

Plants used to treat “tabe rebá” (malaria like fever) in Iranian Traditional Medicine

Saeedeh Ghafari^{1,2}, Somayeh Esmaeili^{1,2}, Farzaneh Naghibi*^{2,3}, Mahmoud Mosaddegh^{1,2}

- 1- Department of Traditional Pharmacy, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences. Tehran. Iran
- 2- Traditional Medicine and Materia Medica Research Center (TMRC), Shahid Beheshti University of Medical Sciences. Tehran. Iran.
- 3- School of Pharmacy Shahid Beheshti University. Tehran. Iran.

***Corresponding Author:** Farzaneh Naghibi

Abstract

This study used fifteen of the most important Iranian Traditional Medical and Pharmacy books written by Iranian scholars who lived within the period of the 9th century to 20th century AD in order to obtain a list of materia medica of plants commonly used to treat “Tabe Rebá” (malaria like fever), in the specified time era and their scientific names were determined subsequently. In ITM (Iranian Traditional Medicine), 51 plants were used to treat “Tabe Rebá” and 61 scientific names were determined subsequently. About 31% of them have shown anti parasitic effect. The listed plants could be a useful starting point for an antimalarial screening strategy.

Keywords: Antimalarial, Iranian Traditional Medicine (ITM), anti-parasitic, Avicenna, Razes

Introduction

Among all parasitic agents causing disease in human, malaria is undoubtedly the most destructive and dangerous infectious agent in developing world (Batista et al., 2009). Nowadays, plants are invariably resource for new drugs in use, namely quinine and artemisinin (Gessler et al., 1994). The resistance of *Plasmodium spp.* to drugs – such as chloroquine, artemisinin- derivatives and to drug combination therapies) – has become a serious problem in areas of endemic malaria and in malaria-free areas with occasional imported cases (Batista, et al. 2009).

One possible approach to the identification of new antimalarial drug candidates is to search for compounds that cure or prevent malaria in plants empirically used to treat malaria. Thus, it is worth documenting the traditional medicinal data, and testing the antiplasmodial activity of the extractive from plants. There is also a need to generate reliable scientific data to determine whether the plants used to treat malaria in old traditional books are actually effective.

Knowledge of medicine in Iran dates back more than 6000 years (Sarmadi, 1991). Iranian scientists such as Avicenna and Razes have theorized medical knowledge in Iran. Their works were translated into different languages, and some of them, such as *the Canon (Qanon)* of Avicenna, were used in European scientific centers for more than 600 years (Bodeker, et al. 2005). In Iranian Traditional Medicine (ITM) throughout this time, there is many of materia medica of plants used treatment disease has yet to be fully verified experimentally.

This study aims to identify the fever like malaria disease in ITM and then presents a list of materia medica of plants named in traditional books. In this way it seeks to point pharmacologist toward a study of traditional substances and their potential for investigating antimalarial properties.

Material and methods

The target of the first part of this study was to find out if malaria was known as a disease in Iranian Traditional Medical manuscripts or not. And if yes, what was it called. In the first step, ten books written by Iranian old physician including disease descriptions were chosen regarding to their importance and availability among other Iranian Traditional Medical books and listed in table 1.

Table 1-The list of Iranian Traditional Medical books from 9th century to 20th century AD

Title	Author	Century produced (A.D)
<i>Ferdous-ul-hekmah</i>	Ali-ibn-e Raban Tabari	9
<i>Al-Maleki (Kamel-os-sana'at fi-tebb)</i>	Ali-ibn-e Abbas Majusi Ahvazi	10
<i>Hedayat ul-moteallemin fi-tebb</i>	Akhaveini Bokharaei	10
<i>the Canon (Qanun fi-tebb)-Volume 4</i>	Avicenna	11
<i>Zakhireh Kharazm shahi</i>	Seyyed Ismaeel Jorjani	12
<i>Al-Asbab val `alamat</i>	Najeebeddin Samarqandi	12
<i>Sharhu'l-asbab va'l-`alamat</i>	Nafis bin Avaz bin Hakim	13
<i>Kholasato Al Tajareb</i>	Bahaeddolehe Razi	15
<i>Tebbe akbari</i>	Hakim Mohammad Akbar Arzani	17
<i>Maghame or rashigh lemonkera tebb- ul- atigh</i>	Haj Mirza Hoseyn Eatemad- ul -Atebba	20

Two of these, the fourth volume of *the Canon* of Avicenna and *Zakhireh kharazm shahi* of Seyyed Ismaeel Jorjani were studied to find the equivalent disease name for malaria since all the books are written in Arabic or Persian and the term malaria was not usual at those times. "Tabe Rebá" is the first choice among many disease accompanied by fever (Jorgani, 2003; Abu Ali Sina, 2004,).

