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REVIEW

GIST OF MEDICINAL PLANTS OF PAKISTAN HAVING ETHNOBOTANICAL EVIDENCES TO CRUSH RENAL CALCULI (KIDNEY STONES)

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Abstract: Human civilization is facing the problem of kidney stones since ancient ages. Although mortality rate is not so high, yet it affects the victim's quality of life. The patient suffers from intense pain and many other symptoms modifying his life style and affecting his socioeconomic status. Many drugs and invasive methods have also been developed for the treatment, but these are highly costly and unaffordable for poor people and the rate of reoccurrence is also high. The use of medicinal plants is both affordable and effective in this respect. In this article, 35 medicinal plants of Pakistan origin and their crucial information have been enumerated in alphabetical order of plant's scientific name, family, place (distribution), part used, local name, habit, major constituents and references. It can also be seen that all parts are used for the treatment of kidney stones. Leaves represent 28% contribution, whole plants and seeds 12%, fruits and roots 11% contribution in this respect. Flowers contribute 8% in the treatment of kidney stone while branches, bark, bushes, buds, milk and shoots contribute only 3% in the removal of kidney stones. Habits of plants were also taken under consideration. It was noticed that herbs are the most useful life form in this regard which contributed 63% for the removal of kidney stone. Shrubs contributed 20%, trees 11% while bushes and weeds contributed 3% for the removal of kidney stones.

Keywords: renal calculi, Pakistan, medicinal plants, crush

One of the major diseases that affect human population since ancient ages are the kidney stones (renal calculi). Kidney stones result in the modification of the victim's behavior with great fear of intense pain and threaten with failure of the kidneys. Urinary stones contain both crystalloid and colloid components. The crystalloid components are mainly calcium oxalate, calcium phosphate, calcium carbonate, magnesium-ammonium phosphate, uric acid and cysteine. Various drugs are available for the treatment of this disease. Moreover, advancements in medical techniques have led to the development of invasive methods of stone disruption like lithotripsy and surgical methods. But these are very expensive methods which are non-affordable by the poor people and the rate of reoccurrence is also high from 50 to 80% (1). The remedy that is the safest and cheapest includes the use of medicinal plants. Medicinal plants have occupied an important place in the society of developing countries, not only as a source of economy but also for improving quality of life, because 80% of human population prefer using herbal remedies (2).

Modern pharmacopoeia includes at least 25% of the drugs coming from plant origin, 121 of such active substances are being in use currently or synthetic analogs are obtained from natural precursors. Hence, potential of medicinal plants cannot be underestimated (3). Various plants have been reported to be used for the treatment of kidney stones.

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However, to the best of our knowledge and according to the literature survey, a majority of the medicinal plants of Pakistan have not been scientifically evaluated for their potential in the treatment of kidney stones.

In this article, 35 medicinal plants of Pakistan origin and their crucial information have been enumerated in alphabetical order of plant's scientific name, family, place (distribution), part used, local name, habit, major constituents and references.

METHODOLOGY

Data collection was carried out through internet search on Science Direct, Google and PubMed using biological and chemical abstracts. The key words used for the literature survey for this article were "Medicinal plants of Pakistan, kidney stones, renal calculi, ethnobotanical evidence and natural products". Selection of plants was focused on their use in the treatment of kidney stones in folklore remedies and studied their references in detail. Chemical constituent of medicinal plants were also searched. The outcome of results were rechecked and compared with the literature.

