TRADITIONAL AND INTEGRATIVE MEDICINE

Trad Integr Med, Volume 1, Issue 3, Summer 2016

Research Article

Renovation and Standardization of a Historical Pharmaceutical Formulation from Persian Medicine: Chamomile Oil

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Received: 16 Jan 2016 **Revised:** 1 Feb 2016 **Accepted:** 10 Feb 2016

Abstract

Medicinal oils were of the pharmaceutical dosage forms used since ancient Persian times to now in Iran. Chamomile oil is one of the medicinal oils prepared by the extraction of the chamomile flowers to sesame oil as an oily vehicle. It was widely used in the history of Persian medicine and is currently used by traditional practitioners of Persian Medicine in various disorders mainly in topical form. In this study, traditional chamomile oil was prepared based on the Qarabadin books. In advanced, 600 g of chamomile flower powder was boiled in 3.6 liter of water for 3 hours. Then, powder was removed and remained water (aqueous extract of chamomile) was boiled with 0.5 liter of sesame oil for 2 hours (until all the water was vaporized and oil remained). For standardization, the essential oil of chamomile oil was obtained via Clevenger apparatus method and then analyzed with the help of gas chromatography (GC)-mass method. In addition, total phenolic and flavonoid contents of the chamomile oil were calculated based on galic acid and quercetin, respectively. The results show that the main component of the essential oil were Caryophyllene (7.45%), Bisabolol Oxide B (2.05%), Bisabolone Oxide A (62.35%), Chamazulene (2.05%), Bisabolol Oxide A (15.54%) and Methyl ester 5,8,11-Heptadecatriynoic acid (5.52%). Besides, total phenolic and flavonoid contents were 11.0043 ± 0.4514 and 2.7640 ± 0.1776 mg/l, respectively. Our results show that the historical dosage form of chamomile oil in Persian medicine can be reproduced and is an stable and homogeneous oil and be standardized in our investigation.

Keywords: Persian Medicine; Chamomile oil; Pharmaceutic; Traditional medicine

Citation: Zargaran A, Faridi P, Daneshamouz S, Borhani-Haghighi A, Azadi A, Hashempur MH, et al. **Renovation and Standardization of a Historical Pharmaceutical Formulation from Persian Medicine: Chamomile Oil**. Trad Integr Med 2016; 1(3): 108-14.

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1. INTRODUCTION

Using medicine dates back to the creation. From the beginning the history, human followed any ways to decrease his/her pains and diseases; and herbal raw materials were as the most accessible remedies for this purpose. But, formulating the complicated pharmaceutical dosage forms was as the main critical point in the history of pharmacy [1].

It has a long history in the ancient developed civilizations. Persian medicine is a traditional system of medicine used currently in Iran and many Middle Eastern countries belonging to thousands years ago in Iran [2]. Pharmaceutical sciences were well developed in Persia from ancient era. Archeological evidences show us many advanced pharmaceutical tools even from prehistoric times. Some pharmaceutical medicines remained in the historical texts show us progressed pharmacy in ancient Persia (from the beginning the history to 637 AD) [3].

Prahaoma syrup (containing *Ephedra distachya* L. and pomegranate tree branches), as the first antidepressant formulation in the history of medicine, is of such examples [4]. Later, in Islamic Golden Age (early medieval period, 9th to 12th century AD), pharmacy was progressed and the first pharmacopeias (*Qarabadin* in the Persian language) were written by Persian scholars. The first remained *Qarabadin* is *Qarabadin-Kabir* (Great pharmacopeia) written by Shapour-ibn-Sahl in Jondishapour University in southwest Persia at 869 AD [5].

Medicinal oils were of the pharmaceutical dosage forms used since ancient Persian times to now in Iran [6], [7]. These formulations categorized into two main groups: oils bearing directly from oily parts of a plant (such as oily seeds), and extraction of the content of a non-oily part of a herb to an oily vehicle. Second group is a pharmaceutical procedure to prepare a group of medicines in a pharmaceutical dosage forms. There are many methods described in the historical books to prepare them [7], [8].

Chamomile oil is one of the best examples of the second group of oils widely used in the history of Persian medicine and is currently used by traditional practitioners of Persian Medicine in various disorders mainly in topical form [9].

Current findings show that chamomile flowers have a high amount of various flavonoids such as apigenin and its glucosid derivates, quercetin and luteolin [10]. In addition, the essential oil of chamomile flowers contains high amount of chamazulene and bisabolol oxide A and B [11].

We tried to consider the historical applications of the traditional chamomile oil as well as how this formulation (chamomile oil) was prepared historically to reformulate this historical formulation based on historical pharmacopeias (*Qarabadins*). Then, we aimed to standardize it based on its essential oil content and total polyphenols and flavonoids.