The semiology of malaria (Wilson, et al. 1991; Saebi, 2005) compared to the signs and symptoms of "Tabe Rebá" as describe in ten Iranian Traditional Medical books (Akhawayini al Bukhari, 1992; Eatemad- ul –Atebba, 2003; Arzani, 2005; Raban, 2008; Majusi, 2008; Nafis, 2008; Razi, 2008; Samarghandi, 2009).

In the second part of the study, five traditional important books from pharmacist angle of view were listed in table 2.

Table 2- The list of Iranian Traditional Pharmacy books from 9th century to 18th century AD

Title	Author	Century produced (A.D)
<i>Al-Hawi fi-tebb</i>	Rhazes	9
<i>Al-Abniyah an haqaiq al-adviyah</i>	Abu Mansour Ali-ol Heravi	10
<i>the Canon (Qanun fi-tebb)- second volume</i>	Avicenna	11
<i>Tuhfat ul-mumenin</i>	Seyyed Mir Muhammad Mumin	17
<i>Makhzan ul-adviiyah</i>	Seyyed Muhammad Hoseyn Aghili Khorasani	18

The second volume of *the Canon* and also *Makhzan ul-adviiyah* of Seyyed Muhammad Hoseyn Aghili Khorasani were reviewed by keyword of "Tabe Rebá" to screen medicinal plants useful to treat "Tabe Rebá" (Abu Ali Sina, 2004; Aghili Khorasani, 2008). In this way we were able to conclude a preliminary list of plants used to treat "Tabe Rebá".

Then each plant in the list was used as a keyword in the three other major pharmaceutical books of ITM namely *Al-Hawi fi-tebb* of Rhazes (Rhazes, 2005), *Al-Abniyah an haqaiq al-adviyah* of Abu Mansour Ali-ol Heravi (Heravi, 1992), *Tuhfat ul-Mumenin* of Seyyed Mir Muhammad Mumin (Mumin Tonekaboni, 2007) to compare the opinion of different famous physicians about the exact type of fever effect of plants. Noteworthy is that plants used for treatment of chills are also included.

One major problem in researches in Traditional Medicine of non European culture is the *Latin binominal nomen cluture* of plants mentioned in the old manuscripts. For this purpose we used *Pezeshkinameh* (Nafisi, 1897), *Matching the old medicinal plant names with scientific terminology* (Ghahreman, Okhovvat, 2009), *Investigation of various common names of plants used in traditional medicine* (Dini, 2005) and *Encyclopedia of*

traditional medicine, medicinal plants (Soltani, 2005). If more than one Latin name is suggested for a plant, the most cited name was chosen. Otherwise all suggestions are included in the list. Finally these plants were screened in modern literature for anti parasitic effects. Positive results are summarized in the result section.

Results

Etiology, symptoms, manifestation, transmission season, rate Risk, diagnosis of malaria disease in classic medicine and “Tabe Rebá” in Traditional Medical books has been compared in table 3.

Table 3- Comparison of malaria disease in classic medicine and “Tabe Rebá” in Iranian Traditional Medical (IT Medical) books

