



A critical comparison between dosage forms in traditional Persian pharmacy and those reported in current pharmaceutical sciences

M. Baranifard^{1,2}, M.M. Khazaei¹, S. Jamshidi¹, M.M. Zarshenas^{1,3}, A. Zargaran^{4,5}

¹Department of Phytopharmaceuticals, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

²Research Office for the History of Persian Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

³Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.

⁴Department of History of Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran.

⁵Department of Traditional Pharmacy, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

There were many natural pharmaceutical dosage forms cited by Persian pharmacists and physicians in the historical pharmacopeias (*Qarabadins*). This work aimed to perform a comprehensive study on “*Qarābādīn-e-Sālehi*” (1765 A.D.), one of the main Persian pharmaceutical manuscripts defining traditional dosage forms. All traditional dosage forms as well as their definitions, descriptions and considerations were extracted by reviewing “*Qarābādīn-e-Sālehi*”. Then, the textbook of “Aulton's Pharmaceutics; the design and manufacture of medicines” was considered to compare the medieval knowledge of pharmaceutics with current ones. Overall, there were 226 different dosage forms which have been cited in traditional Persian pharmacy. Since many of them were related to the preparation method, the final list of dosage form was shortened to nearly 60 items including solid, semisolid, liquid and gaseous forms. On the other hand, almost 40 forms with oral, topical, nasal, parenteral, vaginal and rectal routes of administration are mentioned as current dosage forms. Some of the dosage forms are similar or as the same in traditional and current pharmacy. But, there were too many novel dosage forms in traditional Persian pharmacy. There were 11 types of traditional nasal forms whereas, this route is still known as a novel route of administration. Also 5 different ophthalmic dosage forms have been cited in the textbook. Many of traditional dosage forms were designed according to the medical purposes. Several current dosage forms have roots in the historical definitions and can be found in Persian medicine. However, there are forgotten traditional dosage forms which can be modified and optimized in pharmacy nowadays.

Key words: dosage form, Persian medicine, pharmaceutics, traditional medicine

Introduction

It is well accepted that the official separation of pharmacy from medicine has been occurred in the 13th century. But, historical documents show

that pharmacy was an individual science in Persian medicine (PM) from antiquity [1,2]. According to PM manuscripts, medicine and

pharmacy have been practiced in two related branches. The first remained pharmacopeias (called as “*Qarābādin*” in PM) was written by “*Shapur ibn Sahl*”, Persian physician and pharmacist in Gundishapur in 831AD [3]. Also, there were a group of pharmacists who worked in the Gundishapur University and hospital located in south-west of Persia from 3th century AD [4]. Therefore, there was a well-developed traditional pharmacy in PM created during centuries and generation by generation experiences until 19th century. In PM, “*Qarābādins*” were pharmaceutical encyclopedias or pharmacopeias authored by pharmacist-physicians and mainly included a list of multi-ingredient preparations encompassing mineral, animal and herbal medicaments [5,6]. The natural medicaments reported in “*Qarābādins*” have been compounded in different traditional dosage forms, preparation methods, clinical activities and other related considerations [7].

The structures, patterns and approaches of these books are mainly related to the authors. Some of the “*Qarābādin*”s have been written by a physician or a scholar who has had main concentration on medical aspects. Accordingly, the pattern of key points in these texts was practically based on diseases. On the other hand, there are “*Qarābādin*”s mainly structured in line with dosage forms and pharmaceutical aspects. Among those Persian pharmacopeias, “*Qarābādin-e-azam*” (written by Hakim Azam Khān, 1853 AD) [8], as a famous textbook, has been written particularly according to different types of dosage forms alphabetically. On the contrary, “*Qarābādins-e-Ghāderi*” (written by Ahmad-shah Arzani, 1714 AD) has been authored in accordance with various types of diseases differentiated from head to toe [9].

More comprehensive than these textbooks, “*Qarābādin-e-Kabir*” (written by Aghili Khorasani Shirazi, 1772 AD) consists of 20 chapters on pharmaceutical practice in the first section of the book, followed by 28 parts on dosage forms. In this extensive pharmacopeia, multi-compound preparations in different dosage forms were alphabetically categorized based on a

main component [10].

Among all PM pharmaceutical manuscripts, “*Qarābādin-e-Salehi*” (Ghaeni Heravi, 1766 AD) is a well-known pharmacopeia which involves more than 200 types of dosage forms in alphabetic order. For each dosage form, numerous preparations with a specific name according to the inventor, the main medicament or the predominant portion of a medicine have been cited. For each preparation, name, constituents with related portions, preparation method, considerations and effects on diseases or body organ have been included [11].

