




Materia Medica Used in Jaundice Based on Persian Medicine

Hossein Bakhshi Jouybari^{1,2,3}, Amir Saeed Hosseini⁴, Ali Davoodi^{1,2,3}, Fatemeh Mirzaee^{1,2},
Mohammad Azadbakht^{1*} 

¹Department of Pharmacognosy, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

²Pharmaceutical Sciences Research Center, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

³Medicinal Plants Research Center, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.

⁴Traditional and Complementary Medicine Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran.

Abstract

Jaundice is recognized by increased bilirubin level of blood and yellow appearance in skin, sclera and mucous membrane. Natural products have been used for treatment of jaundice for a long time and Persian Medicine can be a good source of natural drugs for this purpose. This study was done to find the materia medica used for jaundice based on Persian medicine (PM) texts including The Canon of Medicine (al-qanun), Al Hawi Fi Al Tibb, Tuhsat al-Mu'minin, Hedayat al-Motealemin fi Tibb, Zakhireye Khwarazmshahi, Al-Abniah 'an Haqaeq al-Adwia, Makhzan ul-Adwia and Ikhtiyarat Badie. One hundred eleven materia medica belonging to 51 families were identified as herbal remedies for treating jaundice. Apiaceae, Asteraceae, Cucurbitaceae, Fabaceae, Lamiaceae, Rosaceae and Zingiberaceae were the most dominant families. The results of this study may be present sources for pharmacological studies and development of new herbal medicines for jaundice. Asparagus, echium, arnebia, chicory, citron and purgative manna could be good candidate Materia Medica for future studies.

Keywords: bilirubin; herbal remedy; jaundice; materia medica; Persian medicine

Citation: Bakhshi Jouybari H, Hosseini AS, Davoodi A, Mirzaee F, Azadbakht M. Materia medica used in jaundice based on Persian medicine. Res J Pharmacogn. 2018; 5(4): 83-93.

Introduction

The word jaundice has French origin which implicates yellow color. Jaundice is recognized by yellow appearance in skin, sclera and mucous membrane due to bilirubin [1]. Normally, bilirubin is conjugated with glucuronic acid in hepatocytes and excreted in bile. Bilirubin is a product of haem catabolism and mainly results from the hemoglobin breakdown in the reticuloendothelial system [2,3]. In newborns, a degree of serum non-conjugated bilirubin increases in the first few days of life that is called physiological jaundice. The neonatal jaundice is observed in about 60% of term and 80% of preterm infants. Jaundice is more common in

infants than adults [1,4,5]. Normal serum level of bilirubin in adults is 0.3-1.0 mg/dL and levels higher than 3 mg/dL indicate jaundice [6]. It is categorized into three types based on location of bilirubin metabolism and stage of aggregates in body.

i. Pre-hepatic jaundice that is divided as haemolytic and nonhaemolytic. The most important causes of hemolytic jaundice can be blood incompatibility, G6PD deficiency, thalassemia, autoimmune disorders, drugs, etc.

ii. Hepatic jaundice, Gilbert syndrome, intrahepatic cholestasis, drugs, alcohol, autoimmune disorders, viruses (hepatitis A, B, C

*Corresponding author: Azadbakhtm@hotmail.com, MAzadbakht@mazums.ac.ir

and Epstein-Barr virus), bacteria, malaria which can create jaundice caused by damage to liver cells.

iii. Post-hepatic jaundice which is divided into two types: internal and external. In internal type, obstruction in the bile duct is caused by stones, tumors or infections leading to increased levels of bilirubin. However, in the external type, the cause is outside of the hepatobiliary tract (e.g., pancreatitis and cancer) [1,6-9]. Bilirubin can be toxic and cause serious side effects, especially in infants [10]; high levels of bilirubin in the brain cause encephalopathy and life-threatening events [11].

High alcohol consumption in developed countries [12] and contamination of some foods such as cereals with pesticides, aflatoxins and some plant toxins such as pyrrolizidine alkaloids in Boraginaceae family and Senecio genus and industrial pollution are some risk factors for liver damage and cancer [13-18]. Nowadays there is a concern about the incidence of liver disorders and jaundice. Natural products are main sources in drug discovery thus half of approved drugs since 1994 have natural origins mostly from plants. Humans have used plant as medicine for long time, and this goes back to 60,000 years ago. From 250000-500000 of estimated plant species throughout the world, only about 6% have been screened for biological activities. Bioactive compounds isolated from plants can be used directly as drugs (e.g., morphine, digoxin, taxol), or as lead compound for synthesis of novel bioactive molecules with high efficacy and low toxicity (e.g., oxycodon, taxotere, verapamil, which are based on morphine, taxol, khellin, respectively) [19]. In some cases, the whole or a part of a plant can be used as an herbal remedy (e.g., butcher's broom, calendula, garlic, ginkgo, St. John's wort). Traditional medicine plays an important role in introducing medicinal plants. Plants have been used for long time in traditional medicine around the world. They are sources of new bioactive compounds with potential therapeutic activities [19-21]. In recent years, many studies have been done about medicinal plants and their traditional uses from different regions around the world [22]. Persian medicine (PM), known by prominent physicians Avicenna and Rhazes, has a long history, more than 4000 years [23]. It encompasses considerable topics in prevention, diagnosis and treatment of diseases

(figure 1). Natural materials especially herbs were predominantly used as therapeutic agents [24]. PM scholars believed that the quiddity of all beings originated from the nature of four elements: water, fire, air and soil.