Topic	Malaria in Classic medicine	Tabe Rebá in IT Medical	IT Medical References
Etiology	<i>Plasmodium vivax</i> Grassi <i>P. malariae</i> feletti and Grassi <i>P. ovale</i> Stephens <i>P. falciparum</i> Welch	Soda or soda infected phlegm	a, b, c, d, e, f, g, h, i, j,
Manifestation	Fever is once in every four or three days long fever or persistent fever for <i>P.Falciparum</i> infection	Fever (Intermittent fever) is once in every four days sometimes long fever	a, c, d, e, g, h, i, j
Symptoms	1. The initial chill, nausea, vomiting and headache, fatigue, abdominal discomfort, muscle pain and diarrhea 2. Fever, the temperature body to 40 ° C for several hours 3. Sweating The incidence of enlarged spleen and liver enlargement	1. high chills, cold with serious bone pain 2. Fever , high the body temperature for 24 hours 3. Excessive sweating ascites and swollen and raised spleen	c , d, e, f, g, h, i c , d, e, f, g, h, i d, e, h c , d, e, g , h,
Transmission season	Peak in late summer and early autumn	Autumn	a, e, d, h, g, i
Rate Risk	malaria disease of <i>vivax</i> , <i>ovale</i> , <i>malariae</i> almost all recovered without treatment after several weeks	Most quarter of fevers are low risk	c , d, e, h, i
Diagnosis	Identification of parasites in thin and thick smears Other methods (QBC, PCR, ELISA...) Black urine and jaundice, in Backwater fever disease	Patient examination: Swollen and raised spleen There is no swelling of the spleen but pain and hurt At the first, the patient's urine color greenish white, raw and undercooked and the end dark urine	c ,d, e, g , h a, c, d, e, g, h, i

Ferdous-ul-hekmah (a) , *Al-Maleki* (b), *Hedayat ul-moteallemin fi-tebb* (c), *the Canon* (d), *Zakhireh Kharazm shahi* (e), *Al-Asbab val `alamat* (f), *Sharhu'l-asbab va'l-' alamat* (g), *Kholasato Al Tajareb* (h), *Tebbe akbari* (i), *Maghame or rashigh lemonkera tebb- ul- atigh* (j)

Traditional names of plants used in treat “Tabe Rebá” and chills in ITM according to *the Canon and Makhzan ul-Adviyyah* was listed in table 4 and checked other Iranian Traditional Pharmacy books that listed in table 2.

Table 4- Plant names found in the five Iranian Traditional Pharmacy books

Traditional name	Used to treat Tabe Rebá	Used to treat Chills
B d ward- Shokkat ol bayz	A,H,Q,M,T	
Bondoq hendi	A,H,Q,M,T	
Gh fes	A,H,Q,M,T	
Koshuth	A,H,Q,M,T	
khardel	A,H,Q,M,T	
R zey naj	A,H,Q,M,T	
Shuniz	A,H,Q,M,T	
Sous	A,H,Q,M,T	
Afsantin	A,Q,M,T	
B bunaj	A,Q,M,T	
Hheltit - Anjodan siy h	A,Q,M,T	
Jóhdah	A,Q,M,T	
N nk h h	A,Q,M,T	M
Sh htaraj	A,Q,M,T	
Shokaee	A,Q,M,T	
Lesan ol hhamal	H,Q,M,T	
Oshtorq r	H,Q,M,T	
R vand	Q,H,M,T	
Abukhals - Shank r	Q,M,T	
Àqherqherha	M,A,T	H,Q
Anjod n sefid	Q,M,T	
Bent phalon- Nit filii	Q,M,T	
Qantaureion	H,Q,M	
Qaysum	A,M,T	H,Q
H lileh	Q,M,T	
Hendeb	Q,M,T	
J vshir	Q,M,T	M
Labl b	A,M,T	H
Soád	Q,M,T	
Varde ahmar	M,A,H	
Anisun	A,Q	
Chube chini	M,T	
Dins qus	M,T	
Hhandaquqi	Q,M	
Huf riqun	M,T	
Im r nut li	M,T	
Jadv r	M,T	
Mor	M,T	Q,H
Rati naj	M,T	
S maryoma	M,T	
Shár ol Jayr d	M,T	
Shih	M,T	Q
Esghil - Onsul	T	H,Q
Qost	T	A,H,Q,M
khel f	T	M
Labakh	Q	
Ósaj	Q	
Shár ol qul	M	
Zar vand tavil	Q	
Zar vand modahhraj	Q	M,H
Zarnab- Rejj ol jar d	Q	

Al-Hawi fi-tebb (H) Al-Abniyah an haqaiq al-adviyah (A), the Canon (Q), Tuhfat ul-Mumenin (T), Makhzan ul-Adviyyah (M)

The scientific name of plants were mentioned in table 4 according to the four references which used to matching the traditional name with scientific names and also anti parasitic effect of proposed plants in ITM that has been reported in previous studies were reviewed in table 5.

