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Traditionally used Medicinal Plants in the Treatment of Kidney Stone: a Review on Ethnobotanical Studies in Iran

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Abstract

Urinary tract stone are considered as the third leading disease of the urinary tract, which is still increasing in prevalence mainly due to ever-changing dietary and lifestyle. Kidney stone removal treatments never give a guarantee against the recurrence of stone and the employed technique may lead to certain side effects. It is thus, necessary to develop a medical prophylactic program to prevent stone recurrence. This review is to identify and report the plants that are used for prevention and treatment of kidney stone in traditional culture from various regions of Iran. We found 56 plants which belong to the 23 floral families are in use as traditional medicine, to specifically treat kidney stone in Iran. Most of the reported plants were from Asteraceae and Rosaceae families with respective 12 and 6 species. Though most of the plants evaluated in this study contain phenolic compounds, their effects in treating nephrolithiasis may be explained antioxidant activities.

Introduction:

Urinary tract stones are considered as one of the prevalent urinary tract diseases with a prevalence of 1%-15% worldwide (Yuvanc *et al.*, 2015). Although the causes of formation of such stones are not fully understood, various complex internal and environmental factors are involved in evolving this disease. Inherited factors, age, and gender are some of the internal factors. Whether, the amount of water its associated minerals, and some specific diet as some of the external factors that may effect in the formation of urinary tract stone are still under debate. The stone is considered to be one of the most common reasons for hematuria, abdominal pain, flank pain, and groin pain which can increase the risk of urinary tract infections (UTIs) and even renal failure (Yuvanc *et al.*, 2015). Currently, adjuvant therapy (over-hydration and analgesic) is considered for treatments in the majority of the cases. For a large stone that does not pass through urinary tract spontaneously, cause severe complications, which required invasive and surgical treatments, including chemical dissolution therapy (to remove stone through urinary tract), percutaneous nephrolithotomy, extracorporeal shock wave lithotripsy, and if needed, surgery (Yuvanc *et al.*, 2015). In addition to imposing heavy costs on patients, surgical treatment or stone crushing

may cause several complications including UTI which may lead to infection of all the body and also severe damage to renal tissue (Khan & Thamilselvan, 2000, Yuvanc *et al.*, 2015). In this regard, it is necessary to identify and use nature-based compounds that are able to prevent the formation of a kidney stone or to facilitate removing small stones.

In the recent years, ethnobotanical investigations are growing largely and identifying new medicinal plants used to prevent and treat various diseases through phytotherapy. Ethnobotanical studies conducted in various regions of Iran have reported various traditional uses of many medicinal plants (Bahmani *et al.*, 2016; Jivad *et al.*, 2016a; Jivad *et al.*, 2016b; Parsaei *et al.*, 2016a; Parsaei *et al.*, 2016b; Rouhi-Boroujeni *et al.*, 2016; Asadi-Samani *et al.*, 2016; Samarghandian *et al.*, 2016; Mahmoudian-Sani *et al.*, 2016), leading to developing new study designs to discover medicinal plants (Bahmani *et al.*, 2015; Baradaran *et al.*, 2012; Kooti *et al.*, 2015; Moradi *et al.*, 2012; Moradi *et al.*, 2016b; Moradi *et al.*, 2016c; Moradi *et al.*, 2013a, Moradi *et al.*, 2013b; Nasri *et al.*, 2013; Shahrani *et al.*, 2007; Moradi *et al.*, 2016a; Moradi *et al.*, 2015). In this regard, some modern studies have demonstrated that some medicinal plants used in traditional medicine have useful effects in treating kidney stone (Akanae *et al.*, 2010; Cao *et al.*, 2004;

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Jeong *et al.*, 2006; Park *et al.*, 2008; Premgamone *et al.*, 2001). Therefore, we identified here the plants that are used for prevention and treatment of kidney stone in the traditional culture of Iran's various regions.