2. METHODS

2.1. Literature review: At first, we considered some historical medical books (from early Islamic period) including *Hidāyat al-Muta'allimin fi al-Tibb* (The Students' Handbook of Medicine; written by Akhawayni, 10th century AD) [12], *Qanun fi al-Teb* (Canon of Medicine; written by Avicenna, 11th century AD) [13], *Al-Abnieh an Haghaiegh al-Advieh* (written by Heravi, 11th century AD) [14], and *Zakhireye Kharazmshahi* (Treasure of the Khwarazm Shah, written by Jorjani, 11th century AD) [15] to consider the historical uses of chamomile oil in Persian Medicine. Then, we used two main historical pharmacopeias, *Qarabadin-e-Kabir* written by Aghili Shirazi, 1772 AD [16], and *Qarabadin-e-Salehi* written by Mohammad Saleh Ghaeni Heravi, 1766 AD [17] to design its traditional preparation method.

2.2. Preparing the historical chamomile oil: We prepared chamomile oil via one of the methods cited in the historical documents; according to historical method mentioned in *Qarabadin* books [16], [17], 600 g of chamomile flower powder was boiled in 3.6 liter of water for 3 hours. Then, powder was removed and remained water (aqueous extract of chamomile) was boiled with 0.5 liter of sesame oil for 2 hours (until all the water was vaporized and oil remained). The remained oil

was the traditional chamomile oil prepared via traditional direct heat method.

2.3. Gas chromatography (GC)-Mass analysis: We obtained the essential oil of the chamomile oil (100 g of the oil in 2.5 liter of water) using Clevenger apparatus method (5 liter balloon). Then, the essential oil was analyzed using Gas chromatography-mass spectrometry (GC-MS) instrument (Agilent 7890) with mass specific detector (Agilent 5975C), a fused silica capillary column (Agilent DB-1MS; 30 m, 0.25 mm id and film thickness 0.25 μm) and helium as the carrier gas (at 1 ml/min flow rate). In addition, mass spectrometer was regulated in EI mode (70eV) and 30-600 m/z mass range with 280 ºC interface temperature. Finally, identification of the components was carried out via NIST, Willy mass spectra and Adams libraries spectra. Besides, to compare the essential oil of the preparation with the essential oil of the plant, we did the same method for 200 g of the herb and analyzed its essential oil and compared it with the essential oil of the chamomile oil.

***2.4. Total phenolic content*:** Total phenolic content was analyzed based on galic acid content determined by Folin Ciocalteu reagent [18]. The sample of oil was dissolved in methanol, then centrifuged (with Pecolab centrifuge instrument) at 4000 rpm for 13 minutes to get clear. In addition, gallic acid (Sigma) was used as standard. Folin Ciocalteu reagent (5 ml, 1:10 diluted with distilled water) and aqueous Na_2CO_3 (4 ml, 1 M) were mixed with both sample and standard solutions. After 15 minutes, the total phenol was determined via colorimetry at 765 nm [19]. The procedure was done three times. The solutions of gallic acid of concentrations of 0.0000, 50.0000, 100.0000, 150.0000, 200.0000, 250.0000 mg/l in methanol:water (50:50 v/v) were used to prepare standard curve. The results were presented as gallic acid equivalent (mg/l of sample oil).

2.5. *Total flavonoid content:* We determined the total flavonoids content of the traditional oil based on the quercetin using Dowd method as adapted by Arvouet-Grand et al [20]. At first, 5 ml of 2% aluminium trichloride in methanol was mixed with the same volume of a sample of oil. Then, the mixture was centrifuged (with Pecolab centrifuge instrument) at 4000 rpm for 8 minutes to be clear. Finally, after 10 minutes, absorption was read at 415 nm (with Pecolab centrifuge spectrophotometer) against a blank sample consisting oil and methanol without AlCl3. Quercetin (Sigma, Aldrich) was used to determine the total flavonoid content using a standard curve (quercetin solution concentrations: 0.0000, 5.0000, 20.0000, 50.0000 and 80.0000 mg/l). The mean of three readings was used to express of the total flavonoid content as mg of quercetin equivalents per liter of chamomile oil.