Table 5- Scientific names and families of plants used to treat “Tabé Rebá”, recent anti parasitic results relevant to the plants

Traditional name	Scientific name	Family	A	B	C	D	Anti parasitic effect	Source of research
Abukhals - Shank r Afsantin	<i>Alkanna tinctoria</i> Tausch	Boraginaceae	+	+	+	+	Inhibition of <i>Leishmania major</i> antimalaria	(Yousefi, et al., 2009)
	<i>Artemisia absinthium</i> L.	Asteraceae	+	+	+	+		(Zimmerman, et al. 2012)
Àqherqherha	<i>Anacyclus pyrethrum</i> (L.) Lag.	Asteraceae	*	+	+	+	antimalaria	(Zimmerman, et al. 2012)
Anisun Anjod n sefid	<i>Pimpinella anisum</i> L.	Apiaceae	+	+	+	*	larvicidal properties antimalaria	(Moshafi, et al. 2009)
	<i>Heracleum persicum</i> Desf.	Apiaceae	+	+	+	+		
B bunaj	<i>Anthemis nobilis</i> L.	Asteraceae	+	+	-	+	(Saxena, et al. 2003)	
Bad ward – Shokkat ol bayza	<i>Picnomon acarna</i> Cass.	Asteraceae	*	-	+	-		
	<i>Echinops sphaerocephalus</i> L.	Asteraceae		+	-	-		
	<i>Fagonia cretica</i> L.	Zygophyllaceae		-	-	+		
Bondoq hendi	<i>Caesalpinia bonduc</i> (L.) Roxb.	Caesalpinaceae	*	+	+	+		
Nit fili- Bent phalon	<i>Potentilla reptans</i> L.	Rosaceae	*	+	+	*		
Chube chini	<i>Smilax glabra</i> Roxb.	Smilacaceae	+	+	*	*		
	<i>Dipsacus fullonum</i> L.	Dipsacaceae	*	+	+	+		
Dins qus Esghil -Onsul	<i>Urginea maritima</i> (L.) Baker	Hyacinthaceae	+	+	+	*	antiplasmodial	(Sathiyamoorthy, et al. 1999)
	<i>Eupatorium cannabinum</i> L.	Asteraceae	*	+	+	-	antitrypanosomal	(Pyrek, 1985)
Gh fes	<i>Agrimonia eupatoria</i> L.	Rosaceae		-	+	+		
	<i>Terminalia chebula</i> Retz.	Combretaceae	*	*	+	*	antiplasmodial	(Pinmai, et al. 2010)
Hende b	<i>Cichorium intybus</i> L.	Asteraceae	+	+	-	+	antiplasmodial	(Pyrek, 1985; Bischoff, et al. 2004)
Hhandaquqi	<i>Trigonella caerulea</i> (L.) Ser.	Fabaceae	*	+	+	*		
Hheltit- Anjodan siyah	<i>Ferula assa-foetida</i> L.	Apiaceae	+	+	+	*		
	<i>Hypericum perforatum</i> L.	Clusiaceae	+	+	+	*	antiplasmodial	(Zimmerman, et al. 2012)
Im r nut li Jadv r	<i>Verbena officinalis</i> L.	Verbenaceae	*	+	+	*		
	<i>Curcuma zedoaria</i> (Christm.) Roscoe	Zingiberaceae	*	+	+	+		
J vshir	<i>Opopanax chironium</i> W.D.J.Koch	Apiaceae	+	+	+	*		
Jóhdah	<i>Teucrium polium</i> L.	Lamiaceae	*	+	+	*	antiplasmodial	(Sathiyamoorthy, et al.1999)
Koshuth	<i>Cuscuta monogyna</i> Vahl	Convolvulaceae	*	+	-	+		