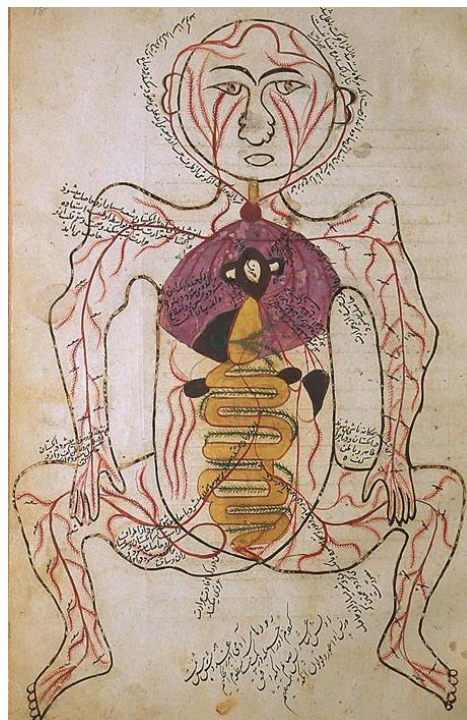


Figure 1. A part of human anatomy adopted from “Mansur's anatomy” by Mansur Ibn Ilyasin 14-15th A.D [26]

Hence these elements were called “quadruplet pillars” and each of these had specific quality. Accordingly; water is cold and wet; fire is hot and dry; air is hot and wet and soil is cold and dry. Difference between creatures is due to differences in the amount and proportion of the elements. These qualities in beings are called temperament [25,26]. Based on PM during the four steps of digestion, foodstuffs in the body would convert to four types of materials (“Khelt” or humor); “Saphra” or yellow bile with hot and dry qualities, “Souda” or black bile with cold and wet qualities, “Balgham” or phlegm with cold and wet qualities, “Dam” or blood with hot and wet qualities”. Each of the humors plays a specific role within the body and is essential for health. Different conditions and factors can produce abnormal humor and their accumulation will cause diseases [27,28].

Based on PM texts, jaundice was known by changing the color of the face and eyes to yellow (figure 2). “Yaraghan” and “Zardi” were related

to jaundice in PM literatures. About 15 factors have been considered for jaundice that were divided into two categories:

- i. Jaundice caused by excess bile production as a result of some foods, drugs, toxins and increase in body temperature
- ii. Jaundice due to obstruction in bile ducts [29].

Methods

This survey has investigated important traditional medicine books including; i. The Canon of Medicine (al-qanun), Al Hawi Fi Al Tibb, Tuhfat al-Mu'minin, Hedayat al-Motealemin fi Tibb, Zakhireye Khwarazmshahi, Al-Abniah 'an Haqaeq al-Adwia, Makhzan ul-Adwia and Ikhtiyarat Badie, which have been written between the 9 and 19 centuries. The terms “Yaraghan”, “Yaraghan-e-asfar”, “Yaraghan-e-zard”, “Zardi” were all keywords indicated to jaundice in reviewed references. Thus, these keywords were searched in the texts. Then, plant and herbal product were selected among all results. Finally, the traditional names collected from the texts and were matched with scientific names using descriptions of Iranian physicians about morphological, anatomical and ecological characteristics of the plants [30-33]. Electronic databases including PubMed, Scopus, ScienceDirect, and Google Scholar were searched for jaundice, Persian medicine, neonatal jaundice, bilirubin, hepatitis and hepatotoxicity keywords.

Results and Discussion

In the present study, we investigated the main ancient Iranian herbal books to detect materia medica used for treatment of jaundice. We obtained 111 materia medica including 110 plant products and one fungus. Table 1 has exhibited materia medica (with the Iranian traditional name) that were arranged by plant family in alphabetical order and scientific name, common name, parts used and the data collection sources. All herbals belong to 51 families; Apiaceae, Asteraceae, Cucurbitaceae, Fabaceae, Lamiaceae, Rosaceae and Zingiberaceae were the most dominant families. The classification of plants according to Angiosperm Phylogeny Group (APG) have been shown in table 2. Among aforementioned materia medica, some with the following properties such as data frequency in the literatures, high therapeutic effects in jaundice based on PM, safety and long-

term use in various disorders were selected (figure 3). These have been briefly introduced in the following section.

Asparagus

Asparagus officinalis L. (Asparagaceae) (figure 3, A) is a spring vegetable, flowering perennial and rhizomatous plant with woody tenuous branches that is harvested when it is 20-30 cm high. Asparagus genus has 150 species and five species that grow in Iran. It is cultivated in most parts of the world and is a popular edible plant [31,34-36]. In PM literatures, Asparagus has been called “Halyoun” and “Marchoobeh” and is used for toothache palliation, diuretic and increase in libido [37]. In recent studies, polysaccharides, flavonoids and steroidal saponins isolated from Asparagus have shown anti-inflammatory and anti-cancer effects [34,38].



Figure 2. The frontispiece of the Jaundice chapter of Zakhireye Khwarazmshahi [36].

Echium

Echium amoenum Fis. & Mey. (Boraginaceae) (figure 3, B) is a biennial or perennial herb with abundant rough trichomes [39]. It grows widely in north of Iran. Its Persian name is Gol-e-gavzag that means ox tongue [40].

Table 1. Mareria medica used for jaundice treatment based on Iranian ancient herbal books