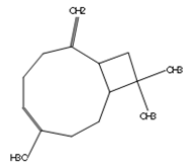
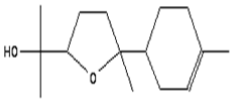
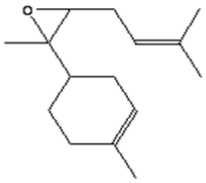
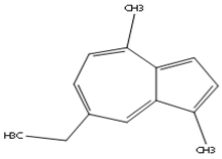
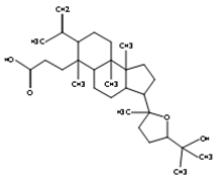
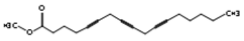
3. RESULTS

As we reviewed, some of the historical uses of chamomile oil in Persian Medicine (PM) are shown in table 1.

Table 1. The physical characteristics of the subjects

Characteristics	Uses	References
Topical on forehead	Migraine-cold headaches	[12], [13], [15]
Massage with oil	Fatigue	[13]
Massage with oil	Chronic fevers	[13], [15]
Topical	Analgesic	[13]
Topical	Spasm	[13], [14]
Oral	Eye tonic	[13]
Ear drop	Otitis	[13]
Oral	Hiccough	[13]
Topical	Jaundice	[13], [15]
Topical	Kidney inflammation	[13]
Topical	Joint pain	[13]
Nose drop	Sedative (for geriatrics)	[15]
Warm oil in oral cavity	Toothache	[15]

Table 2. Main components in the essential oils (EO) of the plant flowers and historical chamomile oil preparation

Component	Structure	Retention Time	Concentration in the plant flowers the essential oils (%)	Concentration in the historical chamomile oil preparation the essential oils (%)
Caryophyllene		25.252	6.86	7.45
Bisabolol Oxide B		32.283	1.88	2.05
Bisabolone Oxide A		33.050	57.37	62.35
Chamazulene		34.456	9.75	2.05
Bisabolol Oxide A		35.204	14.29	15.54
Methyl ester 5,8,11-Heptadecatriynoic acid		38.693	5.08	5.52
TOTAL			95.23	94.96

We reformulated chamomile oil according to traditional direct heat method as is mentioned in methods. The prepared oil has light clean green color and chamomile odor.

Figure 1 shows the GC-MS spectra of the essential oils obtained from chamomile oil and raw flower powder of the chamomile.

The main components in both essential oils are almost the same and listed in table 2, but the amount of chamazulene is decreased from 9.75% to 2.05% in the preparation.

Figure 2 shows calibration curves of galic acid and quercetin to determine total phenolic and flavonoid content; these amounts were 11.0043 ± 0.4514 and 2.7640 ± 0.1776 mg/l, respectively.

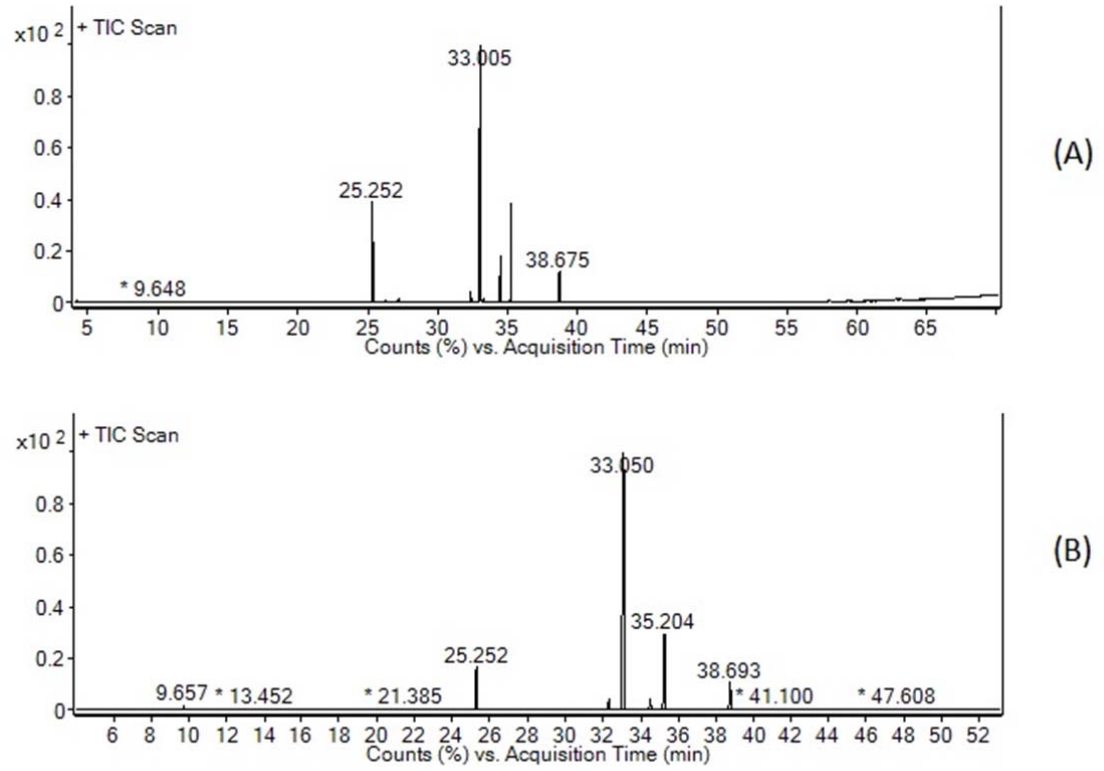


Figure 1. The spectra of essential oils obtained from chamomile flowers (A) and historical chamomile oil preparation (B)

