REPORT

Renovation of a traditional *Ergh-al-Nassa* pill (*Hab*) to a standard Pharmaceutical molded tablet

Arman Zargaran[1,2,3], Saeid Daneshamouz[1,4], Gholamreza Kordafshari[6] and Abdolali Mohagheghzadeh[3,4]

[1]Pharmaceutical Sciences Research Center and Department of Traditional Pharmacy (Phytopharmaceuticals), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Traditional Pharmacy, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3]Research Office for the History of Persian Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[5]Department of Traditional Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract: The *Ergh-al-Nassa* pill (*Hab*) is a traditional combination suggested as one of the most effective preparations useful for treatment of sciatica. Although traditional preparations can be applied as new therapeutic drugs for investigations and clinical trials, they need to be reformulated to achieve pharmacopoeial standards for modern medicine. In this research, based on seven traditional Persian pharmacopeias for *Ergh-al-NassaHab*, nine different molded tablets were reformulated. Each formulation comprised the same amount of colchicum, ginger, aloe and yellow myrobalan fruit. Swe*et al*mond oil had to be added in the maximum amount needed to be absorbed by the yellow myrobalan fruit according to its particle size (30-40 mesh sizes). The studies were performed in order to optimize the formulation process according to the role of three levels in particle size of the herbal ingredients (60-70, 80-100, 100-150 mesh sizes) and three levels of initial water for granulation. The molded tablets were evaluated according to standard quality controls for tablets (mass uniformity, LOD, hardness, friability, and disintegration time at 20 and 30 min). Myrobalan powdered to 30-40 mesh size absorbed the maximum amount of swe*et al*mond oil (1:0.75 w/v). The best formulations occurred when the particle size of colchicum, ginger, and aloe was 60-70 mesh size with an initial moisture content of 0.47 ml per 1g of dried powder. The outcome of this research is a pharmaceutical standardized formulation from the traditional *Ergh-al-Nassa* pill which can be suggested as a sample drug discovery based on traditional knowledge.

Keywords: Traditional Pharmacy, *Ergh-al-Nassa,* Sciatica, pharmaceutical biology, Persia.

INTRODUCTION

Sciatica is one of the most common variations of low back pain (LBP). It is known by various terms, including nerve root entrapment, nerve root pain, radiculopathy and lumbosacral radicular syndrome (Konstantinou and Dunn, 2008). Although many therapeutic approaches are used to manage this disorder, such as spinal manipulative therapy (Rubinstein, 2012) and drugs such as NSAIDs, opioid analgesics, muscle relaxants, anticonvulsants, corticosteroids and antidepressants (Pinto, 2012) etc., no complete and definite treatment has yet been found, and recovery is less frequent than expected. Especially prolonged disability and further related problems can be seen in severe types (Konstantinou and Dunn, 2008; Tubach *et al*., 2004). For this reason, it is good subject for investigation to find and introduce new potential drugs.

Regarding, Traditional systems of medicine whole around the world are one of the potential sources to find new approaches to treat and drugs. The popularity of traditional, complementary, and alternative medicines is on the rise all around the world. The main reasons for this phenomenon can be categorized according to the following factors: a) the positive valuation of traditional approaches, b) the often ineffectiveness and occurrence of side effects with current medicine, c) concern about communication with physicians, d) the more economical cost of traditional medicines, and e) the availability of complementary medicine (Vincent and Furnham, 1996).

Amongvarious kinds of traditional and complementary systems of medicine, Medieval Persian medicine, also known by other names such as humoral medicine, Unani medicine, or Islamic medicine, is one important traditional approach to medicine (Leslie, 1976). The origin of this paradigm of medicine dates back to ancient Persia and Greece (Modanlou, 2008). In the first centuries of the Islamic period, Muslims, especially Persians, gathered the ancient knowledge of medicine from great civilizations of the past and promoted it throughout medieval times (Zargaran *et al*., 2012). Although this

**Corresponding author:* e-mail: daneshamuz@sums.ac.ir

medical approach is still used by traditional medical practitioners in the east, especially in Iran and India, and has been found effective (Lodha and Bagga, 2000; Asefzadeh and Sameefar, 2001), more scientific evaluations and standards are still needed in order for it to be accepted and used as a modern medical approach (Abolhassani *et al*., 2012).