As spreading scientific views on PM in Iran during recent decades and founding PhD courses of Traditional Medicine and Traditional Pharmacy for physicians and pharmacists, respectively; defining these dosage forms and presenting standard definitions comparable with current terminologies are necessary. Searching through the book, “*Qarābādin-e-Salehi*”, revealed that it was well written and may also be structurally similar to current pharmacopeias. Also, it was one of the latest Persian “*Qarabādins*” written in the 18th century AD. On the other hand, the book is well-arranged in regard of the dosage forms’ descriptions, examples, and mode of administrations. Furthermore, it seems that the book has mainly focused on pharmaceutical concepts and is easier for pharmacists to study. Finally, there is a new and recent version of this book which is rewritten and published recently [12]. Accordingly, the present study aimed to extract and cite the main dosage forms from this book, define them and compare the data with those recently reported and defined in current pharmaceutical sources.

Methods

In this paper, a copy of a well-known pharmacopeia, “*Qarābādin-e-Salehi*” [11] which included traditional dosage forms of our study was considered to extract all reported dosage forms from the beginning to the end of the book. On the other side, one of the main pharmaceutical textbook, the book of “*Pharmaceutics, The science of dosage forms design*” authored by

Michael E. Aulton [13] which comprehensively covers the design of current dosage forms and related aspects of drug delivery systems was employed as our current dosage forms-containing reference to compare the derived dosage forms from traditional aspect with those mentioned in contemporary pharmacy. Besides, concerned definitions, descriptions and considerations of both current and traditional dosage forms were collected and scrutinized/read carefully for better similarity verification/identification between them based on their routes of administration, physical properties, pharmaceutical characteristics and target organ.

Results and Discussion

In all, 226 different types of dosage forms administrable via oral, topical, nasal, ophthalmic, vaginal and rectal routes were extracted from “*Qarabadin*”. Table 1 has summarized the information about fractions of dosage forms which have been reported and administered via those aforementioned routes. These formulations were prepared in solid, semisolid, liquid and gaseous forms; solid and liquid forms included the most phases.

Table 1. distribution of all reported dosage forms in *Qarabadin-e-Salehi*, based on the route of administration

Route of administration	Distribution of related dosage forms
Oral	≈ 75
Topical	≈ 13
Nasal	≈ 8
Ophthalmic	≈ 4

It is considerable that nearly 30% of all 226 dosages in the textbook were medicinal foods or those foods that were used for dietary treatment of diseases. Medicinal foods are known as a type of food with specific or general benefits to be formulated for the management of various diseases. However, these formulations are not spoken as drugs or dietary supplements [14]. Medicinal foods such as “*Halva*” (*halwā*) prepared by oil, barley, wheat or other grain flour [15], or “*Hareesa*”, a dessert from meat, wheat

and oil, are two examples of those dosage forms. From all cited traditional dosage forms, 54 were determined as practical dosage form based on similarities in their route of administration and physical properties with a specific group of dosage forms in modern medicine. Particularly, many of those dosage forms (figures 1-6) were invented according to the clinical target or a specific organ. “*Laooq*” is an example of a respiratory dosage form which is not current in today’s pharmaceutical sciences. This dosage form seems to be a sustain-release form of a preparation with efficient and optimum delivery of drugs to the respiratory tract. A similar dosage form known as linctus may be a related form in current pharmacy [16,17].

Current and traditional dosage forms were divided into 4 groups and those with identical features were located in front of each other in related figures. The first group has been made of oral dosage forms which has been consisted of 23 traditional dosage forms like “*Laooq*” (linctus) and “*Habb*” (pill) and 9 current dosage forms such as powders on the opposite side of the figure. The second, third and fourth groups include 15, 6 and 10 topical, ophthalmic and nasal traditional dosage forms and 15, 1 and 2 current items, respectively. Figures 1 and 2 represent the oral dosage preparations, either traditional or current. Figures 3 and 4 show traditional and current topical dosage forms, including liquid or semisolid preparations. It is notable that in this study, in line with the citation in the “*Qarābādīn*”, vaginal and rectal dosage forms were cited in the category of topical forms. Figures 5 and 6 indicate ophthalmic and nasal dosage forms, respectively.