Traditional name	Scientific name	Family	A	B	C	D	Anti parasitic effect	Source of research
	<i>Cuscuta epithymum</i> Murray	Convolvulaceae		+	+	-		
khardel	<i>Brassica nigra</i> (L.) W.D.J. Koch	Brassicaceae	+	+	+	+		
khel f	<i>Salix. sp.</i>	Salicaceae ae	*	+	*	*		
Labakh	<i>Albizia lebeck</i> (L.) Benth.	Mimosaceae	*	+	+	+		
Labl b	<i>Dolichos lablab</i> L.	Fabaceae	*	-	+	+		
Les n ol hamal	<i>Plantago major</i> L.	Plantaginaceae	+	+	+	*	antiplasmodial	(Clarkson, et al. 2004)
Mor	<i>Commiphora myrrha</i> Engl.	Burseraceae	+	-	+	+		
N nkx h	<i>Trachyspermum copticum</i> L. Link	Apiaceae	*	+	+	*		
Ósaj	<i>Lycium sp.</i>	Solanaceae	*	+	-	*	antiplasmodial	(Abdel-Sattar, et al. 2009)
	<i>Rhamnus cathartica</i> L.	Rhamnaceae	*	-	+	*		
Oshtoq r	<i>Alhagi persarum</i> Boiss. & Bushe	Fabaceae	*	+	*	-		
	<i>Alhagi mannifera</i> Desv.	Fabaceae		+		-		
Qantaureion	<i>Fagonia arabica</i> L.	Zygophyllaceae		-		+		
	<i>Centaurea centaurium</i> L.	Asteraceae	*	+	+	-		
Qaysum	<i>Artemisia abrotanum</i> L.	Asteraceae	-	+	+	+	antimalaria	(Zimmerman, et al. 2012)
Qost	<i>Costus speciosus</i> (J.Koenig) Sm.	Costaceae	*	+	+	+		
Rati naj	<i>Picea excelsa</i> (Lamb.) Link	Pinaceae	*	-	+	*		
	<i>Pinus pinea</i> L.	Pinaceae		+	-			
R vand	<i>Rheum palmatum</i> L.	Polygonaceae	*	+	+	*		
R zeyanaj	<i>Foeniculum vulgare</i> Mill.	Apiaceae	+	+	+	+	antitrypanosomal, antimalarial	(Abdel-Sattar, et al. 2009)
S maryoma	<i>Heliotropium europaeum</i> L.	Boraginaceae	*	+	+	*	antimalaria	(Abdel-Sattar, et al. 2010)
Sh htaraj	<i>Fumaria officinalis</i> L.	Papaveraceae	*	+	*	*		
Shár ol qul	<i>Asplenium trichomanes</i> L.	Aspleniaceae	*	+	*	+		
Shár ol Jayr d	<i>Adiantum capillus-junonis</i> Rupr.	Adiantaceae	*	+	*	*		
Shih	<i>Artemisia santonicum</i> L.	Asteraceae	+	-	*	+		
Shokaee	<i>Onopordum acanthium</i> L.	Asteraceae	*	+	+	*		
Shuniz	<i>Nigella sativa</i> L.	Ranunculaceae	*	+	+	*	antiplasmodial	(Okeola, et al., 2011)
Soád	<i>Cyperus longus</i> L.	Cyperaceae	*	+	+	+		
Sous	<i>Glycyrrhiza glabra</i> L.	Fabaceae	+	+	+	+	antiplasmodial	(Esmaeili, et al., 2009)
Varde ahmar	<i>Rosa damascena</i> Mill.	Rosaceae	*	+	-	*		

Traditional name	Scientific name	Family	A	B	C	D	Anti parasitic effect	Source of research
	<i>Rosa gallica</i> L.	Rosaceae		-	+			
Zar vand tavil	<i>Aristolochia longa</i> L.	Aristolochiaceae	*	+	+	+		
Zar vand modahhraj	<i>Aristolochia rotunda</i> L.	Aristolochiaceae	*	+	+	+		
Zarnab-Rejl ol jar d	<i>Taxus baccata</i> L.	Taxaceae	*	-	+	*		

Nafisi (A), Ghahreman (B), Dini (C), Soltani (D). *: This name is not mentioned in this book. +: This book agrees with this scientific name. -: This book does not agree with this scientific name

61 scientific names related to 51 traditional names used in traditional pharmacy books to treat malaria have been found. Out of them 11 plants belong to the Asteraceae, 6 belong to the Apiaceae and the rest belong to other families.

