



RESEARCH ARTICLE

Herbal remedies used for the management of urolithiasis in Abbottabad, Northern Pakistan

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ABSTRACT

The current study was performed to evaluate the ethnobotanical uses of medicinal plants to treat and prevent kidney diseases, especially urolithiasis in the Abbottabad region, Northern Pakistan. Field surveys were conducted from 2014–2016 in various rural and tribally dwelled hilly areas like Ayubia National Park, Sherwan and Thandiani. Ethnobotanical information about the medicinal plants employed to treat urinary ailments was obtained from well-informed sources like local healers (hakims) and residents (men/women), who had vast knowledge of local plants uses. The questionnaire method was adopted to record the information and queries were made to verify the information. Informed consent was obtained from each informant before conducting the interview process. Quantitative ethnobotanical indices were calculated for each recorded species. Correlation analysis between the RFC, UV and FL% was tested by Pearson's correlation, SPSS (ver. 16). A total of 38 plant species belonging to 27 families were being used in the study area to treat Urolithiasis or kidney stone diseases. Asteraceae was the most dominant family with 5 species. Local people used different methods of preparation for different plant parts; among them, decoction was the popular and dominant way of preparation (52.6%), followed by powder (18.4%), extracts (15.7%), juice (7.8%) and cooked (5.2%). The highest UV was recorded for *Rumex acetosa* L. (1.14) followed by *Agrimonia eupatoria* L. (1.1), *Equisetum ramosissimum* Desf. (1.05), *Aerva lanata* L. (1.04), *Eclipta alba* Hassak. (1.03). Moreover, twenty-three species were recorded with above 50% Fidelity level. It was found that most of the plant species (16 species) were explicitly used to remove kidney stones. All the obtained data about the ethnomedicinal uses of plants to treat urinary tract ailments are alphabetically categorized to their botanical name/family, local name, phytoconstituents, dosage and route of administration, along with quantitative indices value. All the collected ethnomedicinal plants require a thorough scientific investigation for isolation, identification, biochemical assays, toxicities and evaluation of pharmacological activities of the phytoconstituents, especially of the plants recorded with a high-fidelity level before their usage in clinics.

Introduction

Urolithiasis or kidney stone formation is the third leading urinary system disease affecting 10–15% of the population worldwide. Generally, it emanates from tiny crystals, which later results in stone, and subsequently grows further and accumulates on the interior surfaces of the kidney (1). Kidney stones or calculi are named based on the identified locations in

the urinary system, such as renal calculi, urinary tract stone disease, urinary calculi, urolithiasis, nephrolithiasis and ureterolithiasis. Urinary stones can be removed/expelled via urine if smaller in size through the ureter from the kidney (2). It is observed that sometimes the stones may not pass through the ureter, which produces severe pain if not managed properly, resulting in serious medical consequences

like extreme obstruction, infection, haemorrhage and hydronephrosis in the urinary system.

The major health problems faced by the people of Pakistan are linked to the kidney, and recently more than 1 million cases of kidney stones were reported (3). It is estimated that 15 % of all the people in Pakistan will suffer from urolithiasis at some point in life. Men tend to be affected more frequently than women (4). Moreover, urolithiasis is the most common illness amongst the people of Northern Pakistan. Different treatment options are available to remove calculi, such as surgical removal, lithotripsy and laparoscopy. Despite the higher treatment costs, these techniques may produce a risk of causing acute renal injury, which decreases renal function and also recurrence of calculi observed in some cases with a possible recurrence rate of 10%, 33% and 50% at 1st, 5th and 10th year respectively (5). Costly diagnostic and treatment procedures for the therapeutic management of patients require better adequate alternative therapies. Phytochemicals are responsible for the therapeutic activity of plant species and can treat various ailments and possess potential anti-inflammatory, antibacterial, analgesic, diuretic, antioxidant and antifungal properties. Natural products derived from medicinal plants, either as pure compounds or as extracts, provide opportunities for developing new drug leads due to the unmatched chemical diversity and lower cost compared to their synthetic chemical counter-parts (6). Due to the recent surge in demands for chemical diversity in screening programmes, search for therapeutic drugs of herbal origin increased due to their attractive properties worldwide. Botanicals and herbal preparations for medicinal purposes contain different types of bioactive compounds like flavonoids, alkaloids, saponins, tannins, sterols and other organic and inorganic constituents. Some medicinal plants and marketed herbal preparations are reported to be effective in treating and preventing kidney stones recurrence with fewer side effects (7). In recent times, the discovery of anti-lithiatic drugs from natural products has gained a lot of importance.