Nasal drug delivery was a beneficial route of drug administration in traditional Persian pharmacy. Natural medicaments have been administered nasally for local effect on the mucosa from long time ago. However, Persian pharmaceutical literatures have presented the route for various diseases especially those affecting the nervous system [3].

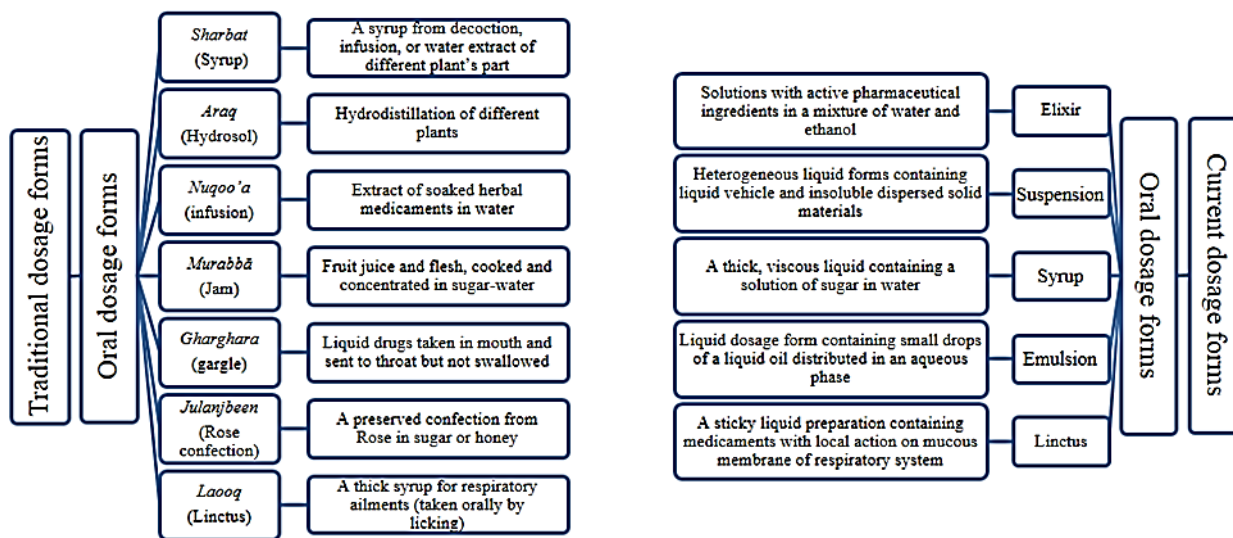


Figure 1. Liquid and semisolid oral dosage forms in traditional Persian pharmacy and current terminologies