In this regard, this research tried to evaluate one Persian traditional dosage form, namely *Ergh-al-NassaHab*, by current pharmaceutical aspects and standards. *Hab* is the common name of a traditional, spherical-shaped pill similar to a molded tablet, which is formed by hand (hand rolling) with natural binders. *Ergh-al-Nassa* means Sciatica (Rhazes, 906/2008; Minaee *et al*., 2012) and *Ergh-al-NassaHab* is a pill for Sciatica. *Ergh-al-Nassa Hab* is used successfully by traditional practitioners based on traditional knowledge in Iran. By standardizing the formulation in this research, it can be evaluated in clinical trials and further investigations in order to reach a standard formulation.

To reach a complete formulation of *Ergh-al-Nassa Hab*, some important traditional pharmacopeia and other medical manuscripts as well as recent texts about traditional Persian medicine were considered. The final formulation presented is based on these documents.

Although the traditional procedure for preparing *Ergh-al-Nassa Hab* (pill) was found in these resources, researchers followed current concepts of pharmaceutical standards to develop a standard procedure for preparing these pills. In this research, *Ergh-al-Nassa Hab* was investigated pharmaceutically to evaluate how component specificity (particle size and moisture content) influences physical nature and standard pharmaceutical controls.

MATERIALS AND METHODS

Reviewing traditional Persian manuscripts to find the formula:

The manuscripts used to find the definition and preparation method of *Ergh-al-Nassa Hab* were *Qarabadin Kabir* (originally written in the 18th century AD by Aghili Shirazi) (AghiliShirazi, 1772/1855), *Qarabadin Salehi* (originally written in 1765 AD by GhaeniHeravi) (Ghaeni Heravi, 1765/1873), *Zakhireh Kharazmshahi*(originally written in 1110 AD by E. Jorjani) (Jorjani, 1110/1637), *Mansouri fi Teb* (originally written circa 906 AD by Rhazes) (Rhazes, 906/2008), *Qarabadin Shafaei* (originally written prior to 1627 AD by M. Shafaei) (Shafaei, 1627/1889), *Qarabadin Azam* (originally written in 1852 AD by Hakim Mohammad Azam Khan) (Azam Khan, 1852/1884), *Qarabadin Mazhari* (originally written in 1793 AD by Hakim Mazhar Ali ibn Tahour Ali [Tahour]) (Tahour Ali, 1793) and *Tohfat al Momenin* (originally written in 1669 AD by Hakim Moemen Tonekaboni) (Tonkaboni, 1669/2007). According to the mentioned traditional resources, the *Ergh-al-NassaHab* pills were comprised of ginger, autumn crocus, yellow myrobalan fruit, aloe, and almond oil as listed in table 1. The procedure used in this research as well as the type and amount of ingredients were similar to that in the traditional texts.

Ergh-al-Nassa Hab (pill) preparation according to the traditional pharmacopeias

According to the selected traditional Persian resources (*Qarabadins*), the procedure for preparing *Ergh-al-NassaHab*, the type of herbal ingredients used, and the amount of the components were as mentioned below:

Equal amounts of four herbal powders, comprising autumn crocus, aloe dry extract, yellow myrobalan fruit (as the main components), and ginger (for decreasing adverse gastric effects of autumn crocus) are used. The autumn crocus, aloe dry extract, and ginger should be crushed and powdered using a mortar and pestle. The yellow myrobalan fruit should be crushed separately and mixed to absorption with almond oil. The components must be mixed thoroughly and wetted using water to form slurry, then shaped or molded.

It must be noted that some parameters were unclear in the traditional manuscripts and needed to be developed: 1st) the mesh size of the ingredient herbal powders, 2nd) the amount of almond oil and 3rd) the amount of water needed to prepare a slurry suitable to molding and easily removable from the mold while maintaining the best stability of form.

