: hints for further research. Inter J Prevent Med 2014, 5:1480-1481.
10. Avicenna H. "Al-Qanun fit-tib". Beirut, Lebanon: Alaalami Beirut library Press 2005.
11. "GINA report," Global Strategy for Asthma Management and Prevention, 2017, http://www.ginasthma.org/.
12. Mohamed WA, Schaalan MF, El-Abhar HS. Camel milk: potential utility as an adjunctive therapy to Peg-IFN/RBV in HCV-4 infected patients in Egypt. Nutr Cancer 2015, 67:1305-1313.
13. Al-Ayadhi LY, Elamin NE. Camel milk as a potential therapy as an antioxidant in autism spectrum disorder (ASD). Evid Based Complement Alternat Med 2013, 2013: 602834.
14. Arab HH, Salama SA, Eid AH, *et al*. Camel's milk ameliorates TNBS-induced colitis in rats via downregulation of inflammatory cytokines and oxidative stress. Food Chem Toxicol 2014, 69: 294-302.
15. Zhu WW, Kong GQ, Ma MM, *et al*. Short communication: camel milk ameliorates inflammatory responses and oxidative stress and downregulates mitogen-activated protein kinase signaling pathways in lipopolysaccharide-induced acute respiratory distress syndrome in rats. J Dairy Sci 2016, 99: 53-56.
16. Ebaid H, Abdel-salam B, Hassan I, *et al*. Camel milk peptide improves wound healing in diabetic rats by orchestrating the redox status and immune response. Lipids Health Dis 2015, 14:132.
17. Soliman MM, Hassan MY, Mostafa SA, *et al*. Protective effects of camel milk against pathogenicity induced by Escherichia coli and Staphylococcus aureus in Wistar rats. Mol Med Rep 2015, 12: 8306-8312.
18. Al-Asmari AK, Abbasmanthiri R, Al-Elewi AM, *et al*.. Camel milk beneficial effects on treating gentamicin induced alterations in rats. J Toxicol 2014, 2014: 917608.
19. Zibaee S, Hosseini SM, Yousefi M, *et al*. Nutritional and therapeutic characteristics of camel milk in children: a systematic review. Electron physician 2015, 7: 1523-1528.
20. Aghili Khorasani MH. "Makhzan -ol- Advieh". Tehran-iran: Bavardaran Institute; 2004.
21. Mo'men H. *Tohfat-ul-mo'menin* Tehran-iran:

Nashr-e Shahr; 2011.
22. M AK. *Aksir Azam*. Tehran-iran: Institute of Medicine Studies and Islamic medicine press; 2004.
23. Rhazes. *Al-Hawi: The Continence*. Tehran, Iran: Alhavi Pharmaceutical Company; 1990.
24. Jarjani HSI. *Zakhireye Kharazmshahi*. Tehran, Iran: Academy of Medical Sciences; 1387.
25. Razi, Muhammad ibn Zakariyya, "Khawi, S al-ashya" (Properties of Things). Qom-iran1999.
26. Ahvazi A. Kamil al-Sanate al-Tebie. Translated by Ghaffari MK. In: MK TbG, ed. Tehran, Iran: The Institute of Islamic Studies, University of Tehran-McGill University; 2009.
27. Aghili Khorasani MH. "Qarabadin Kbir". Tehran-iran: University of Medical Sciences; 2005.
28. Sahiner UM, Birben E, Erzurum S, *et al*. Oxidative Stress in Asthma. World Allergy Organ J. 2011, 4: 151-158.
29. Mansour A, Nassan M, Saleh OM, *et al*. Protective effect of camel milk as anti-diabetic supplement: biochemical, molecular and immunohistochemical study. AJTCAM 2017, 14: 108-119.
30. Dubey US, Lal M, Mittal A, *et al*. Therapurtic potential of camel milk. Emir J Food Agric 2016, 28: 164-176.
31. Jilo K. Chemical composition and medicinal values of camel milk. IJRSB 2016, 4: 13-25.
32. Nimrouzi M, Mahbodi A, Jaladat AM, *et al*. Hijamat in traditional persian medicine: risks and benefi ts. J Evid Based Complement Altern Med 2014, 19: 128-136.
33. Zargaran A, Zarshenas MM, Karimi A, *et al*. Management of stroke as described by Ibn Sina (Avicenna) in the Canon of Medicine. Int J Cardiol 2013; 169: 233-237.
34. Feyzabadi Z, Jafari F, Feizabadi PS, *et al*. Insomnia in Iranian traditional medicine. Iran Red Crescent Med J 2014, 16:e15981.
35. Latifi SA, Minaiee B, Kamalinejad M, *et al*. Complementary treatment in chronic pelvic pain syndrome: a case report study. Iran Red Crescent Med J 2014, 16: e13681.
36. Alhaider AA, Abdel Gader AG, Almeshaal N, *et al*. Camel milk inhibits inflammatory angiogenesis via downregulation of proangiogenic and proinflammatory cytokines in mice. APMIS. 2014, 122: 599-607.