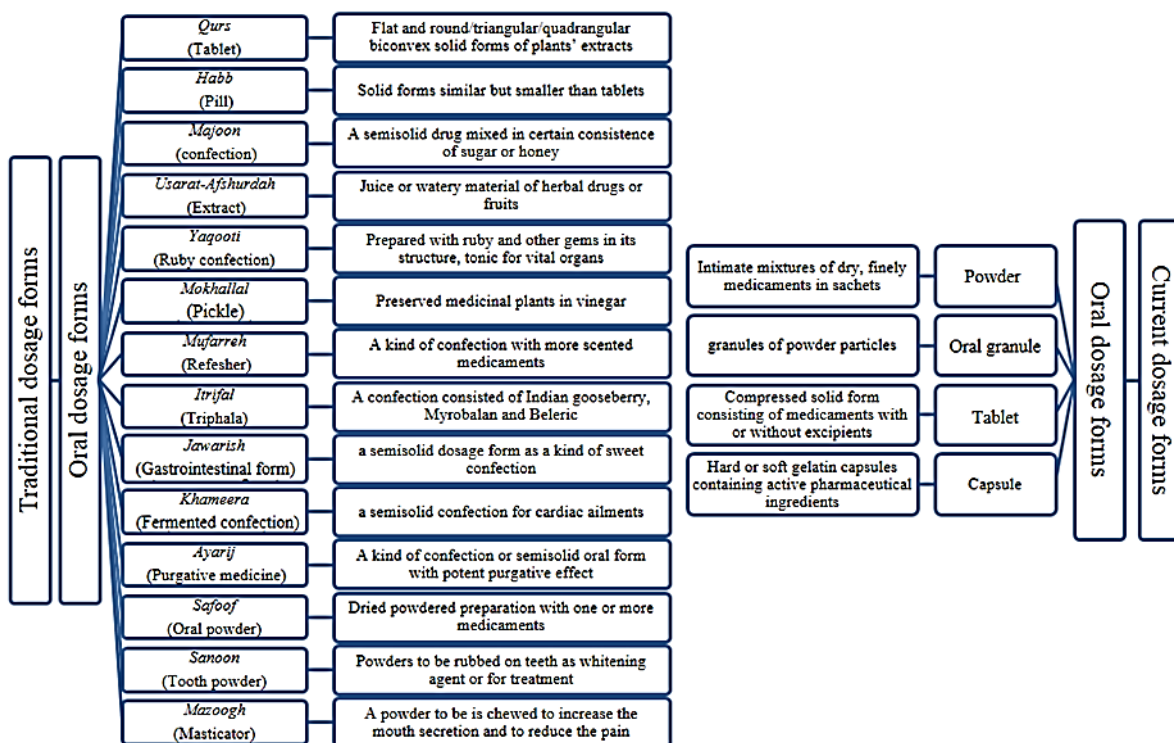


Figure 2. Solid oral dosage forms in traditional Persian pharmacy and current terminologies

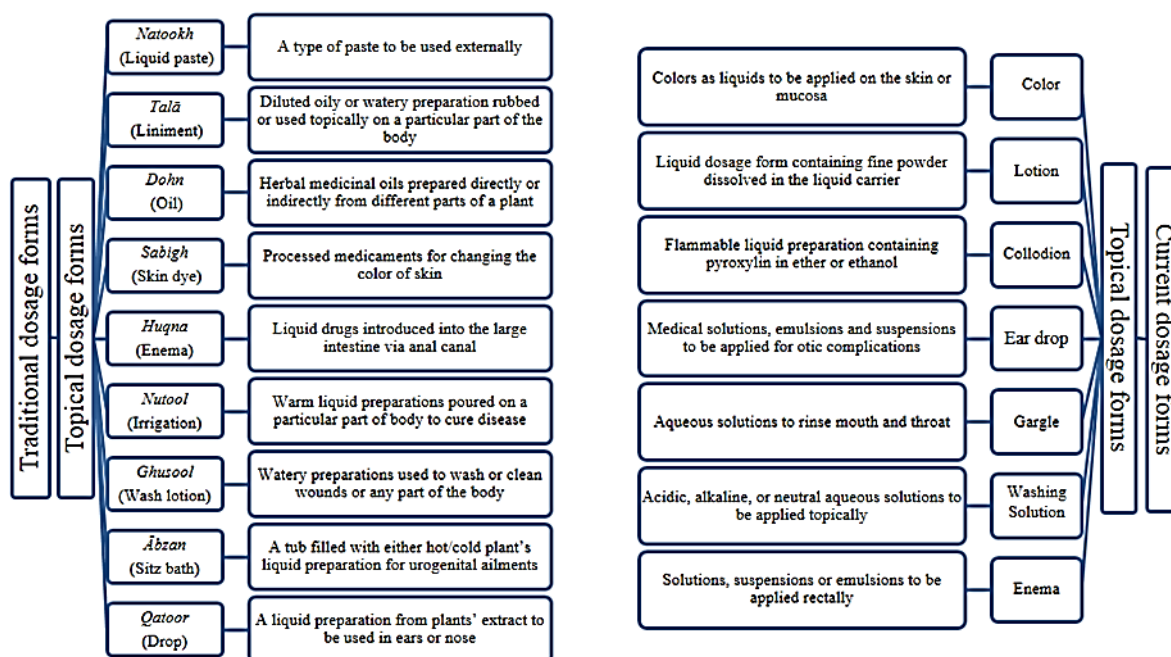


Figure 3. Liquid topical dosage forms in traditional Persian pharmacy and current terminologies