In this regard, particle size reduction of the herbal ingredients was obtained using an electrical mortar and pestle (RM200, Retsch, Germany). The powders of autumn crocus, aloe dry extract, and ginger were produced in three levels (60-70, 80-100, 100-150 mesh size range). Also, a medium particle size of yellow myrobalan fruit powder was used as reported elsewhere (Zargaran, 2010). According to the preparation process, the almond oil must be added drop wise during trituration to the yellow myrobalan until it is completely absorbed. In this process, the role of particle size and the amount of almond oil were examined. Additionally, the amount of water needed to prepare a good slurry suitable to molding and easily removable from the mold while maintaining the best form stability without any compression forces was examined. Finally, by changing the unclear parameters, nine various formulations were produced to arrive at the best formula, as is listed in table 2.

The prepared slurries were molded in round molds (20 mm in diameter and 5 mm thickness) to form traditional pills. The molded tablets were allowed to dry in a room with a controlled temperature of between 25 and 27 degrees C. At intervals of 24 and 48 hours, the pills were examined by removing them from the molds and other pharmaceutical tests were performed.

Pharmaceutical quality control

At first, to determine the flow of ingredient powders, Carr index and then Hausner ratio of powder of the mixture of autumn crocus, aloe dry extract, and ginger in different particle size ranges are measured by following formulations (Baviskar *et al*., 2014):

$$C = 100\frac{V_T - V_B}{V_T}$$

C: Carr index, V_B: the volume of bulk powder occupied, V_T: the volume of tapped powder occupied

$$H = \rho_T/\rho_B$$

H: Hausnerratio ρ_B: bulk density of the powder, ρ_T: tapped bulk density of the powder

To calculate the densities, we use below formulations:

Bulk density (gm/cm3) = W/V0

Tapped density (gm/cm3) = W/Vf

W: weight of powder; V: volume occupied by powder

Measuring the volume of powders was done using an scaled cylinder.

After the formulations of pills were prepared, pharmaceutical quality control tests were done on each group based on the United States Pharmacopoeia (USP32-F 27, 2010).

Mass uniformity

After drying the products in the mold to produce the pills, 36 pills of each formulation were weighed separately (digital balance, BL 120 s, Sartorius, Germany), and the average weight, standard deviation, and coefficient of variation were calculated.

Loss on drying (LOD) after 24 and 48 hrs

The moisture content of the pills was examined after intervals of 24 and 48 hrs of molding. Ten pills of each formula were weighed, then carefully powdered by mortar and pestle and dried in an oven (Reihan Teb, Iran) set at 105°C for two hours. After that, the powder of each formula was weighed and the previous and final weights were compared. The percentage of weight difference was considered as LOD.

Hardness test

The hardness often pills of each formula was determined using Erweka Hardness tester (TB 24, Erweka, Germany).

Friability test

Ten pills of each formula were weighed, then put in the friability tester (Friabilitor, Iran) and rotated at 25 rpm for four minutes. After completing the period, the pills were weighed again and the percentage of weight differences was reported as friability criterion.

Disintegration test

Six pills of each formula were put in the cylinders of the disintegration tester (Zt 34, Erweka, Germany) filled with distillated water (pH=6.5) at 37°C.

Statistical calculations

The means in each group were compared statistically according to ANOVA test using SPSS 16 for windows.

RESULTS

According to the procedure, the maximum amount of almond oil that could be absorbed by yellow myrobalan varied due to the particle size; in this research the medium size (mesh size range 30-40) of yellow myrobalan fruit powder had the maximum ability to absorb almond oil (1.33g for each ml of almond oil) as reported in table 2. Carr index and Hausner ratio of powders are shown in the table 3. The results show group A formulations (with mesh particle size range 60-70) have better and in range flow in comprising with others. Carr index between 5 to 15 and Hausner ratio under 1.25 are mentioned as excellent flowability.

The results of pharmaceutical tests are summarized in table 4. Photographs of the *Ergh-al-Nassa* molded tablets are shown in fig. 1 to 3. The C-2 and C-3 formulations formed without suitable strength and were therefore omitted from the tests.