Discussion

To do necessary experiments for evaluating and confirmation of illness treatment by herbal medicine of ITM, first of all the equivalency of illnesses in classic medicine and traditional medicine should be matched. The term of malaria (mal'aria) was probably first used by the Italian physician FransiscoTorti in 1740 and literary means "bad air" referring to the swamp vapor which supposedly caused the disease (Adams, et al. 2011). There is not the name of malaria in Iranian Traditional Medical and Pharmacy books. In this research according to the studies in some important traditional references, the most likely disease to the malaria can be classified to "tabhaye nubeh" ("intermittent fevers").

By considering known symptoms of malaria and observing different types of "tabhaye nubeh", several similarities between "Tabe Rebá" and malaria has been seen which has been briefed in table 3. Noting the similarity of fever period (quartan) and severe bone pain, strong chills at the beginning of the illness and then fever and sweating, fall season transferring time of the illness, splenomegaly and dark color urine, "Tabe Rebá" may be known as the equivalent of malaria.

In the basis of pharmacy books used in this research, there are 51 medicinal plants (table 4) which were used in ITM to treat "Tabe Rebá". 11 medicinal plants, Aqherqherha, Esghil, Qaysum, Qost, J vshir, khel f, Labl b, Mor, N nkh h, Shih, Zar vand modahhraj are used in chills treatment. Since the red blood cells tearing in malaria is with chills (Wilson, et al. 1991) this matter can be considered in another research.

According to the study for finding different remedies against malaria from the Renaissance time (Adams, et al. 2011) 14% medicinal plants are similar to our study including: *Anacyclus pyrethrum*, *Artemisia absinthium*, *Artemisia abrotanum*, *Eupatorium cannabinum*, *Cichorium intybus*, *Heliotropium europaeum*, *Fumaria officinalis*, *Plantago major*, *Rosa damascene*. Antimalarial/antiplasmodial effects of 6 plants of them, *Anacyclus pyrethrum*, *Artemisia absinthium*, *Artemisia abrotanum* (Zimmerman, et al. 2012), *Cichorium intybus* (Pyrek, 1985; Bischoff, et al. 2004), *Heliotropium europaeum* (Abdel-Sattar, et al 2010), *Plantago major* (Clarkson, et al. 2004) have been reported. Also *Eupatorium cannabinum* has shown antitypanosomal effect (Pyrek, 1985).

In this study, the most cited plants in the traditional pharmacy books are B d ward, Bondoq hendi, Gh fes, Koshuth, Khardel, R zey naj, Shuniz and Sous. R zey naj, *Foeniculum vulgare*, (Abdel-Sattar, et al. 2009), Shuniz, *Nigella sativa* (Okeola, et al. 2011) and Sous, *Glycyrrhiza glabra* (Esmaeili, et al. 2009) have shown antiplasmodial/ antimalarial activity.

Conclusion

Totally about 31% of plants mentioned in this study have been reported as anti parasitic especially antiplasmodial/antimalarial agents. It seems the other plants could be promising candidates for further investigating antimalarial properties.

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The number of plants used to treat malaria or fever in traditional medicine appears almost unlimited, some species of plants are used as antimalarials or antipyretics in all three tropical continents (1). This world-wide experience showing more or less efficacy of various different plant species to clear parasites and fever suggests that the chemical structures of effective plant components may differ considerably. Recently we found that extracts from various plants used in traditional medicine such as *Uncaria tomentosa*, *Hypericum perforatum* For centuries, malaria was treated with the bark of *Cinchona calisaya* and *Cinchona succirubra* plants named "quinas" in Brazil, from which the quinine molecule was isolated. Other plant species known also as "quinas" are used to treat fever and malaria, like *Deianira erubescens* (roots and leaves), *Strychnos pseudoquina* (bark), and *Remijia ferruginea* (bark). Based on this popular knowledge, we evaluated the in vivo antimalarial activity of the ethanol crude extracts of these plant species in mice infected with *Plasmodium berghei*. Only *Remijia ferruginea* showed antimalarial ac