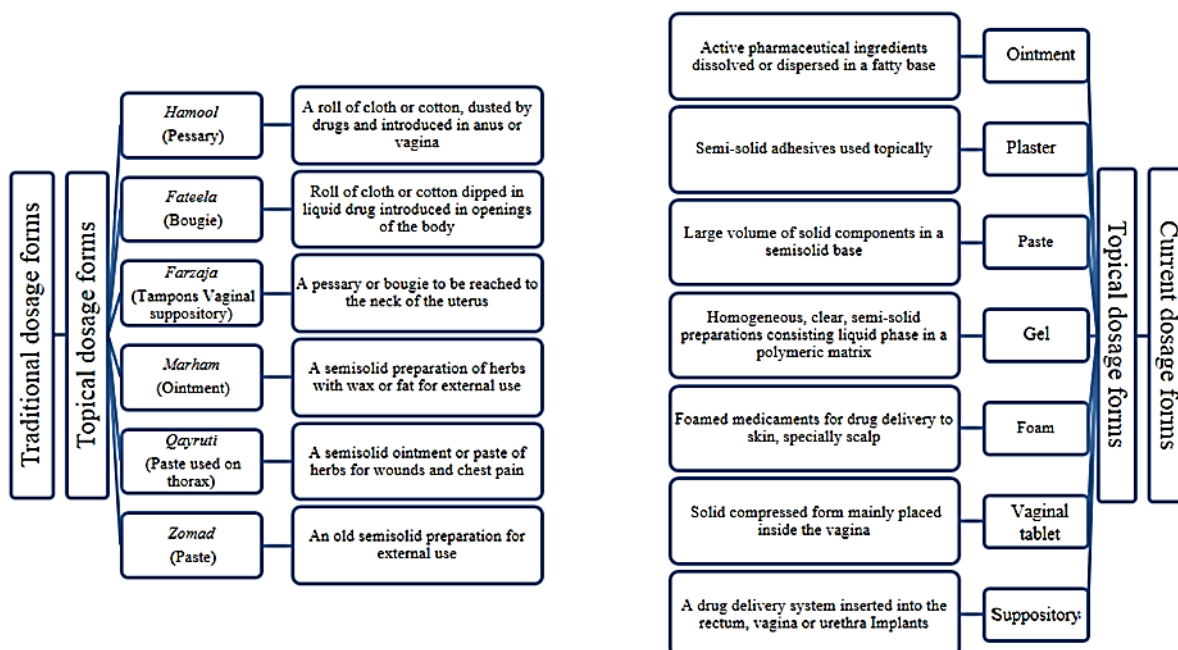


Figure 4. Semisolid topical dosage forms in traditional Persian pharmacy and current terminologies

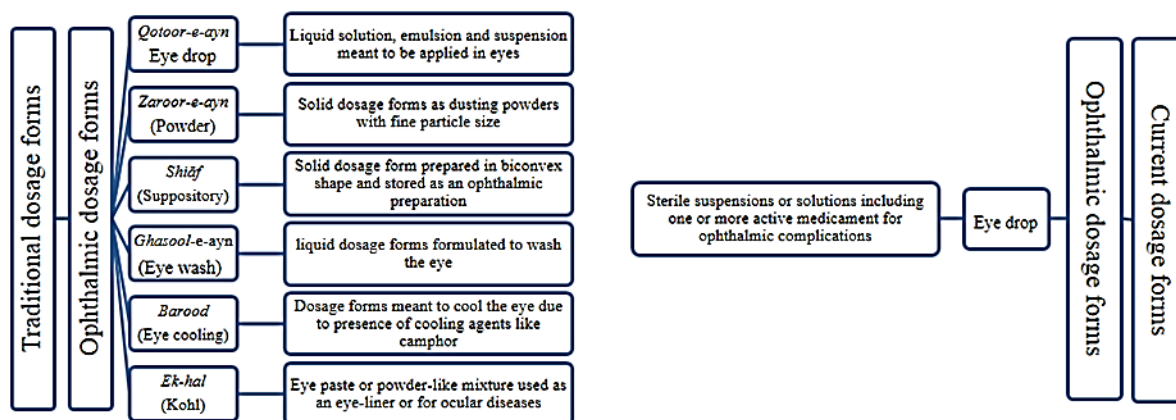


Figure 5. Ophthalmic dosage forms in traditional Persian pharmacy and current terminologies

