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Review

A Brief Review on Vaginal Drug Delivery in Traditional Persian Medicine

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Abstract

Based on numerous written works of Persian scholars of Middle ages, Traditional Persian Medicine (TPM) has its own capabilities and strengths. According to TPM, vaginal drug delivery was prioritized to treat gynecological disorders because of the adjacency of uterine and cervix to vagina. This study was carried out to introduce and extract vaginal multi-component dosage forms, suggested by eight key medicinal manuscripts. Traditional terms of *abzan, bakhour, fetileh, forzjeh, ghatour, jalous, hamoul, hoghneh,* and *shiaf* were sought as keywords. About 680 vaginal formulations were found for various gynecological disorders such as abortion, amenorrhea, and cervical stenosis. Vaginal dosage forms were categorized based on three physical conditions including solid (*forzjeh, fetileh, hamoul,* and *shiaf*), liquid (*abzan, jalous, ghatour and hoghneh*), and gas or smoke (*bakhour*). More detailed analysis of each vaginal dosage form based on traditional documents is suggested .

Keywords: Vaginal drug delivery; Vaginal dosage form; Traditional Persian Medicine

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Introduction

Traditional Medicines (TMs) play a significant role in healthcare systems, particularly in developing countries. Besides, industrialized world has been recently encouraged to practice such methods [1,2]. To put great emphasis on TMs on a regular basis, World Health Organization (WHO) published its recent strategy about TM in December 2013 to give guidelines for the next decade [3]. Traditional Chinese Medicine (TCM), Japanese Kampo Medicine, and Ayurveda are some instances of traditional healing systems [4]. Based on numerous written works of Persian scholars of medieval period, Traditional Persian Medicine (TPM) has its own capabilities and strengths. For instance, different drug delivery methods have been covered by medieval manuscripts [5].

Vaginal drug delivery is not a concept of current century. The earliest vaginal application has been reported in 1850 BC in Egypt [6]. According to TPM, vaginal drug delivery was prioritized to treat gynecological disorders because of the adjacency of uterine and cervix to vagina. Therefore, various vaginal dosage forms such as fumigation, vaginal cotton-load, and vaginal wick were prescribed by Persian physicians [7]. It seems that developed versions of these dosage forms are conventional vaginal formulations including cream, ointment, gel, foam, suspension, solution, emulsion, tablet, and capsule. They are considered advantageous because of no interaction with gastric content, avoidance of hepatic first-pass effect, and potential limitations of oral application [8,9].

This study was carried out to introduce and extract vaginal multi-component dosage forms, suggested by eight key manuscripts of TPM.

Method

In order to extract multi-component vaginal formulations including at least two materia medica, eight key manuscripts of *Qarabadin* (multi-compound encyclopedia) were studied. They belong to a time span of one millennium, from 9th to 19th century. Traditional terms of *abzan, bakhour, fetileh, forzjeh, ghatour, hamoul, hoghneh, jalous* and *shiaf* were sought as keywords in *Qarabadin al-adviye al-morakabe* (9thAD), *Kitab al-Maleki* (10thAD), *Qanon fi- Tib* (11thAD), *Qarabadin-e Shafaii* (17thAD), *Qarabadin-e Salehi* (18thAD), *Qarabadin-e Kabir* (18thAD), *Qarabadin-e Azam* (19thAD), and *Tib-e Faridi* (19thAD) [10-17]. Ear *fetilehs*, ocular *shiafs*, ear and ocular *ghatours* were excluded from extracted results.

Results

In eight traditional manuscripts, 677 vaginal formulations were found for various gynecological disorders such as abortion, amenorrhea, cervical stenosis, displacement of uterus, dysmenorrhea, false pregnancy, hysteria, impaired libido, infertility, labour dystocia, lower abdominal pain, oligomenorrhea, pelvic pain, polymenorrhea, postpartum hemorrhage, rupture of uterus, uterine abscess, uterine dystemprament, uterine pain, uterine prolapse, vaginal dryness, and vaginitis besides contraception and diagnosis of pregnancy. Numbers of each traditional dosage form mentioned in eight qarabadin manuscripts have been summarized in table 1.

Vaginal dosage forms were categorized based

on three physical conditions including solid (*forzjeh, fetileh, hamoul, and shiaf*), liquid (*abzan, jalous, ghatour,* and *hoghneh*), and gas or a mixture of solid in gas (*bakhour*). Table 2 demonstrates further details such as basic of formulation, possible bases and carriers for each traditional dosage form. Three samples of original handwritten formulations including solid, liquid, and gas (*smoke*) vaginal dosage forms have been depicted in figure 1.

Ingredients of a vaginal formulation were either of herbal sources (cinnamon, saffron, chamomile, olive oil), or of animal sources (horse milk, duck fat, chicken skin, bone marrow), or from mineral ones (sulfur, petroleum oil, kohl). Table 3 has exemplified some vaginal formulations in detail (ingredients, plant family, and proportion).