DISCUSSION

Molded tablets include active ingredients and require suitable excipients (binder and disintegrant agent) to shape a solid dosage form using a mold without any compression force (Lieberman *et al*., 1989). It seems traditional herbal pills are too similar to molded tablets where synthetic and potent ingredients are replaced by natural components. *Ergh-al-NassaHab* (molded tablets) were formed with suitable strength only by using natural ingredients, binders, and disintegrants without any compression forces. In exploring the role of components in *Ergh-al-NassaHab* as a molded tablet, it seems that yellow myrobalan fruit could be a binder due to the presence of tannins that act as an astringent agent (Li *et al*., 2011). On the other hand, aloe extract might have a disintegration role, because it can be swelled with water (Kim *et al*., 2009). It also acts as a binder, due to the presence of mucilage (Okorie and Nwachukwu, 2011). It must be noted that the astringent effect of yellow myrobalan fruit can reduce the laxative effect of aloe. Autumn crocus could be the most important ingredient of this pill, because it contains colchicine as a potent analgesic ingredient (Ellington *et al*., 2003). The analgesic effect of ginger is approved (Terry *et al*., 2011), and also has a gastro-protective effect (Alia *et al*., 2008). Its traditional role can also be approved in the formulation.

The role of particle size of herbal powders in the Ergh-al-NassaHab (pill)

As powder characteristics could influence the final molded tablet, the role of particle size of the grinded herbal powder on flow, bulk density, content uniformity, and exposed surface area was considered. Furthermore, non-soluble herbal powders could influence the quality and adherence with a binder in forming mechanical strength and finally production, hardness and disintegration of molded pills.

The C-group (100-150 mesh size) was too fine to produce suitable mass in high humidity and formed viscose granules that could not be molded. These fine particles entrapped water even after 48 hours of drying and might have a negative influence on drying and chemical stability. They had high friability and unsuitable hardness, although they did have a desirable disintegration time.

Fig. 1: Ergh al Nassa Hab, "A" series formulations, Ginger, Aloe, Autumn crocus (Mesh size 60-70), comprised of Ginger: Aloe: Autumn crocus: Yellow myrobalan Fruit: Almond oil (1.6:1.6:1.6:1.6:1.2), from left to right: A-1, A-2 and A-3 (containing 26.3, 36.8, 47.4 ml of water /100g of powder)

In the B-group (80-100 mesh size), the primary humidity for granule preparation was increased, resulting in a higher water content remaining even after 48 hours of drying. This result may be due to the high surface area and the high surface tension of the small particle size that could retain water. The pills had high mechanical strength with suitable hardness and friability but undesirably slow disintegration time. It was assumed, due to the small particle size of the herbal powder, that having close contact using aloe resin would have binding effects that refuse water penetration to the core of the pill and low expansion for disintegration.

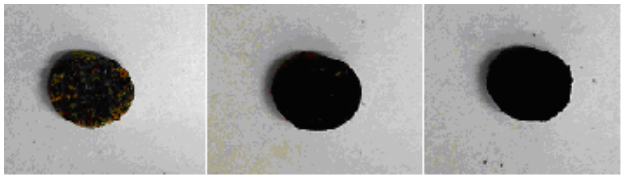

Fig. 2: Ergh al Nassa Hab, "B" series formulations, Ginger, Aloe, Autumn crocus (Mesh size 80-100), comprised of Ginger: Aloe: Autumn crocus: Yellow myrobalan Fruit: Almond oil (1.6:1.6:1.6:1.6:1.2), from left to right: B-1, B-2 and B-3 (containing 26.3, 36.8, 47.4 ml of water /100g of powder)

In the A-group (60-70 mesh size), however, to which water was added for granulation, the water retained after drying was in such a state as to show suitable water migration out of the molded granules. The binding capability could keep the herbal powder granules closely bound to each other and give the tablets suitable mechanical strength and good friability (A2 and A3). In these formulations the greater particle size of aloe resin produced binding and good disintegration due to its expanding capability and suitable disintegrating time.