RESULTS AND DISCUSSION

Urolithiasis is a major problem afflicting human civilization for several centuries. It has been observed that its annual incidence is 0.5% in western world. The major phenomenon responsible for stone formation involves calcium oxalate and calcium phosphate accumulation. The phases involved in the accumulation of these two substances include: nucleation, crystal growth, crystal aggregation and crystal retention (55). Nucleation phase involves the formation of a solid crystal. It is the primary step in the formation of renal stone. The underlying cause for nucleation is super-saturation. The homogeneous nucleation involves the nucleation in pure solution, whereas secondary nucleation involves the accumulation of new crystals on pre-existing crystals. Urine is not a pure substance and nucleation in it involves the presence of an existing surface or structure. This phenomenon is called heterogeneous nucleation (58). Heterogeneous nucleation in urine may occur at epithelial cells, RBCs, bacteria, some other crystals, cell debris and urinary casts. Stone formation involves phase change which results in the condensation of dissolved solids transforming these into solid state because of super-saturation. Nucleation is followed by the crystal growth. The crystal growth process begins with the nucleation stage. Super-saturation facilitates the process of cluster formation. In the 3rd phase (crystal aggregation/crystal agglomeration), the crystals stick together and constitute a larger particle. Stabilization is achieved by the bridge formation among the crystalline substance (24). Finally, these crystals are retained in the kidney. The retention is achieved because of adherence of crystals with epithelial cell line (41).

Stone formation inhibitors forbid the agglomeration and growth by developing a layer on the surface of growing calcium crystals or by forming complexes with calcium and oxalate. There are various substances that inhibit the stone formation including both organic and inorganic substances. Inorganic substances include citrates, magnesium and pyrophosphates while organic substances include Tamm-Horsfall proteins, urinary prothrombin fragment 1, protease inhibitor (inter-α-inhibitor), glycosaminoglycans, osteopontin (uropontin), renal lithostathine and other bikunin and calgranulin. High urine flow is also an important inhibitor of kidney stone formation (55).

Phytochemical investigation for use as urolithiatic agent is still an era of thirst. Only a few phytochemicals have been investigated to have a role in urolithiasis. Some terpenoids have been reported to have this activity (56, 57). Some flavonoids like quercetin, kaempferol-3-rhamnoside and kaempferol-3-rhamnogalactoside and tannins have also been reported to have some effect (60).

Plant extracts may contain chemicals and phytochemicals that inhibit the synthesis and growth of crystals. This character of plants may be of significant importance in preventing kidney stone formation. The extracts of plants may also contain constituents that retard crystal agglomeration (58).

The history of use of herbal remedies starts from the very beginning of human civilization. Various plants have been reported to be used in the treatment of disorders, but the knowledge of treatment differ in various areas and it is just like a hidden treasure. The present study is an effort to bring out the hidden treasure of knowledge used in the treatment of kidney stones in Pakistan. In this article, 35 medicinal plants of Pakistan and their crucial information have been enumerated in alphabetical order of plant scientific name, family, place (distribution), part used, local name, habit, major constituents and references (Table 1). These plants are distributed in 21 families of which, Cucurbitaceae represents the maximum contribution with 4 plants. Asteraceae, Fabaceae and Solanaceae are the families contributing 3 plants. Amaranthaceae, Boraginaceae , Chenopodiaceae, Rosaceae and Rutaceae are

Table 1. Medicinal plants of Pakistan used for the treatment in kidney stone.