In this review article, we used the keywords ethnobotany, ethnomedicine, ethnopharmacology, phytopharmacology, phytomedicine, Iran, and traditional medicine in combination with kidney stone, nephrolithiasis and renal stone to retrieve relevant articles from scientific database. Duplicate articles and the articles without accessible full text were not included in final analysis.

Phytotherapy and Kidney Stone:

Available literature indicates that Iran's people belonging to various cultures and regions use total 56 medicinal plants from 23 families in the treatment of kidney stone. Most of the identified plants were from Asteraceae and Rosaceae family with respective 12 and 6 species (figure1). Table 1 gives further data on the medicinal plants effective on kidney stone disease.

Figure 1: Family wise representation of medicinal plants effective on kidney stone

Discussion:

Till date, the development and increased use of minimally invasive and non-invasive stone treatments such as percutaneous nephrolithotomy, extracorporeal shock wave lithotripsy, and endoscopy have succeeded to large extent in removing kidney stone; nevertheless, the recurrence rates are still high (10 to 23% per year, which exceeds up to 50% within 5 years' time period) (Akanae *et al.*, 2010). Furthermore, such mechanical/surgical techniques often resultant to various side-effects such as hemorrhage, tubular necrosis, hypertension, subsequent kidney fibrosis etc. Thus, stone recurrence is a critical issue and requires an effective prophylactic treatment. It is

necessary to develop a medical prophylactic program to prevent stone recurrence. The use of natural medicine is a constant aspect of current health care. Although, the modern allopathic medicine is easily available across the world, but many people seem to prefer alternative or complementary therapy, including medicinal herbs (Touhami *et al.*, 2007).

The record of 56 medicinal plants use to treat kidney stones directly indicates the richness of Iran's traditional medicine, which has long addressed use to prevent and treat the kidney stone. The existence of widely varied approaches to using plants to treat diseases, including kidney stone, in Iranian traditional medicine is compatible with geographical expansion and indicates vegetation diversity of this country.

Most of the identified plants used in kidney treatments were from Asteraceae family and followed by Rosaceae family that contain large amounts of phenolic compounds. In previous experimental studies, flavonoids from plants or herbs were reported to decrease calcium oxalate stone formation in hyperoxaluria-induced stone in rats (Jeong *et al.*, 2006, Park *et al.*, 2008). Further, rosmarinic acid, as a plant flavonoid, found to inhibit several complement-dependent inflammatory processes, acting through stimulating a host antioxidant response (Akanae *et al.*, 2010). Flavonoids interfere with different free radical-producing systems involving the reduction in ischemia-reperfusion injury by interfering with inducible nitric-oxide synthase activity, direct radical scavenging, leukocyte immobilization during ischemia, inflammation conditions, and the xanthine oxidase pathway, which is an important oxidative injury-inducing route inhibited by flavonoids (Nijveldt *et al.*, 2001). The mechanism and sequence of events by which free radicals interfere with cellular functions have not yet been fully understood, but one of the most significant events may be the lipid peroxidation, which leads to cellular membrane damage. Indeed free radicals attract different inflammatory mediators, playing a role in general inflammatory response and tissue damage.

Conclusively, many of plants referred in this study contain phenolic compounds and have antioxidant activity; their effects in treating nephrolithiasis may be completed by their antioxidant activities (Akanae *et al.*, 2010; Amidi *et al.*, 2016; Karimi & Moradi, 2015). Researchers and relevant physicians are advised to investigate the proper roles of the plants referred to this study by clinical trials to develop anti-kidney stone herbal drugs and make them commercially available.