Family	Traditional name	Scientific name	Common name	Part(s) used	References
Alliaceae	Basal	<i>Allium cepa</i> L.	Onion	Bulb	1-3,34,55
Agaricaceae	Ghareyghoun	Unknown	-	Whole part	1-8,34,55
Amaranthaceae	Ghataf	<i>Atriplex</i> sp.	Saltbush	Seed	1,2,4,7,8,34,55
	Anjodan	<i>Levisticum officinale</i> Koch.	Lovage	Seed	1,2,34,55
	Daryas	<i>Thapsia</i> spp.	Deadly carrots	Fermented	1,2,34,55
	Ghorrat-ol-ayn	<i>Sium latifolium</i> L.	Great water-parsnip	Leave, seed essential oil	1,2,34,55
	Jav'sheer	<i>Opopanax chironium</i> (L.) Kock	Sweet myrrh	Oleo-gum-resin	1,34,55
Apiaceae	Heltit	<i>Ferula assa-foetida</i> L.	Asafoetida	Oleogum resin	1,2,3,8,34,55
	Razyanaaj	<i>Foeniculum vulgare</i> Mill.	Fennel	Seed, root	4,5,34,55
	Razyaneh-e-barry	<i>Hippomarathrum libanotis</i> Koch.	Hippomarathon	Seed	1,2,34,55
	Safeydolioun	<i>Heracleum spondylium</i> L.	Common hogweed	Fruit	1,2,34,55
	Shebbet	<i>Anethum graveolens</i> L.	Common dill	Aerial part	2,5,6,34,55
	Asaroon	<i>Asarum europaeum</i> L.	Wild spikenard	Root	1-4,34,55
Aristolochiaceae	Zaravand-e-modahraj	<i>Aristolochia rotunda</i> L. <i>A. indica</i> L.	Birth wort	Root	1,2,34,55
Asparagaceae	As-e-Barry	<i>Ruscus hyrcanus</i> L.	Butcher's broom	Leave, fruit	1,2,34,55
	Halyoun	<i>Asparagus officinalis</i> L.	Asparagus	Root	3,8,34,55
Asphodelaceae	Sebr	<i>Aloe vera</i> L.	Medicine aloe	Aerial part	1-6,34,55
Aspleniaceae	Osgholohandaryoun	<i>Asplenium scolopendrium</i> L.	Hart's- tongue fern	Whole part	1,2-4,8,34,55
	Afsanteen	<i>Artemisia absinthium</i> L.	Absinthium	Aerial parts	1-7,34,55
	Azaryoun	<i>Calendula officinalis</i> L. <i>C. arvens</i> (Vaill) L.	Calendula	Leave, flower	1,2,34,55
	Baboonaj	<i>Matricaria disciforme</i> L.	Chamomile	Flower	1,2,34,55
	Bad-avard	<i>Echinops</i> spp.	Globe thistles	Root	1,2,34,55
Asteraceae	Lahyat-ol-teys	<i>Tragopogon prantensis</i> L.	Salsify	Root	8,34,55
	Tobagh	<i>Inula</i> sp.	Inula	Leave, flower	1,2,34,55
	Ghantaurioun-e-kabear	<i>Centaurea</i> sp.	Centaury	Root	1,2,5,34,55
	Moondi	<i>Sphaeranthus africanus</i> L. <i>S. indicus</i> L.	Mundi	Aerial part	1,34,55
	Hendebe	<i>Cichorium intybus</i> L.	Cichory, Seris	Leave, seed	1,2,5, 6-8,34,55
Brassicaceae	Fojl	<i>Raphanus sativus</i> L.	Radish	Leave, root	1,3- 6,8,34,55
	Ghonnabari	<i>Lepidium draba</i> L.	Hoary cress	Leave	1,2,34,55
	Kornob	<i>Brassica oleracea</i> L.	Cabbage	Leave	3,5,34,55
Boraginaceae	Abu-khalsa	<i>Arnebia euchroma</i> (Royle) I. M. Johnst	Arnebia	Root	1-4,34,55
	Lesan-ol-soor	<i>Echium amoenum</i> Fis. & Mey.	Iranian borago	Flower	1,2,34,55
Burceraceae	Lythabotes	<i>Boswellia sacra</i> Flueck. <i>B. frereana</i> Birdw.	Frankincense	Fruit	4,34,55
Caryophyllaceae	Kondos	<i>Gypsophila struthium</i> L.	Baby's-breath	Root	1,2,34,55
	Satroonyoun	<i>Saponaria officinalis</i> L.	Soapweed	Root	1,2,4,34,55
	Lakhneys	<i>Lychnis</i> sp.	Lychnis	Seed, leave	2,34,55
Colchicaceae	Soorenjan	<i>Colchicum</i> sp.	Autumn crocus	Bulb	1,2,34,55
Convolvulaceae	Chalapa	<i>Ipomoea jalapa</i> (L.) Pursh.	Jalap	Root	1,34,55
	Koshouth	<i>Cuscuta</i> sp.	Devil's guts	Seed	1,2, 4-8,34,55
	Bet-tikh	<i>Cucumis melo</i> L.	Musk melon	Fruit, seed	1,5,6,34,55
	Bettikh-e-Hendi	<i>Citrullus lanatus</i> (Thunb.) Matsum. & Nakai	Water melon	Fruit	1,2,5,7,34,55
Cucurbitaceae	Bandal	<i>Luffa echinata</i> Roxb.	Luffa	Root, seed	1,34,55
	Ghasd	<i>Cucumis sativus</i> L.	Cucumber	Fruit	1-5,34,55
	Ghar'e	<i>Cucurbita pepo</i> D.C.	Squash	Fruit	1,2,6,8,34,55
	Kareyla	<i>Momordica charantia</i> Descourt.	Bitter melon	Fruit	1,34,55
	Hanzal	<i>Cucum iscolocynthis</i> L.	Colocynth	Fruit	2,4,34,55
	Ghesa	<i>Cucumis flexuosus</i> L.	Snake cucumber	Fruit	4,34,55
Cyperaceae	So'd	<i>Cyperus longus</i> L. <i>C. rotundus</i> L.	kuperios	Root	1,2,34,55
Euphorbiaceae	Afyous	<i>Euphorbia apios</i> L.	Apios	Fruit	1,3,34,55