Table 1. Numbers of vaginal dosage forms mentioned in eight *qarabadin* manuscripts

manuscript (century)	***forzjeh***	***fetileh***	***hamoul***	***shiaf***	***abzan***	***hoghneh***	***bakhour***	***ghatour***	**total**
al-Adviye al-Morakabe [9]	0	0	0	0	0	4	0	0	4
Kitab al-Maleki [10]	45	0	4	1	11	24	6	3	94
Qanon fi-Tib [11]	42	1	12	2	11	7	28	0	103
Qarabadin-e Shafaii [17]	23	0	0	4	0	0	4	0	31
Qarabadin-e Salehi [18]	47	0	39	0	6	8	6	0	106
Qarabadin-e Kabir [18]	80	2	58	6	20	8	21	1	196
Qarabadin-e Azam [19]	36	1	11	12	2	3	1	0	66
Tib-e Faridi [19]	7	0	51	0	10	1	8	0	77
total	280	4	175	25	60	55	74	4	677

Table 2. Vaginal dosage forms in three categories of physical condition (solid, liquid, gas or smoke) and eight types (*forzjeh, fetileh, hamoul, shiaf, abzan, hoghneh, ghatour and bakhour*)

physical condition	**vaginal dosage form**		**basic of formulation**	**base**	**carrier/ device**
	traditional	**conventional**			
S	*Forzjeh*	Cotton-Load	powdered ingredients or semisolids + base (in size of date seed, oak fruit, or middle finger)	extracts, gum, honey, hot water, mallow mucilage, milk, oil in wax, rosewater, sugar, vinegar, yolk	an absorbent material like cotton, linen, wick, or wool
	Fetileh	Wick			
	Hamoul	Cotton-Load			
	Shiaf	Pessary			
L	*Abzan/Jalous*	Sitz-Bath	ingredients + water ➤ boiled until halved ➤ filtrated	oil, water	a tub [a]
	Hoghneh	Douche			a lubricated tube [b]
	Ghatour	-	tablet or shiaf ➤ powdered	oil, milk, mucilage, vinegar	nm [c]
G	*Bakhour*	Fumigation	powdered ingredients + base ➤ dried ➤ burned	cow fat, honey, olive oil, wax	a tube, or a seat with a hole

S: solid, L: liquid, G: gas (mixture of solid in gas)
a. Patient has to seat in a tub filled with therapeutic liquid for 30 minutes to one hour.
b. The tubes for hoghneh were made from the skin of fawn's or yeanling's trotters attached to a wooden straw.
c. Not mentioned

Table 3. Eight examples of vaginal dosage forms (*forzjeh, fetileh, hamoul, shiaf, abzan, hoghneh, ghatour, and bakhour*) in detail

	dosage form	ingredients	used part	family	unit(s)[a]
1	*forzjeh* for menorrhagia [16]	1.*Acacia nilotica* (L.) Delile 2.*Cinnamomum camphora* (L.) J.Presl 3.*Coriandrum sativum* L. 4.*Punica granatum* L. var. pleniflora Hayne	Exudate Exudate Seed Flower	Fabaceae Lauraceae Apiaceae Lythraceae	1 1 7 3
2	*fetileh* for hysteria [12]	1.*Boswellia serrata* Roxb. ex Colebr. 2.Duck fat 3.*Liquidambar orientalis* Mill. 4.*Piper nigrum* L. 5.*Urtica dioica* L.	Exudate - Exudate Fruit Seed	Burseraceae - Altingiaceae Piperaceae Urticaceae	2 4 3 2 2
3	*hamoul* for vaginal itching [12]	1.*Lens culinaris* Medik. 2.*Mentha spicata* L. 3.*Punica granatum* L.	Fruit Leaf Peel	Fabaceae Lamiaceae Lythraceae	nm[b]
4	*shiaf* for polymenorrhea [15]	1.Kohl 2.*Myrtus communis* L. 3.*Punica granatum* L. var. pleniflora Hayne 4.*Quercus ilex* L.	Mineral Leaf Flower Peel	- Myrtaceae Lythraceae Fagaceae	nm
5	*abzan* for amenorrhea [11]	1.*Apium graveolens* L. 2.*Artemisia vulgaris* L. 3.*Brassica oleracea* L. 4.*Foeniculum vulgare* Mill. 5.*Juniperus sabina* L. 6.*Matricaria chamomilla* L. 7.*Mentha pulegium* L. 8.*Ruta graveolens* L.	Seed Flower Seed Seed Fruit Flower Leaf Leaf	Apiaceae Asteraceae Brassicaceae Apiaceae Cupressaceae Asteraceae Lamiaceae Rutaceae	nm
6	*hoghneh* for post-partum pain [11]	1.*Apium graveolens* L. 2.*Foeniculum vulgare* Mill. 3.*Trigonella foenum-graecum* L.	Seed Seed Seed	Apiaceae Apiaceae Fabaceae	nm
7	*ghatour* for uteritis [11]	1.*Coriandrum sativum* L. 2.*Plantago major* L. 3.*Rosa* × *damascena* Mill.	Leaf [c] Seed [d] Flower [e]	Apiaceae Plantaginaceae Rosaceae	nm
8	*bakhour* for abortion [15]	1.*Commiphora mukul* (Hook. ex Stocks) Engl. 2.*Commiphora myrrha* (Nees) Engl. 3.*Juniperus sabina* L.	Exudate Exudate Fruit	Burseraceae Burseraceae Cupressaceae	nm

a. units show the proportion of ingredients in formulation
b. nm: not mentioned
c. juice of leaf is used
d. mucilage obtained from seeds
e. Rosa oil which is prepared by maceration of petals in sesame oil