Scientific Name	Family	Location	Constituent	Constituents active against urolithiasis	Habit	References
Acacia Jacquemontii Benth.	Fabaceae	Sindh*****, Punjab*, Baluchistan**	Diterpenoids	Terpenoids	An erect shrub	4, 56
Achillea millefolium L.	Asteraceae	Himalayan Region and Azad Kashmir *	Saponins, essential oils, flavanoids	Flavonoids	Herb	5, 6, 60, 63
Achyranthus aspera L.	Amaranthaceae	Swat, Bhimber, Azad Jammu and Kashmir*	Saponins, oleanolic acid, flavonoids, dihydroxyketones, alkaloids	Flavonoids	Wild herb	7, 8, 60, 64-66
Aervajavanica (Burm, f.) Schult.	Amaranthaceae	Parachinar, Kurram Agency, Kohat***	Alkaloids, flavonoids, tannins	Flavonoids, tannins	Herb	9-14, 60
Asphodelus tenuifolius Cavan.	Liliaceae	Bhimber****	β-Sitosterol, 1-octacosanol, 1-triacontanol, hexadecanoic acid, tetracosanoic acid, triacontanoic acid, 3-hydroxybenzoic acid and β-sitosterol 3-O-β-D-glucopyranoside	Not yet identified	Herb	15, 16
Bergenia ciliate (Haw.) Sternb.	Saxifragaceae	Azad Kashmir****	Wax, gallic acid, tannin, bergenin, mucilage	Tannin	Herb	17, 60
Bryophyllum pinnatum (Lam.) Oken	Crassulaceae	Bhimber****	Alkaloids, triterpenes, glycosides, flavonoids, steroids, bufadienolides, lipids and organic acids.	Terpenoids, flavonoids	Herb	15, 18, 56, 60
Calendula officinalis L.	Asteraceae	Pooch valley****	Triterpenoids, flavonoids, coumarins, quinones, volatile oil, carotenoids and amino acids	Terpenoids, flavonoids	Herb	19, 20, 56, 60
Chenopodium album L.	Chenopodiacea	Tank***	Oxalic acid, essential oil, vitamin A and C, alkaloid, flavonoid	Flavonoid	Weed	17, 21, 60, 67
Cichorium intybus L.	Asteraceae	Swat****	Inulin, esculin, volatile compounds (monoterpenes and sesquiterpenes), coumarins, flavonoids and vitamins	Flavonoids	Herb	22-24, 60
Citrullus colocynthis (L.) Schrad.	Cucurbitaceae	Dadu*****	Alkaloids, anthraquinones, flavonoids, terpenes, tannins, steroids, cardiac glycosides and saponins	Terpenoids, flavonoids, tannins	Herb	4, 9-11, 25, 26, 56, 60
Citrullus vulgaris Schrad. ex Eckl. and Zeyh.	Cucurbitaceae	Tehsil Pindigheb, District Attock*	Tannin, phytate, oxalate, iron, calcium, zinc	Tannins	Herb	27, 28, 60
Citrus sinensis (L.) Osbeck, Reise Ostind	Rutaceae	Sindh*****	Reducing sugar, saponins, cardiac glycosides, tannins and flavonoids	Flavonoids, tannins	Tree	4, 29, 60

Table 1. cont.

Scientific Name	Family	Location	Constituent	Constituents active against urolithiasis	Habit	References
Citrus aurantifolia (L.) (Christman) Swingle	Rutaceae	Sindh*****	Polymethoxyflavones (PMFs), polymethoxylated flavones, O-glycosylated flavones	Flavonoids	Tree	4, 60
Cucumis melo L.	Cucurbitaceae	Nara Desert, Sindh*****	Alkaloids, triterpenoids, carbohydrates, proteins, flavonoids, phytosterols	Terpenoids, flavonoids	Shrub	30-32, 56, 60
Cucumis sativus L.	Cucurbitaceae	Kohat***	Alkaloids, glycosides, steroids, saponin tannins	Tannins	Herb	30, 33-35
Dolichos biflorus L.	Fabaceae	Sindh*****	Falconoid phenolic	Not yet identified	Herb	30, 36, 37
Ficus carica L.	Moraceae	Chagharzai Valley***	Flavonoid, alkaloid, tannin, saponin	Flavonoids, tannins	Tree	38-40, 60
Haloxylon stocksii (Boiss.)	Chenopodiaceae	Coastal of Karachi*****	Dillenic acid	Not yet identified	Srubs	9-11, 41-43
Heliotropium strigosum Willd.	Boraginaceae	Bhimber****	Flavonoids, essential oil	Flavonoids	Wild herb	15, 35, 60
Micromeria biflora (Buch.-Ham. ex D. Don) Benth.	Labiatae	Pooch valley****	Essential oils	Not yet identified	Herb	17, 19, 44
Nigella sativa L.	Ranunculaceae	Bahawalpur, Bhakkar, Faisalabad, Hasilpur, Lahore, Multan*	Alkaloids, tannins, flavonoids, sterols	Flavonoids, tannins	Herb	38, 45, 46, 60
Rubus ellipticus Smith.	Rosaceae	Swat****	Flavonoids, carbohydrates, steroids, tannins and phenolic compounds, terpenoids, alkaloids	Flavonoids, tannins, terpenoids	Shrub	17, 22, 56, 60, 62
Rosa indica L.	Rosaceae	Sindh*****, Punjab*, Baluchistan**	Linoleic acid, α-linolenic acid, oleic acid, palmitic acid, stearic acid, octadecenoic acid, eicosanoic acid, eicosadienoic acid, erucic acid and minor fatty acids, alkaloids, flavonoids, saponins, tannins and phenols	Flavonoids, tannins	Shrub	4, 60, 65
Rumex hastatus D. Don.	Polygalaceae	Poonch vally****	Phenols, tannins	Tannins	Herb	5, 47, 60
Senna italica/ *Cassia italica* Mill	Fabaceae	Sindh*****	β-Sitosterol, stigmasterol, α-amyrin, 1,5-dihydroxy-3-methylanthraquinone, anthraquinone, alkaloids, steroids and flavonoids (I)	Flavonoids	Shrubs	4, 60, 66
Solanum nigrum L.	Solanaceae	Upper Dir****	Alkaloids, pregnane saponins, solanigroside A, tannins, flavonoids, proteins	Flavonoids, tannins	Herb	4, 48, 60, 68