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Table 1: Medicinal plants effective on kidney stone in different subcultures and regions of Iran

No.	Scientific name	Family	Local name	Used	Preparation organs	Regions	References*
1	<i>Biarum straussii</i> Engl.	Araceae	Kardeh	Leaves	Edible	Arjan, Fars P.	*(Dolatkhahi et al., 2014)
2	<i>Nasturtium officinale</i> R. Br.	Brassicaceae	Bakaloo	Stem, Leaves	Infusion	Arjan, Fars P.	*(Dolatkhahi et al., 2014)
3	<i>Alhagi camelorum</i> Fisch.	Papilionaceae/ Fabaceae	Khar Shotor Toranjabin	Whole Plant	Decoction	Arjan, Fars P; Mobarakeh, Isfahan P.	*(Dolatkhahi et al., 2014, Mardaninejad et al., 2013)
4	<i>Adiantum capillus-Veneris</i> L.	Pteridaceae	Parsiavashoon	Leaves	Infusion	Arjan, Fars P.	*(Dolatkhahi et al., 2014)
5	<i>Pyrus communis</i> L.	Rosaceae	Anchochak	Seed	Edible	Arjan, Fars P.	*(Dolatkhahi et al., 2014)
6	<i>Tribulus terrestris</i> L.	Zygophyllaceae	Kharkhasak,	Whole Plant	Infusion, Concentrated Decoction	Arjan, Fars P; Maraveh Tappeh Khar Pelangi, Region, North of Iran; Mobarakeh hopanch okorek region, Isfahan P; Turkmen Sahra, north of Iran; Hezar Mountain, SE of Iran; and Kerman, Mashhad, Razavi Khorasan P.	*(Ghorbani, 2005; Mardaninejad et al., 2013; Dolatkhahi et al., 2014; Mirdeilami et al., 2011; Amiri & Joharchi, 2013; Rajaei & Mohamadi, 2012)
7	<i>Allium iranicum</i>	Alliaceae	sirevahshi	Bulb	Decoction	Hamedan P.	*(Esmaeili et al., 2014)