The role of water amount in the formulations of Ergh-al-NassaHab(pill)

In the traditional resources, the necessary amount of water was not noted clearly; thus according to the particle size and content of powdered herbals, the needed amount of binding solution had to be obtained.

Fig. 3: Ergh al Nassa Hab, Group "C" formulations, Ginger, Aloe, Autumn crocus (Mesh size 100-150), comprised of Ginger: Aloe: Autumn crocus: Yellow myrobalan Fruit: Almond oil (1.6:1.6:1.6:1.6:1.2), from left to right: C-1, C-2 (containing 26.3, 36.8 ml of water /100g of powder)

In some formulations of pills, poor strength in molded pills was observed; thus the herbal content could not be attached carefully. Although aloe has the binding role in these formulations, because of the low water content, they had not enough strength in the adhering bridge. Since no compression forces were applied to the molded pill, the binding components in these pills had no capability to dry binding (as occurred in direct compression formulation).

Liberman and coworkers demonstrated if an insufficient amount of water was added, it only wet the powder to form a film on the surface and make some bridge to attach the granules (Lieberman *et al*., 1989). Surface tension and negative capillary pressure in these bridges could form the adhesion forces, and the "Pendular" state could form although it had low mechanical strength. By adding water, the separated bridges merged together to form "Funicular" state, and more granule strength formed. As water content was added, the particles adhered to each other closely, due to the surface tension and negative capillary pressure, to form a "capillary" state that had maximum strength in the wet granules. In this state by hydrating the binder components (e.g. aloe) and increasing the consistency of the binder, forced bridges could connect the herbal powders, even in the absence of compression forces, and the wet mass could be molded. During evaporation of the water, the binder became more viscose and crystallized to

Table 1: The plants and materials, which were used to prepare *Ergh-al-Nassa Hab* (pill)

Plant	Scientific name	Family	Plant num. *
Ginger	*Zingiberofficinale* L.	Zingiberaceae	13 Pm
Autumn crocus	*Colchicum autumnale* L.	Colchicaceae	26Pm
Yellow myrobalan fruit	*Terminaliachebula* Retz.	Combretaceae	27Pm
Aloe	*Aloe* spp.	Xanthorrhoeaceae	28Pm
Almond oil	*Prunusamygdalus* Batsch.	Rosaceae	From Nikan co.

*These plants are numbered and kept in herbal collection of Shiraz University of Medical Sciences.

Table 2: Formulation design of *Ergh-al-Nassa Hab* (pill), according to the change of mesh size of herbal ingredients and the amount of water needed for granulation

Formulation*	Yellow myrobalan Fruit [Mesh size]	Ginger, Aloe, Autumn crocus [Mesh size]	Granulating water (ml/100g of powder)
A-1	# 30-40	# 60-70	26.3
A-2			36.8
A-3			47.4
B-1	# 30-40	# 80-100	26.3
B-2			36.8
B-3			47.4
C-1	# 30-40	# 100-150	26.3
C-2			36.8
C-3			47.4

* Each pill (in A, B and C formulations) includes: Yellow myrobalan (1g); Fruit Almond oil (0.75ml); Ginger (1g); Aloe (1g); and Autumn crocus (1g)

Table 3: Carr Index and Hausner ratio of the mixture of autumn crocus, aloe dry extract, and ginger in different particle size ranges (the groups of A, B and C formulations)

Formulations	Particle size (Mesh)	Carr Index	Hausner ratio
A	60-70	10	1.2
B	80-100	13	1.7
C	100-150	19	2.3

Table 4: Pharmaceutical quality control results of *Ergh-al-NassaHab* (pill) for nine prepared formulations *****