Table 1. Continued					
Family	Traditional name	Scientific name	Common name	Part(s) used	References
	Dand	<i>Croton tiglium</i> L.	Purging Croton	Seed	1,2,34,55
Elaeagnaceae	Ghobayra	<i>Elagnus angustifolius</i> L.	Oleaster	Flower	1,2,34,55
	Oshtorghar	<i>Alhagi mannifera</i> Desv.	Camel thorn	Manna	1,34,55
	Hemmas	<i>Cicer arietinum</i> L.	Garbanzo bean	Seed	1-4,6,34,55
	Khornoub	<i>Ceratonia siliqua</i> L.	Carob	Gum	1,2,34,55
	Ceres	<i>Albizia lebbek</i> (L.) Benth.	Lebbeck	Leaf	1,34,35
	Kaat	<i>Acacia catechu</i> (L. f.) P. J. H. Hurter & Mabb.	Catechu	Gum	1,34,55
Fabaceae	Karasnah	<i>Vicia ervillia</i> L. (Willd.)	Vetch	Seed	1,2,6,34,35
	Handaghoughi	<i>Trigonella caerulea</i> Ser.	Fenugreek	Seed	1,2,34,55
	Bonn	<i>Gymnocladus dioica</i> L. K Koch	Kentucky coffee	Seed	1,34,55
	Retteh	<i>Caesalpinia bonduc</i> (L.) Roxb.	Gray Nicker	Fruit	2,3,8,34,55
	Tamr-e- hendi	<i>Tamarindus indica</i> L.	Indian date	Fruit	5,6,8,34,55
Fumariaceae	Shahtareh	<i>Fumaria</i> spp. <i>Iris florentina</i> L.	Fumitory	Aerial part	1,2,5,6,34,55
Iridaceae	Earsa	<i>I. germanica</i> L. <i>I. ensata</i> Thunb	Iris	Root, rhizome	1,2,34,55
	Foodanaj	<i>Mentha longifolia</i> (L.) Hudson	Wild mint	Aerial part	1-5,7,8,34,55
	Ghastaroon	<i>Stachys officinalis</i> (L.) Trevis.	Hedgenettle	Seed	1,34,55
	Kamazaryous	<i>Teucrium chamaedrys</i> L.	Wall germander	Root	1,2,34,55
Lamiaceae	Komafeytous	<i>Ajuga iva</i> L. <i>A. chamaepitys</i> (L.) Schreb	Bugleweed	Leave	1,2,4,34,55
	Na'na	<i>Mentha</i> spp.	Mint	Aerial part	1,3,6,8,34,55
	Sa'tar	<i>Zataria multiflora</i> Boiss.	-	Seed	1,2,34,55
Lauraceae	Darseyni	<i>Cinnamomum</i> spp.	Cinnamon	Bark	1,2,8,34,55
Liliaceae	Esgheal	<i>Uriginea maritima</i> (L.) Stearn	Skilla	Bulb	1-4,34,55
	Ashras	<i>Asphodelus ramosus</i> L.	Hypocistis	Root	1,2,34,55
Lythraceae	Henna	<i>Lawsonia inermis</i> L.	Henna	Leaf	1,2,34,55
Malvaceae	Khobbazi	<i>Malva neglecta</i> L. <i>M. rotundifolia</i> L.	Mallow	Aerial part	1,2,34,55
Menispermaceae	Kelovi	<i>Tinospora cordifolia</i> (Thunb.) Miers	Guduchi	Stem	1,34,55
Myristicaceae	Joz'boa	<i>Myristica fragrans</i> Hou.	Nutmeg	Fruit	1,2,34,55
Orobanchaceae	Asad-ol-adas	<i>Orobanche</i> spp.	Broomrape	Whole plant	1,2,34,55
Papaveraceae	Mamiran	<i>Chelidonium majus</i> L.	Celandine	Root	1,3,34,55
Pinaceae	Sanobar	<i>Pinus</i> spp.	Pine	Seed	1,2,34,55
Pistachiaceae	Fostogh	<i>Pistacia vera</i> L.	Common pistache	Fruit	1,2,5,6,34,55
	Hammaz	<i>Rumex conglomeratus</i> L.	Sorrel	Root	1,2,3,7,34,55
Polygonaceae	Raavad	<i>Rheum palmatum</i> L.	Chinese rhubarb	Root	1,2,5,6,34,55
	Reybas	<i>Rheum ribes</i> L.	Rhubarb	Aerial part	1,2,34,55
Primulaceae	Bakhor Maryam	<i>Cyclamen purpurascens</i> Miller <i>C. hederifolium</i> Aiton <i>C. persicum</i> Mill.	Cyclamen	Corm	1,2,7,8,34,55
Pteridaceae	Par-e-siavashan	<i>Adiantum capillus-veneris</i> L.	Maidenhair	Whole part	1-6,8,34,55
Punicaceae	Romman	<i>Punica granatum</i> L.	Pomegranate	Fruit	1,2,5,6,34,55
Ranunculaceae	Shoneaz	<i>Nigella sativa</i> L.	Nigella	Seed	1,2,8,34,55
	Kharbagh-e- siah	<i>Helleborus niger</i> L.	Black hellebore	Root	2,7,34,55
Rhamnaceae	Amelyles	<i>Rhamnus alaternus</i> L.	Mediterranean buckthorn	Root	1,34,55
	Bentaphalon	<i>Potentilla reptans</i> L.	Creeping cinquefoil	Leave	1-3,34,55
	Safarjal	<i>Cydonia oblonga</i> Mill.	Quince	Fruit	1,2,34,55
Rosaceae	Loz-ol-morr	<i>Amygdalus communis</i> var. <i>amara</i>	Bitter almond	Seed	1,2,5,6,34,55
	Nasrean	<i>Rosa canina</i> L. <i>R. moschata</i> Herrm.	Rose	Flower	1,2,5,6,34,55
	Shir-e-khesht	<i>Contoneaster</i> spp.	Purgative manna	Manna	1,3,34,55
Rubiaceae	Fov-vah	<i>Rubia tinctorium</i> L.	Eruthrodanon	Root	1,2,34,55
Rutaceae	Otroj	<i>Citrus medica</i> L.	Persian apple, citron	Fruit	1-3,6,7,34,55
	Sodab	<i>Ruta graveolens</i> L.	Rue	Aerial parts	1,2,34,55

Table 1. Continued

Family	Traditional name	Scientific name	Common name	Part(s) used	References
Salicaceae	Khelaph	<i>Salix</i> spp.	Willow	Leave	1-3,7,8,34,55
Solanaceae	Fealzahraj	<i>Lycium afrum</i> L.	kraal honeythorn	Fruit, leave	1,3,4,8,34,55
	Kakanj	<i>Physalis alkekengi</i> L.	Winter cherry	Fruit, seed	1-3,6,8,34,55
Tamaricaceae	Asl	<i>Tamarix</i> spp.	Tamarisk	Fruit	1,2,34,55
Thymelaeaceae	Mazaryoun	<i>Daphne mezereum</i> L.	Mezereon	Leave	1,2,34,55
Valerianaceae	Sonbol	<i>Nardostachys jatamansi</i> D.C.	Nardin	Root	1-3,5,8,34,55
	Sonbol-e-roomi	<i>Valeriana</i> sp.	Valerian	Root	1,2,34,55
Verbenaceae	Eyaranootani	<i>Verbena supine</i> L.	Vervain	Leave	1,34,55
Vitaceae	Zabeyb	<i>Vitis vinifera</i> L.	Grape vine	Fruit	1,2,34,55
	Jadvar	<i>Curcuma zedoaria</i> (Berg.) Roscoe	White turmeric Black turmeric	Rhizome	1,2,34,55
		<i>C. caesia</i> Roxb.			
Zingiberaceae	Zanjabeel	<i>Zingiber officinale</i> Rosc.	Ginger	Rhizome	1,2,34,35
	Oroogh-ol-sophr	<i>Curcuma longa</i> L.	Turmeric	Rhizome	1-4,7,34,55
	Ghost	<i>Alpinia</i> sp.	Ginger-lilies	Rhizome	1,2,34,55
<i>Costus</i> sp.		Spiral gingers			
Zygophyllaceae	Hormal	<i>Peganum harmala</i> L.	Espanid	Seed	1,2,34,55