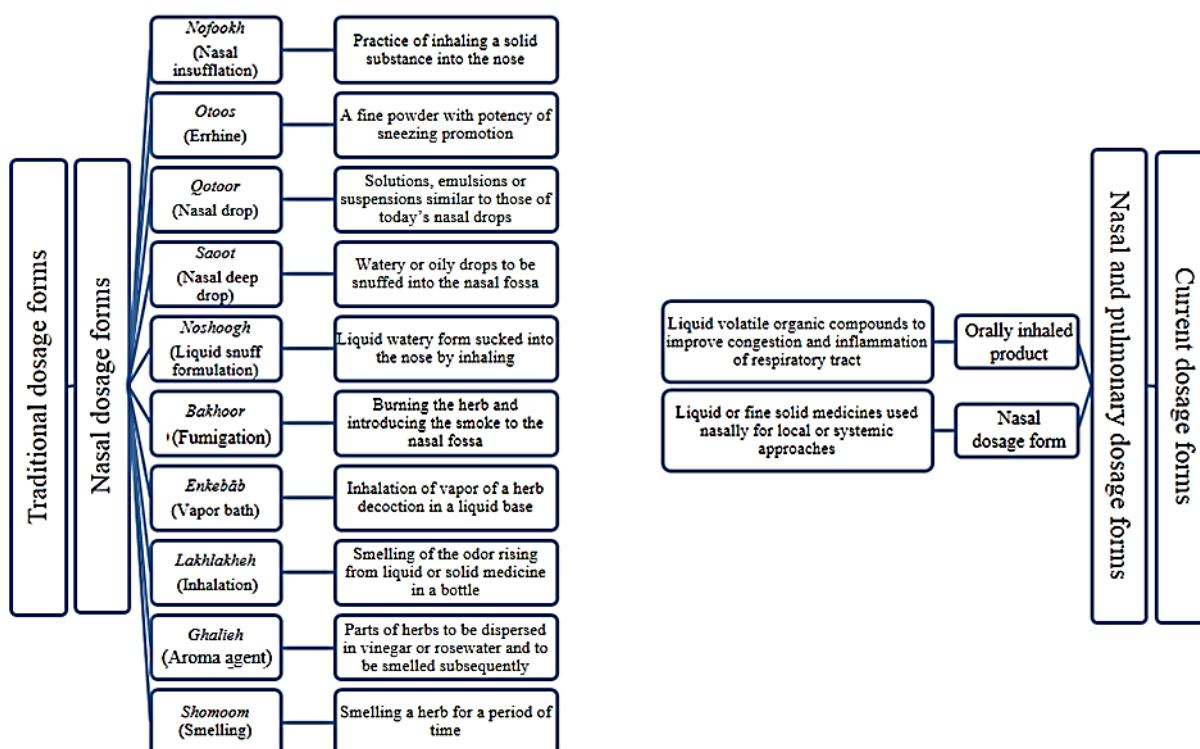


Figure 6. Nasal dosage forms in traditional Persian pharmacy and current terminologies

It is remarkable that the art and science of formulations and designing a particular dosage form have been meticulously considered by early Persian scholars. Based on the route of

administration, Persian traditional pharmacists have defined a procedure which is still considerable. Considering the solid and semisolid oral dosage

forms, it has been cited that based on the particle size, distribution of a medicament in a traditional dosage form may vary within a patient's body. It is mentioned that it is not necessary to reduce the particle size when a remedy is specifically administered for gastrointestinal purposes. However, the particle size has to be thoroughly decreased when a medicine is for "far organs" or those which are far from gastrointestinal system [18].

Although there has been no known sterilization for ophthalmic dosage forms in traditional pharmacy during the aforementioned era, additional processes such as decreasing the particle size of the employed medicament or pre-formulation procedures called "*Tadābir*" (treatment of modifications of the formulation ingredients) have been noted [19]. These treatments have been mainly carried out when mineral ingredients such as ruby, pearl, copper or silver have been used in the eye formulations. Washing, burning and reduction in the particle size were of the most practical treatments [18,19]. Interestingly, there are medieval eye formulations under a specific dosage form ("*Barood*" or cooling agents) which is seemingly neglected in current pharmaceutical sciences (figure 5). Since this type of formulation is now being specified as a cosmetic agent, it can be considered in current eye-related pharmaceutical remedies as well [19].

Apart from similarities in traditional and current topical dosage forms, application of "*Qairooti*" (cerate formulations) is noteworthy. Having numerous ingredients with various formulations, "*Qairooti*" has been used for relieving the joint pain, bone fracture, injuries and wounds. These formulations can also be considered by current medicine [20].

Conclusion

There were various dosage forms not only based on pharmaceutical shape, but also on the route of administration, ingredients and even therapeutic effects in PM. As examples, "*Laoq*" and "*Jawarish*" are two popular dosage forms which

have been administered for respiratory and gastrointestinal ailments, respectively. Therefore, there were a wide range of dosage forms some time covering each other. Defining each one needs a precise attention and consideration to be used correctly. They were presented separately with their own definitions in this study. It seems that many current terminologies and dosage forms rooted in the historical definitions and can be seen in the PM. Some others were developed in current pharmaceuticals and also we can use them in developing traditional remedies for better compliance or effect in traditional pharmacy researches. What is more, there are many forgotten traditional dosage forms which can be used in pharmacy nowadays.