The practiced medicinal plants by traditional healers and locals for the cure of kidney stones possess various bioactive chemical compounds, and some of the chemical constituents from different plant species have been used in anti-urolithiatic formulations (6). Various phytoconstituents have been isolated from traditionally used medicinal plants and have been found to be effective in preventing kidney disease/stones (6, 8). Diet from natural food (vegetative plants and fruits) also plays a vital role in either preventing or promoting the formation of kidney stones, depending on the types of nutrients and chemical constituents found in the plants (6). Those plants which contain phytoconstituents like (flavonoids, alkaloids, tannins, saponins, phenolic compounds, organic and inorganic constituents, plant proteins etc.) are responsible for anti-urolithiatic activity (9). The World Health Organization (WHO) stated that almost 4 billion (80%) people worldwide take advantage of herbal remedies for their healthcare needs. Furthermore, the remaining 25% of conventional

drugs marketed in developed countries are mostly derived from natural products such as vinblastine, quinine, reserpine and aspirin (10). It is estimated that about 50000–70.000 plant species are utilized for medicinal purposes by traditional and modern healthcare systems worldwide (11). Pakistan has different climatic and ecological zones enriched with floral diversity, containing almost 6000 species of important flowering plants, including 500 species of extreme therapeutic importance. Some of these plants are used in the locally practiced medical system (Hikmat) (12).

A thorough literature search revealed that a lot of work had been done on the medicinal plants in the Abbottabad region (13–20). However, yet no report is available regarding kidney diseases. Therefore, it would be important to document these medicinal plants employed for treating kidney stones. The current study will not only be helpful in the conservation of resources but also helps in preserving the fast-disappearing traditional knowledge and may provide a base for pharmacological research.

Materials and Methods

This study was authorized by the Department of Botany and Office of Research, Innovation and Commercialization of Hazara University (ORIC-HU), Mansehra, Pakistan. Informed consent was obtained from each informant before conducting the interview process.

Study area

The Abbottabad district covers an area of 1967 km² and falls between 34° 9'–34° 21' North latitude and 73° 10'–73° 13' East longitude, predominantly mountainous terrain (Fig. 1). The average peak elevation ranges from 2500–2700 m and the Miranjani peak (3313 m) is the highest point in the district. These peaks dominate the landscape and are a part of the lesser Himalayas. The Dongagali

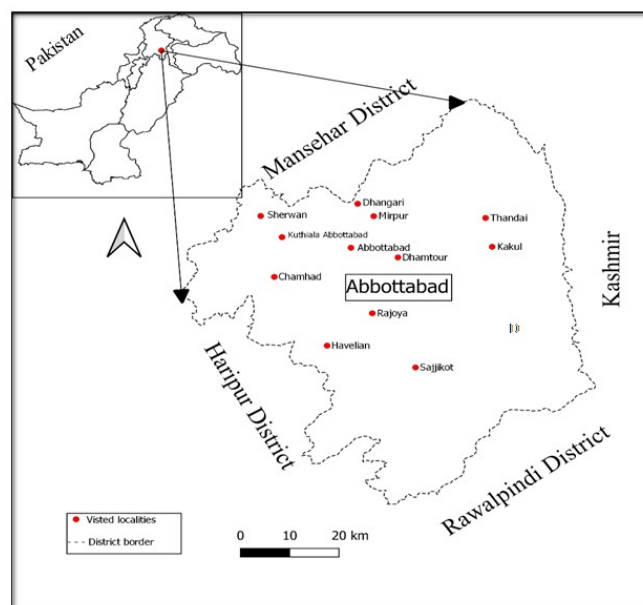


Fig. 1. Map of the study area (visited localities) Abbottabad District, Khyber Pakhtunkhwa, Pakistan.

peaks unite with the right banks of the Jhelum and Kunhar river from the north. It includes various offshoots that differ in altitudes from 2500–2700 m. Several other peaks also project around this range, especially from the west, with 600–1500 m of range. The overall population of Abbottabad is around 1169432 and the urban population is estimated to be 1519751. The topography of Abbottabad is mainly composed of gullies and steep slopes, with metamorphic rocks formed of limestone. Recently, frequent deforestation and pasturage triggered soil erosion, which has made the parent rock shallower and silty loess (21). The average temperature in the region ranges from 34.3–3.4 °C, with occasional snow. Most rainfall occurs in winter and monsoon; the average being recorded is around 1200 mm per year. The major tribes of the region include Gujjar, Awan, Karlal, Syed, Jadoon, Abbasi, Rajput, Kashmiri and Mughal. Most of the population depends on forests and agriculture (primary occupation), although cattle grazing occurs near the adjacent hilly areas. Nevertheless, some people are also involved in local labour and trade. The most commonly grown crops in the area include rice, maize, wheat, tobacco etc. Recently, due to increased illegal tree cuttings, extensive fires, illegal settlements, urban encroachment and growing pollution, the area is under severe threat (22).