Among the four *Echium* species distributed in Iran, *E. amoenum* Fis. & Mey. Has been used as a medicinal plant in PM [41,42]. *Echium* petals are prescribed as tonic, tranquilizer, and anxiolytic in PM and they are also used in modern medicine. Recently, it has been used as anti-inflammatory, antifebrile, laxative, diuretic and protective factor against cancer [40,43]. Its Flowers contains phenolic compounds (e.g. delphinidin, rosmarinic acid), volatile oil and mucilage [44]. Pyrrolizidine alkaloids are plant toxins which are found in different parts of *E. amoenum* Fis. & Mey. Surprisingly, research by Azadbakht and co-workers have shown that the amount of pyrrolizidine alkaloids is very trace and can be safe for oral use [13]. In high doses up to 6 mg/kg, no side effects have been observed [45].

Table 2. Classification of the materia medica based on APG (angiosperm phylogeny group)

group	number
Monilophytes	2 (1.8%)
Gymnosperms	1 (0.9%)
Magnoliids	4 (3.6%)
Monocotyledons	13 (11.7%)
Eudicots	90 (81.0%)
Fungi	1 (0.9%)

Arnebia

Arnebia euchroma (Royle) I.M. Johnston (figure 3, C) is herbaceous plant and belongs to Boraginaceae family. It grows in Asia and north of Africa [46]. *Arnebia* genus consist of 7 annual and perennial species in Iran [31]. In PM as well as traditional Chinese medicine, *Arnebia* root has

been used for treatment of jaundice and burns [37,47]. Naphthoquinone derivatives from *Arnebia* root have shown anti-inflammatory and anti-platelet activation effects [46,48]. *Arnebia* root has also shown to be effective for treatment of second degree burn wounds [49]. Pyrrolizidine alkaloids can also be found in the roots of *A. euchroma*. The total concentration of these compounds was found to be only about 10 ppm [50] and their toxicity has not been reported until now.

Chicory

Cichorium intybus L. (chicory) (figure 3, D) from Asteraceae family is a perennial herb. *Cichorium* genus has three species in Iran. Its Persian common name is "Kasni," while its traditional name is "Hendebe" [31,51]. According to the ancient medical texts, Iranian scientists have believed that chicory could unplug hepatic ducts obstruction [52] and was also used laxative, diuretic, hepatotonic, appetizer and for treatment of jaundice [51]. Recent studies on phenolic compounds of chicory seeds have exhibited hepatoprotective activity [53]. Cichotyboside, a sesquiterpene lactone glycoside, isolated from seeds of *C. intybus* has shown anti-hepatotoxic activity against toxicity induced by CCl₄ [54]. In other studies, anti-diabetic, anti-malarial, anti-inflammatory, diuretic and anti-cancer effects of chicory were proved [55-59].

Citron

Citrus medica L. (citron or Persian apple) (figure 3, E) belongs to Rutaceae family.

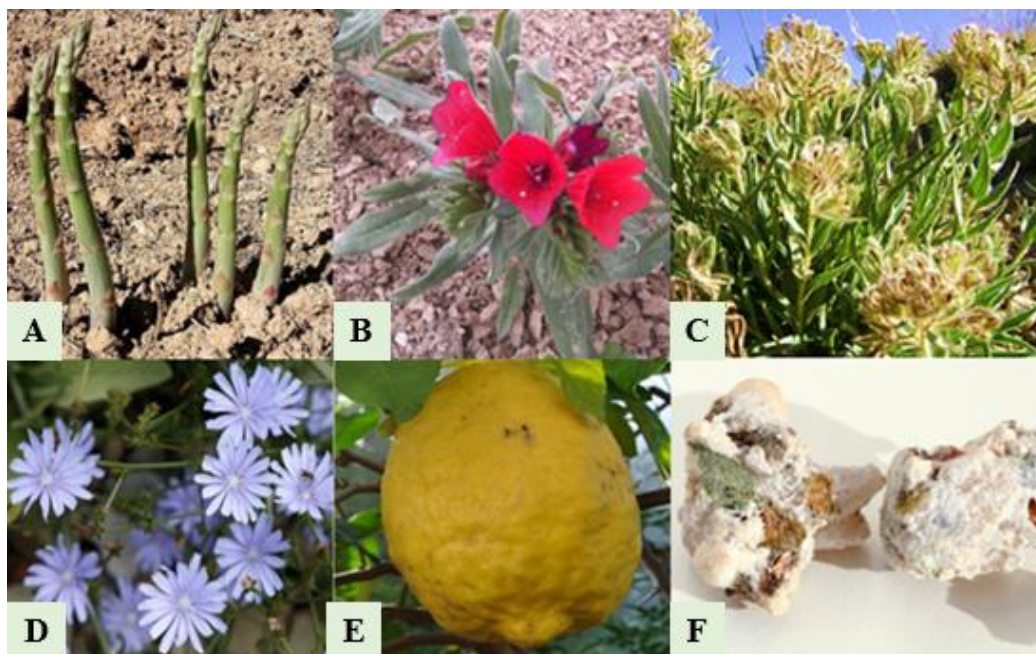


Figure 3. The selected Iranian materia medica used in jaundice; A: Asparagus, B: Echium, C: Arnebia, D: Chicory, E: Citron, F: Purgative manna [42]

Citrus genus has numerous species and hybrids in Iran. This plant is distributed in Asia, Mediterranean region, middle and south of America [31]. In PM literatures the fruit of citron are called “Balang”, “Toranj”, “Torang” and “Otroj”. Different parts of citron fruit have various effects. Based on the Canon of medicine, yellow peel of citron has been used as a tonic for heart, liver, brain, stomach and as anti-nausea. Citron oil has been used for osteoarthritis, sciatica and eczema, and its fruit for treatment of headache [37,60,61]. Recent pharmacological studies on various parts of citron fruit have exhibited as anti-helminthic [62], cytotoxic [63], antidiabetic, hypolipidemic, antifungal [64,65], antimutagenic [66] and antiulcer [67] effects. Citron contains organic acids, polyphenols, flavonoids, pectin, vitamin C, beta-carotene and dietary fibers [61,68,69]. Limonene, γ -terpinen, geranial are major compounds of citron essential oil [70].