Acknowledgments

This work is the result of an approved proposal (No. 14405); supported by Vice Chancellor for Research of Shiraz University of Medical Sciences, Shiraz, Iran.

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] Zargaran A, Zarshenas MM, Hosseinkhani A, Mehdizadeh A. Jawarish, a Persian traditional gastrointestinal dosage form. *Pharm Hist (Lond)*. 2012; 42(2): 24-25.
- [2] Zargaran A, Ahmadi SA, Daneshamouz S, Mohagheghzadeh A. Ancient Persian pharmaceutical vessels and tools in Iranian archaeological museums. *Pharm Hist (Lond)*. 2012; 42(4): 68-71.
- [3] Zarshenas MM, Zargaran A, Muller J, Mohagheghzadeh A. Nasal drug delivery in traditional persian medicine. *Jundishapur J Nat Pharm Prod*. 2013; 8(3): 144-148.
- [4] De Vos P. The "Prince of medicine": Yūhannā ibn Māsawayh and the foundations of the western pharmaceutical tradition. *Isis*. 2013; 104(4): 667-712.

- [5] Hamed A, Zarshenas MM, Sohrabpour M, Zargar A. Herbal medicinal oils in traditional Persian medicine. *Pharm Biol.* 2013; 51(9): 1208-1218.
- [6] Begum M, Ahmad A, Rasheed H, Syeed A. The valuable contributions by Unani physicians in “*Qarabadin*” (Unani medica). *Ayushdhara.* 2016; 2(6): 380-384.
- [7] Hosseinkhani A, Zargar A, Zarshenas M, Mehdizadeh A. Abkama, the first reported antibiotic in gastritis and infections throughout history. *Pharm Hist (Lond).* 2013; 43(2): 39-41.
- [8] Khan M. “*Qarabadeen azam*”. New Delhi: Central Council Research of Unani Medicine, 2009.
- [9] HA A. “*Qarabadeen Qadri*”. New Delhi: Aijaz Publication, 1998.
- [10] Husain S. “*Qarabadeen-e-Kabir*”. Lucknow: Matba munshi nawal kishore, 1897.
- [11] Heravi M. “*Qarabadin-e-Salehi*”. Tehran: Dar-ol-khalafeh, 1765.
- [12] Farjadmand F, Shams Ardekani MR, Zargar A. Wines as pharmaceutical dosage forms in 'Amal Saleh', as the last Persian pharmacopeia in the Zand era. *Pharm Hist (Lond.)*. 2017; 47(1): 8-10.
- [13] Alton M. *Pharmaceutics, the science of dosage forms design*. London: Churchill livingstone, 2002.
- [14] Ramaa CS, Shiode AR, Mundada AS, Kadam VJ. Nutraceuticals-an emerging era in the treatment and prevention of cardiovascular diseases. *Curr Pharm Biotechnol.* 2006; 7(1): 15-23.
- [15] Iqbal SZ, Asi MR, Jinap S. Natural occurrence of aflatoxin B1 and aflatoxin M1 in “halva” and its ingredients. *Food Control.* 2013; 34(2): 404-407.
- [16] Zarshenas MM, Badr P, Moein MR. Laooq: selective respiratory dosage form used in medieval Persia. *Pharm Hist (Lond).* 2013; 43(2): 34-38.
- [17] Karegar-Borzi H, Salehi M, Rahimi R. Lauq: a sustained-release dosage form for respiratory disorders in traditional Persian medicine. *J Evid Based Complement Altern Med.* 2016; 21(1): 63-70.
- [18] Afsharypour S. *Introduction to Iranian traditional pharmacy and pharmaceutical dosage forms*. Tehran: Chogan, 2013.
- [19] Zarshenas MM, Hosseinkhani A, Zargar A, Kordafshari G, Mohagheghzadeh A. Ophthalmic dosage forms in medieval Persia. *Pharm Hist (Lond).* 2013; 43(1): 6-8.
- [20] Mosleh G, Badr P. Qairooti (cerate or cera beeswax salve) in medieval Persia. *Pharm Hist (Lond).* 2016; 46(4): 72-74.