Formulations**,***	Mean weight (g) ±SD(n=36)	LOD %		Disintegrated pills (n=6)		Hardness ±SD(n=6)	Friability (%)
		24hr	48hr	20min	30min		
A-1	0.20±0.018	9.30	8.40	4	6	3.19±0.80	6.0
A-2	0.22±0.019	8.30	7.50	3	6	4.85±0.12	1.4
A-3	0.24±0.016	4.00	3.10	3	6	8.31±0.24	0.5
B-1	0.22±0.011	4.40	4.00	3	5	3.81±0.24	4.3
B-2	0.23±0.008	11.11	8.70	2	3	4.94±0.15	1.3
B-3	0.23±0.017	13.60	12.00	1	1	5.19±0.24	0.9
C-1	0.24±0.025	15.60	10.00	6	6	2.62±0.41	4.0
C-2	0.20±0.018	-	11.00	3	5	4.15±0.23	2.7
C-3	Pills were not formed						

*Each pill (in A, B and C formulations) includes: Yellow myrobalan (1g); Fruit Almond oil (0.75ml); Ginger (1g); Aloe (1g); and Autumn crocus (1g). ** Particle size (mesh size) of Aloe, Autumn crocus and Ginger in "A", "B" and "C" formulations are #60-70; #80-100 and #100-150 respectively. *** Percent of granulation water for "1series", "2 series" and "3series" are 26.3ml; 36.8ml and 47.4ml per 100gram of powder, respectively.

strengthen the granules; thus the molded tablet was released from the mold and passed the friability, hardness, and disintegrating tests. The remaining water was needed for optimum strength and to play a lubricating role.

According to formulation series A, B and C, the more water added (Formulation 1 to 3), the more tablet hardness, and the less in disintegration time as shown in table 4.

If the granules become over-wet (like the C-3 formulation, which had small particle size) the “drop” state with less adhering capability was formed. This state could not be molded easily, and after drying the tablets were too hard to disintegrate easily and showed shrinkage on the surface.

CONCLUSION

In the A-group (60-70 mesh size) formulations, the retained water after drying was in such a state as to show suitable water migration out of the molded granules. The binding capability caused careful and close adherence of the herbal powder granules, which had suitable mechanical strength and good friability (A2 and A3). In these formulations the greater particle size of aloe resin produced binding and good disintegration due to its expanding capability and suitable disintegrating time. The A-3 formulation is in the pharmaceutical tests while disintegrating in 30 minutes, even though pills had to disintegrate in 20 minutes. It is suggested to further investigate and correct this one criterion to formulate this traditional pill. Moreover, determination of the active ingredient of this pill (colchicine) and a dissolution test is the next step to present a final formulation of the *Ergh-al-Nassa* pill that would need further investigation. The standard formulation can be used in clinical trials and pilot industrial studies to present a new traditional formulation for sciatica.

REFERENCES

Abolhassani H, Naseri M and Mahmoudzadeh S (2012). A survey of complementary and alternative medicine in Iran *Chin J Integr Med.*, **18**(6): 409-416.

Aghili Shirazi MHMH (1772/1855). Qarabadin kabir. ostad allah qoli khan qajar publisher, Tehran (lithograph in Persian).

Alia BH, Blundenb G, Taniraa MO and Nemma A (2008). Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): A review of recent research. *Food Chem Toxicol*., **46**: 409-420.

Asefzadeh S and Sameefar F (2001). Traditional healers in the Qazvin region of the Islamic Republic of Iran: A qualitative study. *East Mediterr Health J*., **7**: 544-551.

Azam Khan HM (1852/1884). Qarabadin Azam. Matba Nezami Kanpour, Delhi (lithograph in Persian).

Baviskar D, Rajput A, Bare K, Biranwar Y, Chaudhari H, Narkhede D and Jain D (2014). Development and *in vitro* characterization of mebendazole delayed release tablet for colonic drug delivery. *Pak J Pharm Sci.*, **27**: 249-253.

Ellington E, Bastida J, Viladomat F and Codina C (2003). Supercritical carbon dioxide extraction of colchicine and related alkaloids from seeds of *Colchicum autumnale* L. *Phytochem Anal.*, **14**: 164-169.

Ghaeni Heravi MS (1765/1873). Qarabadin Salehi. Alijah Ezatva Saadat Publisher, Tehran (lithograph in Persian).