8	<i>Centaurea solstitialis</i> L.	Asteraceae		Whole Plant	Decoction	Hamedan P. *(Esmaeili et al., 2014)
9	<i>Ceratocephalus falcata</i> (L.)	Ranunculaceae		Aerial Parts	Decoction	Hamedan P. *(Esmaeili et al., 2014)
10	<i>Cicer anatolicum</i> Alef	Fabaceae	Albaloo vahshi	Fruit	Decoction	Hamedan P. *(Esmaeili et al., 2014)
11	<i>Citrullus lanatus</i> (Thumb.) Matsum & Nakai	Cucurbitaceae	hendev:nedeym	Fruit	Cooked	Hamedan P. *(Esmaeili et al., 2014)
12	<i>Tripleurospermum disciforme</i> (C. A. Mey.) Schultz	Asteraceae	Ryshe gaz	Flower	Decoction	Hamedan P. *(Esmaeili et al., 2014)
13	<i>Urtica dioica</i> L.	Urticaceae	Gaz gaz	Aerial Part	Decoction	Hamedan P., Sardasht, Western Azerbaijan P. *(Esmaeili et al., 2014; Azizi & Keshavarzi, 2015)
14	<i>Salvia sclarea</i> L.	Lamiaceae		-Leaves, Flower, Seed	Infusion	Hezar Mountain, SE of Iran *(Rajaei & Mohamadi, 2012)
15	<i>Adonis aestivalis</i> L.	Ranunculaceae	Teryakoo	Flower	Decoction	Hezar Mountain, SE of Iran *(Rajaei & Mohamadi, 2012)
16	<i>Consolida orientalis</i> (Gay) Schrod.	Ranunculaceae		Flower, Leaves	Poultice, Decoction	Hezar Mountain, SE of Iran *(Rajaei & Mohamadi, 2012)
17	<i>Galium aparine</i> L.	Rubiaceae		Aerial Part	Infusion	Hezar Mountain, SE of Iran *(Rajaei & Mohamadi, 2012)
18	<i>Acanthophyllum squarrosum</i> Boiss.	Caryophyllaceae		Chubakeriz	Root powder	Brew poultice Hormozgan P. *(Safa et al., 2013)
19	<i>Conyza canadensis</i> (L.) Cronq.	Asteraceae	Pirbaharakebagh	Whole plant	Brew	Hormozgan P. *(Safa et al., 2013)
20	<i>Desmostachya bipinnata</i>	Poaceae	Kertaki, kertah	Root	Fresh organ	Hormozgan P. *(Safa et al., 2013)
21	<i>Heliotropium europaeum</i> L.	Boraginaceae	Kolohmu, balghandu	Leaves, flower, seed, twigs	Brew fresh organ	Hormozgan P. *(Safa et al., 2013)
22	<i>Herniaria hirsuta</i> L.	Paranychiaceae	Alafe fatgh korkalud	Aerial parts	Decoction brew	Hormozgan P. *(Safa et al., 2013)
23	<i>Amaranthus caudatus</i> L.	Amaranthaceae	Sorkh Maghz	Fruit, seed, flower	Raw seeds	Kerman P. *(Maymand & Mirtajodin, 2010)
24	<i>Alhagi pseudalhagi</i> (M.Bieb.) Desv	Fabaceae	Adoor, Khare Eshter	Aerial parts	Aromatic water	Kerman P. *(Mahdavi Maymand & Mirtajodin, 2010)
25	<i>Eryngium campestre</i> L.	Apiaceae	Zallash	Flower, Stem	Decoction, Edible	Maraveh Tappeh Region, North of Iran *(Mirdeilami et al., 2011)
26	<i>Teucrium polium</i> L.	Lamiaceae	Bakhshiya ushen	Leaves, Aerial Part	Demulcent, Infusion	Maraveh Tappeh Region, North of Iran *(Mirdeilami et al., 2011)
27	<i>Anthemis nobilis</i> Boiss.	Asteraceae	Tatbashi Golbarmagh	Flower	Decoction, Infusion	Maraveh Tappeh Region, North of Iran *(Mirdeilami et al., 2011)
28	<i>Astragalus hamosus</i> L.	Fabaceae	Nakhonak	Fruit		Mashhad, Razavi Khorasan P. *(Amiri & Joharchi, 2013)
29	<i>Nigella sativa</i> L.	Ranunculaceae	Siah Daneh	Seed	Infusion, decoction	Mashhad, Razavi Khorasan P. and Mobarakeh region, Isfahan P. *(Amiri & Joharchi, 2013; Mardaninejad et al., 2013)
30	<i>Cerasus avium</i> (L.) Moench	Rosaceae	Dome Gilas	Pedicel	-	Mashhad, Razavi Khorasan P. *(Amiri & Joharchi, 2013)
31	<i>Rosa beggeriana</i> Schrenk	Rosaceae	Nastaran	Fruit	-	Mashhad, Razavi Khorasan P. *(Amiri & Joharchi, 2013)
32	<i>Physalis alkekengi</i> L.	Solanaceae	Arusak Posht Pardeh	Fruit	-	Mashhad, Razavi Khorasan P. *(Amiri & Joharchi, 2013)