Ethnobotanical data collection

Ethnobotanical data were collected following ethical guidelines with informed consent. Questionnaires and semi-structured interviews (SSI) were conducted in spring and summer (2014–2016) at 15 different localities in the Lesser Himalayas. About 95 key informants (15–20 per site and aged 25 to 75 years) with reliable and in-depth knowledge of traditionally used medicinal plants against urolithiasis and residing there for (30 years) were interviewed several times regarding the healing properties against urolithiasis (Table 1). Questions asked to the informants about the medicinally used plants were mainly related to the use of the plant, its local name, habitat, place and time of collection, used parts and categories, fruit and vegetable consumption, way of drug preparation and administration and at last, diseases treated. Plant collection was done during the blooming and fruiting stage, approved by local inhabitants to verify the authenticity of the collected plant. After drying, the specimens were pressed, poisoned and

finally mounted on herbarium sheets. Interviews were conducted mostly in fields; otherwise, photographs were shown for identification. Females were interviewed indirectly through male family members. Participants were briefed about the research objectives and were allowed to discontinue the interview at any time. The native language (Urdu and Hindko) has been used as a medium of communication. Later, an English language questionnaire proforma was filled for each informant.

Identification of plants

The collected plant species were identified with the available Flora of Pakistan, and their names were identified through the literature search and key plant-related websites such as the plant list (www.theplantlist.org), international plant name index (<http://www.ipni.org>) and GRIN taxonomy site (<http://www.ars-grin.gov/cgi-bin/npgs/html/queries.p1>). For voucher specimens, standard herbarium techniques (23, 24) were strictly followed and were deposited in the Hazara University Herbarium, Pakistan for future references.

Quantitative and correlations analysis of ethnomedicinal data

The obtained data were analyzed and presented using quantitative indices, descriptive statistics and correlation analysis for all the collected plant species.

Relative Frequency Citation (RFC)

Relative frequency citation was calculated while ignoring the use-categories following the formula (25).

$$RFC = \frac{FC}{N} \quad (0 > RFC > 1)$$

RFC shows the importance of each species in the study area given by the FC (FC is the number of local informants reported the uses of the species) divided by the total number of informants (N).

Use value (UV)

Use value (UV) determines the importance of each plant species utilized by locals. It was calculated using the following formula (26).

$$UV = \sum U_i / N$$

Where “UV” indicates the use-value of individual species, “ U_i ” is the number of uses recoded for a given species by each informant, and “N” represents the total number of informants in the study.

Table 1. Demographic information of rural respondents.

Variable	Demographic categories	Number of informants	%
Gender	Male	75	79
	Female	20	21
Experience	Traditional healers	25	26
	Local people	70	69
Age groups	25-40	13	14
	41-60	19	20
	Above 60	63	66
Education	Illiterate	69	73
	Primary	15	16
	Middle	2	2
	Matric and above	9	9

Fidelity level percentage (FL%)

Fidelity level (FL) is the percentage of plant specimens that the interviewees claim to be used for the same particular purpose. Fidelity level shows the importance of each species for a specific disease. Its value can be calculated for common diseases as follows:

$$FL (\%) = (N_p / N) \times 100$$

N_p is the number of individuals claiming to utilize a group of plant specimens to cure a specific disease, and N is the number of people utilizing herbal remedies to treat any illness (23, 27, 28).

Pearson correlation

Pearson's correlation, SPSS (ver. 16) tested correlation analysis between the RFC, UV and FL%.

Results and Discussion

The study found that 38 species belonging to 37 genera and 27 families are utilized to treat different urinary tract infections (Table 2). The findings on the usage of ethnomedicinal plants for treating urinary tract disorders are displayed alphabetically, along with the botanical/local name, family, habitat, phytoconstituents and type of application. Such traditional medicinal plants have been practiced by the ancient medicinal systems (Ayurveda, Traditional Chinese medicine, Siddha, Unani medicine and Kampo medicine) for a number of diseases (9), like *Asparagus racemosus* Willd. (root, 5-7 g, powder) used by Siddha for the treatments of urolithiasis (29, 30). A large number of preclinical studies support the traditional uses of medicinal plants to prevent kidney stones (31), such as an *in vitro* experiment (32) found that the aqueous extract of *Bryophyllum pinnatum* leaves was effective in dissolving calcium phosphate. Another study (29) used the ethanolic extract of *Asparagus racemosus* on albino rats and found that the concentration of calcium and phosphate was significantly reduced. In short, most of the modern drugs have been originated from the traditional knowledge of medicinal plants by identifying/isolating/modifying the specific chemical constituents for specific diseases and then performing its clinical trials to evaluate their safety and efficacy and also the effective dosage and its route of administration.