Jorjani E (1110/1637). Zakhireh Kharazmshahi. Original manuscript, kept in documents center of Research Office for the History of Persian Medicine, Shiraz, Iran.

Kim SA, Baek JH and Lee SY (2009). Dewatering impregnation soaking; *Aloe vera* gel; Fourier transform infrared spectroscopy; Scanning electron microscopy. *Food Engineering Progress*, **13**: 24-31.

Konstantinou K and Dunn KM (2008). Sciatica: Review of epidemiological studies and prevalence estimates. *Spine (Phila Pa 1976)*, **33**: 2464-2472.

Leslie CM (1976). Asian medical systems: A comparative study. University of California Press, California, pp.8, 149.

Li K, Diao Y, Zhang H, Wang S, Zhang Z, Yu B, *et al* (2011). Tannin extracts from immature fruits of *Terminaliachebula* Fructus Retz. promote cutaneous wound healing in rats. *BMC. Complement. Altern Med*., **11**: 86.

Lieberman HA, Lachman L and Schwarts JB (1989). Pharmaceutical dosage forms, vol. 1. Marcell Dekker, Inc., New York.

Lodha R and Bagga A (2000). Traditional indian systems of medicine. *Ann Acad Med Singapore*., **29**: 37-41.

Minaee B, Abbassian A, Nasrabadi AN and Rostamian A (2012). Prognostic factors of sciatica in the canon of Avicenna *Rheumatol Int*., 33(12):3095-3096.

Modanlou HD (2008). A tribute to Zakariya Razi (865-925 AD), an Iranian pioneer scholar. *Arch Iran Med*., **11**: 673-677.

Okorie O and Nwachukwu N (2011). Evaluation of the suspending properties of *aloe barbadensis* (*Aloe vera*) gum in pharmaceutical suspensions. *Int J Pharm Sci Rev Res*., **6**: 14-17.

Pinto RZ, Maher CG, Ferreira ML, Ferreira PH, Hancock M and Oliveira VC *et al* (2012). Drugs for relief of pain in patients with sciatica: Systematic review and meta-analysis. *BMJ*, **344**: e497.

Rhazes.Mansuri-fi-Teb (906/2008).Trans. (into Persian) Zaker ME. Tehran University of Medical Sciences Press, Tehran.

Rubinstein SM, Terwee CB, Assendelft WJ, de Boer MR and van Tulder MW (2012). Spinal manipulative therapy for acute low-back pain. *Cochrane Database Syst. Rev*., **9**: CD008880.

Shafaei M (1627/1889). Qarabadin Shafaei. Alijah Ezatva Saadat Publisher, Tehran (lithograph in Persian).

Tahour Ali HMA (1793). Qarabadin Mazhari. Original Manuscript in Persian: The copy which is kept in documents center of Research Office for the History of Persian Medicine, Shiraz, Iran.

Terry R, Posadzki P, Watson LK and Ernst E (2011). The use of ginger (*Zingiber officinale*) for the treatment of pain: A systematic review of clinical trials. *Pain Med*., **12**: 1808-1818.

Tonkaboni M (1669/2007). Tohfatol Moeminin. Corrected by Rahimi R, Shams Ardekani MR, Farjadmand F. Nashr Shahr Press, Tehran.

Tubach F, Beaute J and Leclerc A (2004). Natural history and prognostic indicators of sciatica. *J Clinic Epidemiol*., **57**: 174-179.

Vincent C and Furnham A (1996). Why do patients turn to complementary medicine? An empirical study. *Br J Clin Psychol*., **35**: 37-48.

Zargaran A (2010). Study on history of ancient Persian medicine and consideration on Hab as a traditional dosage form. Pharm D dissertation: Shiraz University of Medical Sciences. USP32-NF 27 (2010, Electronic version). U.S Pharmacopeia, US.

Zargaran A, Mehdizadeh A, Zarshenas MM and Mohagheghzadeh A (2012). Avicenna (980-1037 AD). *J Neurol*., **259**: 389-390.