Purgative manna

Purgative manna (Persian name: “Shir-e-khesht”) (figure 3, F) is a manna that is produced by *Cotoneaster* species (Rosaceae family) affected by a type of insects. *Cotoneaster* genus has 19 perennial shrubs in Iran. Purgative manna is amorphous and white to yellow pieces with a

sweet taste and cooling properties. In PM, “Shir-e-khesht” was used as laxative, biliousness and hepatotoxic [71]. It has been prescribed by traditional healers “Attar” for treatment of jaundice [5]. The main ingredient of Purgative manna is mannitol and slight amounts of fructose, glucose, sucrose, mucilage and resin. Radioprotective and anticancer effects of the manna have been reported recently [72]. In a clinical trial about infant jaundice, purgative manna has shown a significant effect in reducing serum bilirubin [71].

Conclusion

Jaundice is a condition caused by increase in serum bilirubin due to various diseases and conditions. The main symptom of this disorder is yellowing of the skin and mucous membranes. According to modern medicine and PM studies in this article, it is suggested that this disorder was well-known by Iranian physicians. In the present study, we have collected numerous materia medica used for treatment of jaundice based on PM texts. Also, according to the ethnobotanical information in some areas of Iran, a number of studies have been done about the medicinal plants used for treatment of jaundice [5,73]. Today, *Cotoneaster* manna is used in Iran extensively. Besides, many clinical trials have

suggested Cotoneaster manna as a good choice in prevention and treatment of Jaundice especially neonatal jaundice [71]. Only about 15% homology with this paper was observed in these studies. The large number of Materia Medica presented by this survey can be good sources for future research to find new herbal remedies for jaundice.

Acknowledgments

This work was supported by the Mazandaran University of Medical Sciences. The authors are grateful to Mazandaran University of medical sciences, Sari, Iran for their support.

Author contributions

Hossein Bakhshi Jouybari was the main study investigator; Amirsaeed Hosseini was a study investigator and contributed to the collection of the data; Ali Davoodi participated in the data interpretation and revised the manuscript; Fatemeh Mirzaee participated in the data interpretation; Mohammad Azadbakht was the study investigator, contributed to the collection of the data, and critically revised the manuscript.

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] Roche SP, Kobos R. Jaundice in the adult patient. *Am Fam Physician*. 2004; 69(2): 299-308.
- [2] London IM, West R, Shemin D, Rittenberg D. On the origin of bile pigment in normal man. *J Biol Chem*. 1950; 184(1): 351-358.
- [3] Dennery PA. Pharmacological interventions for the treatment of neonatal jaundice. *Semin Neonatol*. 2002;7(2): 111-119.
- [4] Brito MA, Silva RF, Brites D. Bilirubin toxicity to human erythrocytes: a review. *Clin Chim Acta*. 2006; 374(1): 46-56.
- [5] Fakhri M, Azadbakht M, Yousefi SS, Mousavinasab SN, Farhadi R, Azadbakht M. Medicinal plants for treatment of neonatal jaundice by community of attars (traditional healers) of several urban areas in Mazandaran province, northern of Iran. *Br J Med Med Res*. 2016; 14(11): 1-13.
- [6] Ho NK. Neonatal jaundice in Asia. *Baillière's clin Haemat*. 1992; 5(1): 131-142.
- [7] Ducci H. Contribution of the laboratory to the differential diagnosis of jaundice. *JAMA*. 1947; 135(11): 694-698.
- [8] Zimmerman HJ, Fang M, Utili R, Seeff LB, Hoofnagle J. Jaundice due to bacterial infection. *Gastroenterology*. 1979; 77(2): 362-374.
- [9] Mohapatra M. The natural history of complicated falciparum malaria-a prospective study. *J Assoc Physicians India*. 2006; 54(1): 848-852.
- [10] Fevery J. Bilirubin in clinical practice: a review. *Liver Int*. 2008; 28(5): 592-605.
- [11] Tiribelli C, Ostrow JD. The molecular basis of bilirubin encephalopathy and toxicity: report of an EASL *Single Topic Conference*, Trieste, Italy, 1-2 October, 2004. *J Hepatol*. 2005; 43(1): 156-166.
- [12] Thursz M, Morgan TR. Treatment of severe alcoholic hepatitis. *Gastroenterology*. 2016; 150(8): 1823-1834.
- [13] Azadbakht M, Nematzadeh G, Azad N, Shokri E. Quantitative and qualitative investigation of pyrrolizidine alkaloids in roots, leaves, petals and seeds of Iranian *Echium amoenum* Fisch. & Mey. *J Mazandaran Univ Med Sci*. 2012; 21(1): 131-137.
- [14] Azadbakht M, Talavaki M. Qualitative and quantitative determination of pyrrolizidine alkaloids of wheat and flour contaminated with Senecio in Mazandaran Province farms. *Iran J Pharm Res*. 2010; 2(2): 179-183.
- [15] Barrett JR. Liver cancer and aflatoxin: new information from the Kenyan outbreak. *Environ Health Perspect*. 2005; 113(12): 837-838.
- [16] Shokrzadeh M, Azadbakht M, Abadean S, Abotorabi M. The effect of *Diospyros lotus* on liver glutathione level in mice administered by *Senecio vulgaris* extract. *J Mazandaran Univ Med Sci*. 2013; 23(98): 200-206.
- [17] Kopelman H, Robertson M, Sanders P, Ash I. The epping jaundice. *Br Med J*. 1966; 1(5486): 514-520.
- [18] Rapisarda V, Loreto C, Malaguarnera M, Ardiri A, Proiti M, Rigano G, Frazzetto E, Ruggeri MI, Malaguarnera G, Bertino N, Malaguarnera M, Catania VM, Di Carlo I, Toro A, Bertino E, Mangano D, Bertino G.