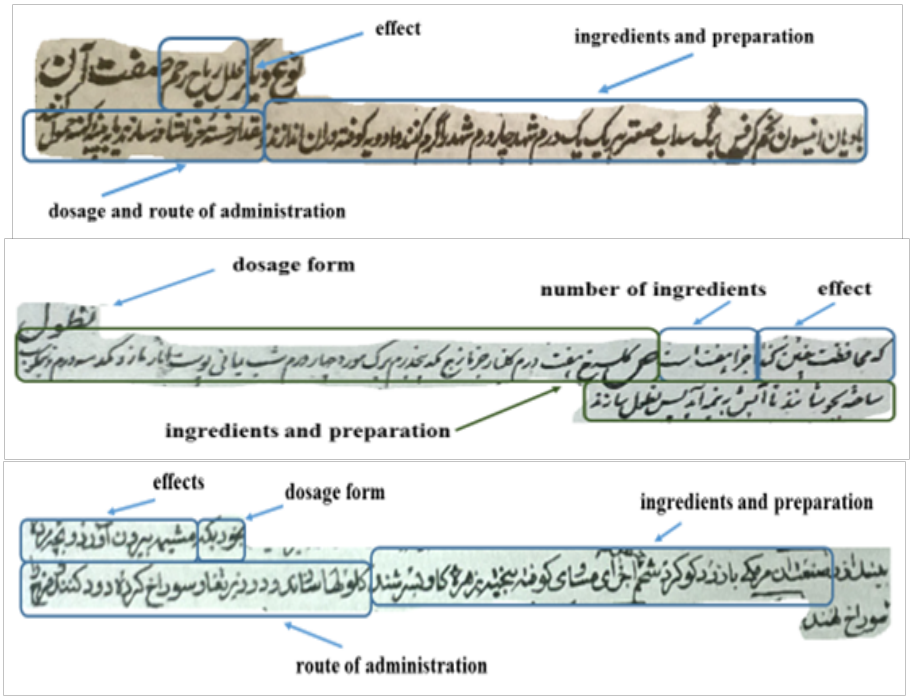

Figure 1. Top to bottom: samples of the original hand-written formulations including solid, liquid, and gas (smoke) vaginal dosage form [14-16]

Discussion

According to table 1, gradual increase in number of formulations throughout the studied timespan (9th -19th century) shows an improvement in expertise and knowledge of Persian scholars. Multi-compound formulations were both simple and of great complexity, including two to fifty-three ingredients. Among the studied manuscripts, *Qarabadin-e Kabir* and *Qarabadin-e Salehi* had mentioned higher numbers of vaginal formulations (195 and 106, respectively). Among total formulations, *forzjeh* was the highest in number followed by hamoul (respectively 280 and 175 out of 677). It can be deducted that such formulations were more common in the past. Two reasons for this acceptability is the adjacency of drug to the location and long continuance of therapeutic effects [14].

All formulations were not ready after preparation. For some, 40 days or 6 months should pass before administration to make medications ripened. To reduce vaginal irritation, lubricating oils like rose oil were used. Also, the absorbent carrier for solid dosage forms should be soft, preventing irritation. To avoid full-body weakness following *abzan*, similar to after-sauna tiredness, massage with rubbing oil was advisable. Fragrant ingredients such as amber, musk, and olibanum had a main role in vaginal formulations because they were believed as uterine tonics that improve functions of uterus. Opposing to oral formulations, the quantities of ingredients in vaginal dosage forms were not usually mentioned, especially in *abzan, hoghneh, ghatour,* and *bakhour,* as shown in table 3. No reason was found for this inexact usage of ingredi-

ents. Similarly, recent ethnomedicinal surveys confirm lack of dose adjustment for medicinal smokes and liquid vaginal preparations which are prescribed by local healers [18-20]

Studied vaginal dosage forms have not been exclusively prescribed in this region and similar formulations are common in other systems of traditional medicine. For instance, fumigation is being used in Argentina, Bolivia, Guyana, India, and South Africa for gynecological disorders [18,21]. Conventional bases for vaginal suppositories are either oleaginous or water-soluble/water-miscible bases [22,23]. Similarly, traditional formulations including *forzjeh, fetileh, hamoul, shiaf, abzan, hoghneh,* and *ghatour* had oily or watery bases. Application of an absorbent material like cotton, linen, wick, or wool as a carrier could control the release of main drug. Traditional manuscripts of different nations account for a valuable heritage that should be wisely worked on. Further detailed analyses of vaginal dosage forms based on these documents is suggested.

Conflict of Interests

None.

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