33	<i>Matricaria chamomilla</i> L.	Asteraceae	Baboneh	Flower	-	Mobarakeh region, Isfahan P. *(Mardaninejad et al., 2013)
34	<i>Achillea santonici</i>	Asteraceae	Gole zardi	Aerial Part brenjas	-	Mobarakeh region, Isfahan P. *(Mardaninejad et al., 2013)
35	<i>Raphanus sativus</i> L.	Brassicaceae	Torobsiah	Root, Leaves, Seed	-	Mobarakeh region, Isfahan P. *(Mardaninejad et al., 2013)
36	<i>Rumex crispus</i> L.	Polygonaceae	Torshak	Root, Leaves, Flower	-	Mobarakeh region, Isfahan P. *(Mardaninejad et al., 2013)
37	<i>Prunus cerasus</i> L.	Rosaceae	Albalo	Peduncle	-	Mobarakeh region, Isfahan P. *(Mardaninejad et al., 2013)
38	<i>Polygonum aridum</i> Boiss	Polygonaceae	Haft band	Aerial parts, latex	-	Mobarakeh region, Isfahan P. *(Mardaninejad et al., 2013)
39	<i>Zea mays</i> L.	Poaceae	Zorat	Stigma, Seed	Decoction	Mobarakeh region, Isfahan P., & Turkmen Sahra, N. Iran *(Mardaninejad et al., 2013; Ghorbani, 2005)
40	<i>Allium akaka</i> Gmel.	Aliaceae	Losha	Shoots	-	Sardasht, Western Azerbaijan P. *(Azizi & Keshavarzi, 2015)
41	<i>Pirus communis</i> L.	Rosaceae	Harmeh	Fruit	-	Sardasht, Western Azerbaijan *(Azizi & Keshavarzi, 2015)
42	<i>Anthemis</i> spp.	Asteraceae	Chofan-telfek Tatbashi	Flower	Decoction	Turkmen Sahra, north of Iran *(Ghorbani, 2005)
43	<i>Calendula persica</i> C.A.Mey.	Asteraceae	Sari-Solmaz	Aerial parts	Decoction, infusion, Juice	Turkmen Sahra, N. Iran; Kohghiluyeh va Boyer Ahmad P & Maraveh Tappeh Region, *(Ghorbani, 2005, Mirdeilami et al., 2011, Mosaddegh et al., 2012)
44	<i>Calendula alata</i> Rech. f.	Asteraceae	Sari-Solmaz	Aerial parts	Decoction, infusion	Turkmen Sahra, N. Iran *(Ghorbani, 2005)
45	<i>Origanum vulgare</i> L.	Lamiaceae	Kakelik-oti	Aerial parts	Flavoring, with yugart	Turkmen Sahra, north of Iran *(Ghorbani, 2005)
46	<i>Olea europaea</i> L.	Oleaceae	Zeytun	Flower, Leaves	Infusion, decoction	Turkmen Sahra, N. Iran *(Ghorbani, 2005)
47	<i>Polygonum arenasterum</i> Boreau	Polygonaceae	Gheq-buqun	Aerial parts	Decoction	Turkmen Sahra, north of Iran *(Ghorbani, 2005)
48	<i>Polygonum hyrcanicum</i> Rech. f.	Polygonaceae	Gheq-buqun	Aerial parts	Decoction	Turkmen Sahra, N. Iran *(Ghorbani, 2005)
49	<i>Thymus kotschyanus</i> Boiss.	Lamiaceae	kakuty	Leaves, nflorescence	Infusion	West Azerbaijan P. *(Miraldi et al., 2001)
50	<i>Rosa canina</i> L.	Rosaceae	Nastaran, Shilan	Flower, Fruits	Infusion	Western Azerbaijan P. *(Miraldi et al., 2001; Azizi & Keshavarzi, 2015)
51	<i>Arctium minus</i> Bernh.	Asteraceae	Baba Adam	Root/leaf	Infusion	Kohghiluyeh va Boyer Ahmad P. *(Mosaddegh et al., 2012)
52	<i>Allium jesdianum</i>	Liliaceae	bonsorkh	Whole Plant	Infusion	Kohghiluyeh va Boyer Ahmad P. *(Mosaddegh et al., 2012)
53	<i>Achillea wilhelmsii</i> K.Koch.	Asteraceae	Berenjas	Flower	Powder & infusion of dried flowers	Kohghiluyeh va Boyer Ahmad P. *(Mosaddegh et al., 2012)
54	<i>Cichorium intybus</i> L.	Asteraceae	kasni	Leaves, stem	Aromatic water & cooked	Northeast Latrine Zone of Persian Gulf *(Dolatkhahi & Nabipour, 2014)
55	<i>Alhagi persarum</i> Boiss. & Buhse	Papilionaceae	kharshotor	Whole Plant	Aromatic water, Decoction	Northeast Latrine Zone of Persian Gulf *(Dolatkhahi & Nabipour, 2014)
56	<i>Peganum harmala</i> L.	Zygophyllaceae	espan	Aerial parts	Infusion	Northeast Latrine Zone of Persian Gulf *(Dolatkhahi & Nabipour, 2014)