Table 1. cont.

Scientific Name	Family	Location	Constituent	Constituents active against urolithiasis	Habit	References
Solanum surattense Shord and Wendl	Solanaceae	Poonch valley****	Oil, alkaloids, potassium nitrate, carbohydrates, tannins phenols, gums and mucilages	Tannins	Herb	5, 17, 60, 69
Tamarix aphylla (L.) Karst.	Tamaricaceae	Sindh*****	Glycosylated isoferulic acid, tamarixetin 3,3'-disodium sulfate, dehydrodigallic acid dimethyl ester and isoferulic acid, ferulic acid, kaempferol 7,4'-dimethyl-ether-3-sulfate, quercetin 3-O-isoferulyl-β-glucuronide, alkaloids, flavonoids, tannins	Flavonoids, tannins	Trees shrub	4, 60, 70
Trianthema portulacastrum L.	Aizoaceae	Bhimber***	Tetraterpenoid 1 (trianthenol), flavonoid, (C-methylflavone) , alkaloid (trianthemine)	Terpenoids	Herb	15, 49, 56
Tribulus teretris L.	Zygophyllaceae.	Bhimber****	Saponins , diosgenins, alkaloids, amides, tannins, flavonoids	Flavonoids, tannins	Herb	15, 50, 60, 71
Trichodesma indicum (L.) R. Br.	Boraginaceae	Poonch valley****	Fatty acids and non-steroidal compounds.	Not yet identified	Herb	5, 17, 51
Vitex agnus-castus L.	Verbenaceae	Khuzdar, Wadh**	Iridoids, flavonoids, diterpenoids, essential oils, ketosteroids	Terpenoids, flavonoids	Shrub	52, 53, 56
Withania somnifera (L.) Dunal	Solanaceae	Khushab, Cholistan desert*	Withanolides, cytotoxic lactones, piperidine, anaferine, anahygrine, alkaloids (withanine, somniferine, somnine, tropine, triterpenes	Terpenoids	Herb	43, 44, 54, 56, 72
Zea mays L.	Poaceae	Sindh*****	Flavonoids, alkaloids, phenols, steroids, glycosides, carbohydrates, amino acids, terpenoids, tannins	Flavonoids, tannins terpenoids	Bushes	4, 56, 60, 61

*East of Pakistan, **West of Pakistan, ***North of Pakistan, ****North-west of Pakistan, *****South of Pakistan