4. DISCUSSION

4.1. Historical uses of chamomile oil in Persian Medicine: Although chamomile oil mainly used in combination of other ingredients to prepare various medicines in Persian Medicine [12], [13], [14], [15], it was used solely as medicine in many cases with different diseases of different organs.

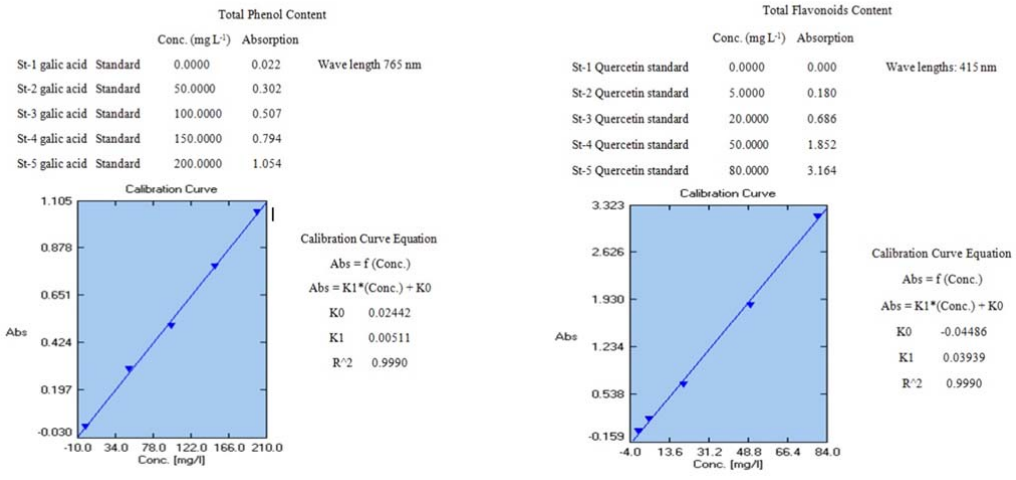


Figure 2. Calibration curves for gallic acid and quercetin standards to determine total poly phenol and flavonoids contents of the historical chamomile oil

4.2. Traditional methods to prepare chamomile oil: There were various methods mentioned in the historical pharmacopeias to prepare chamomile oil. But, two main methods were widely used in Persian medicine. In the first method, 600 g of the chamomile flowers was put in 3.6 l of water and boiled until one third of the water vaporized. Then, the flowers were removed and aqueous content transferred into 0.5 l of Sesame oil and boiled until water vaporized and oil remained. The remained oil was chamomile oil prepared via traditional direct heat method. In another method, 280 g of chamomile flower should be put in a vessel with 949.2 ml of sesame oil and the vessel put in expose to the sun light for 40 days during summer. Then, oil was filtrated and plant would be removed. The remained oil was traditional chamomile oil prepared via traditional indirect heat method. In this study we reformulate chamomile oil according to the first method, direct heat method. [16], [17]

4.3. Preparation of the chamomile oil: We prepared the chamomile oil according to historical books as we mentioned in the material and methods [12], [13]. The prepared oil has light clean green color and chamomile odor.

4.4. GC-Mass analysis: As we found, the main components in both essential oils were almost the same, but the amount of chamazulene was decreased from 9.75% to 2.05% in the preparation.

4.5. Summary: Our results show that the historical dosage form of chamomile oil in Persian medicine can be reproduced and is an stable and homogeneous oil. On the other hand, analysis of the content of the oil showed that it contains chamazulene in its essential oil and poly-phenolic compounds and flavonoids. Current findings support antioxidant and radical scavenging activities of chamazulene [21]. Besides, flavanoids (apigenin and its glucoside derivatives as main component in chamomile) have anti-inflammatory and analgesic [cyclooxygenase (COX)-II inhibitory] effects [9], [22]. In addition, they can decrease NO level [23] and posse neuroprotective effect [24]. These properties can support historical applications of the traditional chamomile oil.

5. Conflict of Interests

Authors have no conflict of interests.

6. Acknowledgments

None

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