- Hepatocellular carcinoma and the risk of occupational exposure. *World J Hepatol.* 2016; 8(13): 573-580.
- [19] Shafiee F, Khoshvishkaie E, Davoodi A, Dashti Kalantar A, Bakhshi Jouybari H, Ataee R. The determination of blood glucose lowering and metabolic effects of *Mespilus germanica* L. hydroacetic extract on streptozocin-induced diabetic Balb/c mice. *Medicines.* 2018; 5(1): 1-7.
- [20] Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. *Environ Health Perspect.* 2001; 109(1): 69-75.
- [21] Harvey AL. Natural products in drug discovery. *Drug Discov Today.* 2008; 13(19): 894-901.
- [22] Heinrich M. Ethnobotany and its role in drug development. *Phytother Res.* 2000; 14(7): 479-488.
- [23] Rossato SC, De Leitão-Filho HF, Begossi A. Ethnobotany of caiaçaras of the Atlantic Forest coast (Brazil). *Econ Bot.* 1999; 53(4): 387-395.
- [24] Mikaili P, Shayegh J, Asghari MH, Sarahroodi S, Sharifi M. Currently used traditional phytomedicines with hot nature in Iran. *Biol Res.* 2011; 2(5): 56-68.
- [25] Rezaeizadeh H, Alizadeh M, Naseri M, Ardakani MS. The Traditional Iranian medicine point of view on health and disease. *Iranian J Publ Health.* 2009; 38(1): 169-172.
- [26] Shoja MM, Tubbs RS. The history of anatomy in Persia. *J Anat.* 2007; 210(4): 359-378.
- [27] Parvinroo S, Kamalinejad M, Sabetkasaei M. Pharmacological concepts of temperament in Iranian traditional medicine. *Iranian J Publ Health.* 2014; 43(10): 1463-1465.
- [28] Mirzaee F, Hosseini A, Jouybari HB, Davoodi A, Azadbakht M. Medicinal, biological and phytochemical properties of *Gentiana* species. *J Tradit Complement Med.* 2017; 7(4): 400-408.
- [29] Emtiazy M, Keshavarz M, Khodadoost M, Kamalinejad M, Gooshahgir SA, Shahrab Bajestani H, Hashem Dabbaghian F, Alizad M. Relation between body humors and hypercholesterolemia: An Iranian traditional medicine perspective based on the teaching of Avicenna. *Iran Red Crescent Med J.* 2012; 2012(3): 133-138.
- [30] Emtiazy M, Choopani R, Khodadoost M, Tansaz M, Nazem E. Atheroprotector role of the spleen based on the teaching of Avicenna (Ibn Sina). *Int J Cardiol.* 2013; 167(1): 26-28.
- [31] Arzani S. Teb-e Akbari. Qom: Jalal-al-din, 2008.
- [32] Ghahreman A, Okhovvat AR. Matching the old medicinal plant names with scientific terminology. Tehran: University of Tehran Press, 2004.
- [33] Mozaffarian V. A dictionary of Iranian plant names. Tehran: Farhang -e-Mo'aser, 1996.
- [34] Mozaffarian V. Identification of medicinal and aromatic plants of Iran. Tehran: Tehran Publications, 2013.
- [35] Hooper D, McNair JB, Field H. Useful plants and drugs of Iran and Iraq. Chicago: Field Museum of Natural History Publications, 1937.
- [36] ZE J. Zakhireye Khwarazmshahi. Tehran, Iran. Tehran: Research Institute for Islamic and Complementary Medicine Publications, 2012.
- [37] Shao Y, Chin CK, Ho CT, Ma W, Garrison SA, Huang MT. Anti-tumor activity of the crude saponins obtained from *Asparagus*. *Cancer Lett.* 1996; 104(1): 31-36.
- [38] Sarabi B, Hassandokht MR, Hassani ME, Masoumi TR, Rich T. Evaluation of genetic diversity among some Iranian wild asparagus populations using morphological characteristics and RAPD markers. *Sci Hort.* 2010; 126(1): 1-7.
- [39] Soltani F, Kashi A, Arghavani M. Effect of magnetic field on *Asparagus officinalis* L. seed germination and seedling growth. *Seed Sci Tech.* 2006; 34(2): 349-353.
- [40] Sharafkandi A. The Canon of medicine of Ibn Sina. Tehran: Soroush Publications, 1987.
- [41] Zhou Y, Li Y, Zhou T, Zheng J, Li S, Li HB. Dietary natural products for prevention and treatment of liver cancer. *Nutrients.* 2016; 8(3): 156-160.
- [42] Azadbakht M. Medicinal plant systematics: according to APG. 2nd ed. Tehran: Arjmand publication, 2013.
- [43] Amirghofran Z, Azadbakht M, Keshavarzi F. *Echium amoenum* stimulate of lymphocyte proliferation and inhibit of humoral antibody synthesis. *Ir J Med Sci.* 2000; 25(3): 119-124.
- [44] Noroozpour Dailami K, Azadbakht M, Lashgari M, Rashidi Z. Prevention of