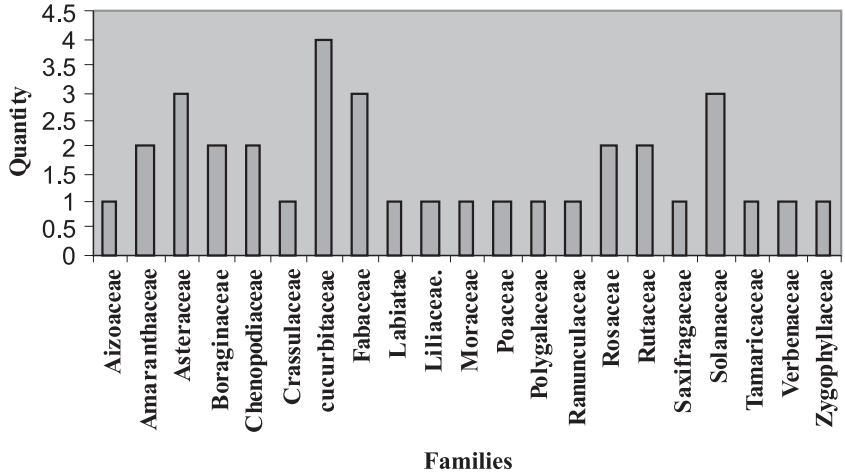

Figure 1. Various families and their number of plants

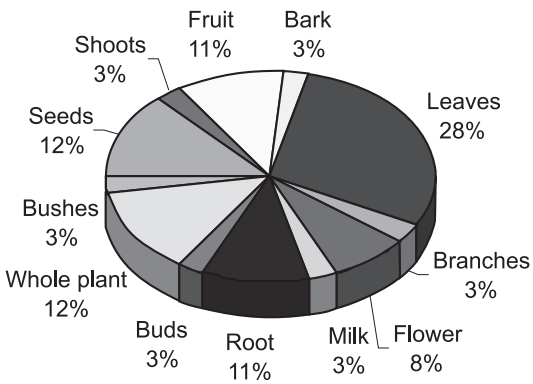

Figure 2. Percentages of various parts used for treatment of kidney stones

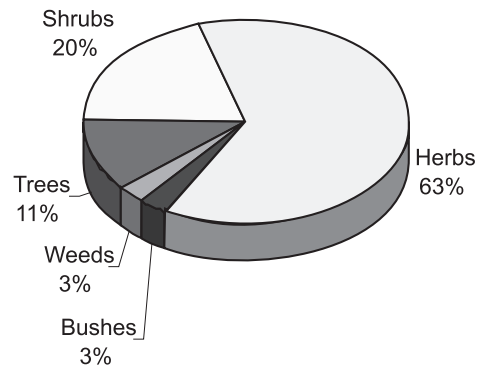

Figure 3. Percentage of different life forms

the families contributing 2 species, while, Aizoaceae, Crassulaceae, Labiatae, Liliaceae, Moraceae, Poaceae, Polygalaceae, Ranunculaceae, Saxifragaceae, Tamaricaceae, Verbenaceae and Zygophyllaceae, were found with single medicinal plant of such potential (Fig. 1). These plants are distributed throughout Pakistan in all the provinces. It can also be seen that all parts are used for the treatment of kidney stones. Leaves represent 28% contribution, whole plants and seeds 12%, fruit and roots 11% contribution in this respect. Flowers contribute 8% in the treatment of kidney stone while branches, bark, bushes, buds, milk and shoots contribute only 3% in the removal of kidney stones (Fig. 2). Habits of plants were also taken under consideration. It was noticed that herbs are the most useful life form in this regard which contributed 63% for the removal of kidney stones. Shrubs contributed 20%, trees 11% while bushes and weeds contributed 3% for the removal of kidney stones (Fig. 3).

During ethnobotanical search of Pakistan 35 medicinal plants belonging to 21 families were recorded as effective remedies used by the local people for the removal of renal calculi (kidney stones). These crude drugs cause dissolution or breakage of the renal calculi with subsequent expulsion from the body. The phenomenon of dissolution or destruction may be caused by the phytochemicals present in the crude drugs so plants were also searched for chemicals.

CONCLUSION

The present article enlists 35 medicinal plants used by the local people for the treatment and removal of renal calculi in various areas of

Pakistan. The medicinal plants used for the treatment of renal calculi contain such constituents which are active against urolithiasis. These active constituents include flavonoids, terpenoids, and tannins. Chemical investigation of medicinal plants is another important thirsting era that may lead to the understanding of physiology, pathology and pharmacology and use of these plants for various other diseases.

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