- selenite-induced cataractogenesis by hydroalcoholic extract of *Echium amoenum*: an experimental evaluation of the Iranian traditional eye medication. *Pharm Biomed Res.* 2015; 1(4): 40-47.
- [45] Safaeian L, Tameh AA, Ghannadi A, Naghani EA, Tavazoei H, Alavi SS. Protective effects of *Echium amoenum* Fisch. and CA Mey. against cerebral ischemia in the rats. *Adv Biomed Res.* 2015; 4(1): 107-115.
- [46] Ranjbar A, Khorami S, Safarabadi M, Shahmoradi A, Malekirad AA, Vakilian K, Mandegary A, Abdollahi M. Antioxidant activity of Iranian *Echium amoenum* fisch & CA Mey flower decoction in humans: a cross-sectional before/after clinical trial. *Evid Based Complement Alternat Med.* 2006; 3(4): 469-473.
- [47] Mehrabani M, Ghassemi N, Ghannadi ESA, Shams-Ardakani M. Main phenolic compound of petals of *Echium amoenum* Fisch. and CA Mey., a famous medicinal plant of Iran. *Daru Journal of Pharm Sci.* 2005; 13(2): 65-69.
- [48] Sayyah M, Sayyah M, Kamalinejad M. A preliminary randomized double blind clinical trial on the efficacy of aqueous extract of *Echium amoenum* in the treatment of mild to moderate major depression. *Prog Neuropsychopharmacol Biol Psychiatry.* 2006; 30(1): 166-169.
- [49] Kaith B, Kaith N, Chauhan N. Anti-inflammatory effect of *Arnebia euchroma* root extracts in rats. *J Ethnopharmacol.* 1996; 55(1): 77-80.
- [50] Shen CC, Syu WJ, Li SY, Lin CH, Lee GH, Sun CM. Antimicrobial activities of naphthazarins from *Arnebia euchroma*. *J Nat Prod.* 2002; 65(12): 1857-1862.
- [51] Ko FN, Lee YS, Kuo SC, Chang YS, Teng CM. Inhibition on platelet activation by shikonin derivatives isolated from *Arnebia euchroma*. *Biochim Biophys Acta.* 1995; 1268(3): 329-334.
- [52] Nasiri E, Hosseinimehr SJ, Hosseinzadeh AZ, Azadbakht M, Akbari J, Azadbakht M. The effects of *Arnebia euchroma* ointment on second-degree burn wounds: a randomized clinical trial. *J Ethnopharmacol.* 2016; 189(1): 107-116.
- [53] Roeder E. Medicinal plants in China containing pyrrolizidine alkaloids. *Pharmazie.* 2000; 55(10): 711-726.
- [54] Ghannadi A, Minaiyan M, Abed A. Kasni (*Cichorium intybus* L.). *J Islam Iran Trad Med.* 2011; 1(4): 365-372.
- [55] Aghili Khorasani M. Makhzan ol Advieh. Tehran: Tehran University of Medical Sciences Press, 2009.
- [56] Ahmed B, Al-Howiriny T, Siddiqui A. Antihepatotoxic activity of seeds of *Cichorium intybus*. *J Ethnopharmacol.* 2003; 87(2): 237-240.
- [57] Ahmed B, Khan S, Masood M, Siddique A. Anti-hepatotoxic activity of cichotyboside, a sesquiterpene glycoside from the seeds of *Cichorium intybus*. *J Asian Nat prod Res.* 2008; 10(3): 218-223.
- [58] Bischoff TA, Kelley CJ, Karchesy Y, Laurantos M, Nguyen-Dinh P, Arefi AG. Antimalarial activity of Lactucin and Lactucopicrin: sesquiterpene lactones isolated from *Cichorium intybus* L. *J Ethnopharmacol.* 2004; 95(2): 455-457.
- [59] Pushparaj P, Low H, Manikandan J, Tan B, Tan C. Anti-diabetic effects of *Cichorium intybus* in streptozotocin-induced diabetic rats. *J Ethnopharmacol.* 2007; 111(2): 430-434.
- [60] Kaur N, Gupta AK. Applications of inulin and oligofructose in health and nutrition. *J Biosci.* 2002; 27(7): 703-714.
- [61] Ahmed N. Alloxan diabetes-induced oxidative stress and impairment of oxidative defense system in rat brain: neuroprotective effects of *Cichorium intybus*. *Int J Diabetes Metabol.* 2009; 17(1): 105-109.
- [62] Hassan H. The prophylactic role of some edible wild plants against nitrosamine precursors experimentally-induced testicular toxicity in male albino rats. *J Egypt Soc Toxicol.* 2008; 38(4): 1-11.
- [63] Al-Yahya M, Mothana RA, Al-Said M, El-Tahir K, Al-Sohaibani M, Rafatullah S. *Citrus medica* "Otroj": Attenuates oxidative stress and cardiac dysrhythmia in isoproterenol-induced cardiomyopathy in rats. *Nutrients.* 2013; 5(11): 4269-4283.
- [64] Jafarpour M, Yousefi G, Hamed A, Shariat A, Salehi A, Heydari M. Effect of a traditional syrup from *Citrus medica* L. fruit juice on migraine headache: A randomized double blind placebo controlled clinical trial. *J Ethnopharmacol.* 2016; 179(1): 170-176.

- [65] Raj RK. Screening of indigenous plants for anthelmintic action against human *Ascaris lumbricoides*: Part-II. *Indian J Physiol Pharmacol*. 1974; 19(1): 1-10.
- [66] Monajemi R, Oryan S, Haeri-Roohani A, Ghannadi A, Jafarian A. Cytotoxic effects of essential oils of some Iranian *Citrus* peels. *Iran J Pharm Res*. 2005; 4(3): 183-187.
- [67] Govindachari T, Suresh G, Gopalakrishnan G, Masilamani S, Banumathi B. Antifungal activity of some tetranortriterpenoids. *Fitoterapia*. 2000; 71(3): 317-320.
- [68] Sah AN, Joshi A, Juyal V, Kumar T. Antidiabetic and hypolipidemic activity of *Citrus medica* Linn. seed extract in streptozotocin induced diabetic rats. *Pharmacogn J*. 2011; 3(23): 80-84.
- [69] Entezari M, Majd A, Falahian F, Mehrabian S, Hashemi M, Lajimi AA. Antimutagenicity and anticancer effects of *Citrus medica* fruit juice. *Acta Med Iran*. 2009; 47(5): 373-377.
- [70] Nagaraju B, Anand S, Ahmed N, Chandra JNS, Ahmed F, Padmavathi G. Antiulcer activity of aqueous extract of *Citrus medica* Linn. fruit against ethanol induced ulcer in rats. *Adv Biol Res*. 2012; 6(1): 24-29.
- [71] Tomar A, Mall M, Rai P. Pharmacological importance of citrus fruits. *Int J Pharm Sci Res*. 2013; 4(1): 156-160.
- [72] Ahmed H, Zahran M, Emam H. Heatless synthesis of well dispersible Au nanoparticles using pectin biopolymer. *Int J Biol Macromol*. 2016; 91(1): 208-219.
- [73] Lota ML, de Rocca Serra D, Tomi F, Bessiere JM, Casanova J. Chemical composition of peel and leaf essential oils of *Citrus medica* L. and *C. limonimeditica* Lush. *Flavour Fragr J*. 1999; 14(3): 161-166.

Abbreviations

PM: Persian medicine; G6PD: glucoe 6-phosphate dehydrogenase; APG: Angiosperm Phylogeny Group