Species richness for the treatment of urolithiasis

A total of 38 species from 37 genera belonging to 27 families were documented, which were used by local

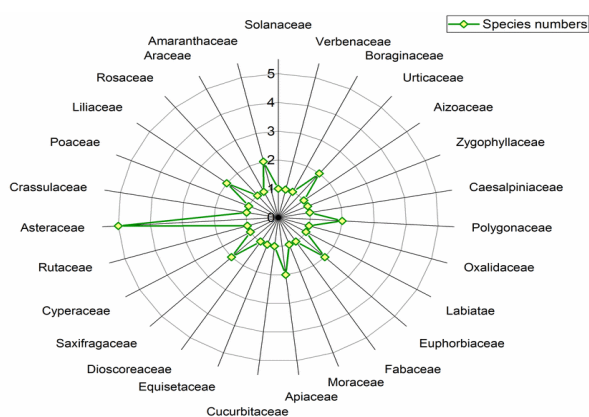


Fig. 2. Taxonomic diversity of medicinal plants used for urolithiasis treatment in Abbottabad District.

people for the treatment of urolithiasis in the study area. Asteraceae family (5 species) was the most frequently mentioned among plant families, followed by Amaranthaceae, Liliaceae, Saxifragaceae, Apiaceae, Euphorbiaceae, Polygonaceae and Urticaceae (2 species each) and the other plant families were recorded with only one medicinal plant species each (Fig. 2). Most of the registered plant species in the study area have been practiced by the Ayurveda Pharmacopoeia of India, TCM, Siddha, Unani for the urolithiasis treatment (2, 9); some of them have been tested in preclinical studies and some of the claims were scientifically proved for the same diseases as in the therapy/practice.

Ethnomedicinal utilization of plant parts for the treatment of urolithiasis

A total of eight different plant parts were used for the management of urolithiasis by the local community (Fig. 3). Leaves were the most widely used part (28.94%), followed by the whole plant

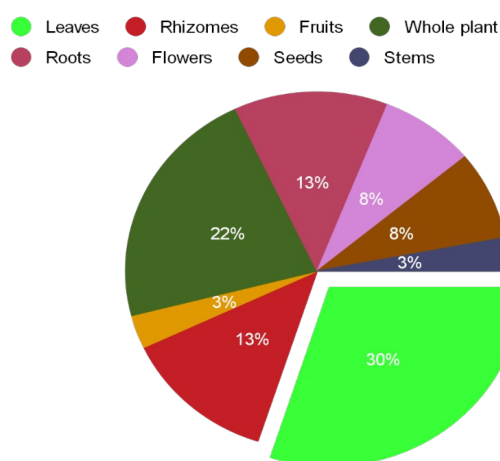


Fig. 3. Ethnomedicinal utilization of plant parts for the treatment of urolithiasis.

(21.05%), rhizomes and roots (13.5%), flowers and seeds (7.89%) and fruits and stem (2.63%). Because of the lower level of communication means, ignorance, poverty and the absence of modern therapeutic facilities, the people of the rural areas still depend on traditional medicines for curing various ailments (Table 1). Plant parts and the way of their utilization have a significant role in preventing any disease. It has been found that some of the traditionally used plant parts contain phytoconstituents which can be used as anti-urolithiasis agents, such as *Bergenia ciliata* leaves (ethyl acetate extracts) (33) and *Bryophyllum pinnatum* leaves extracts (32). In a study, the pulp extracts of *Citrullus lanatus* were found to be effective against urolithiasis, while the seed extracts did not show any effectiveness (34). In contrast, the seeds of *Citrullus lanatus* were used traditionally against urolithiasis. However, in this study, most of the reported species based on the part of utilization and their purpose against urolithiasis matched with the phytoconstituents used in pre-clinical stages. Some species were found with no pharmacognostic study records, therefore, recommended for further screening.

Table 2. Ethnomedicinal plants used for the treatment of urolithiasis.

Botanical Name, family, voucher number	Local name	Plant parts used	Type of preparation	Disease Treated	Route and Dosage	Quantitative Indices				
						FC	RFC	ΣU_i	UV	FL%
<i>Achyranthes aspera</i> L. (Amaranthaceae), HUP-0002	Puthkanda	Leaves	Decoction	Treatment of calculi	Orally, twice daily for 7-10 days	40	0.421	70	0.73	50
<i>Acorus calamus</i> L. (Araceae), HUP-0003	Bach	Rhizome	Powder	Diuretic and useful for calculous affections	3 g twice daily for 7-12 days	29	0.305	60	0.63	25
<i>Aerva lanata</i> L. (Amaranthaceae), HUP-0004	Not Known	Whole plant	Extract	Diuretic and lithotriptic and is used in lithiasis	Half of the teacup twice daily for one month	55	0.578	99	1.04	30
<i>Agrimonia eupatoria</i> L. (Rosaceae), HUP-0001	PeeliBooti	Leaves	Decoction	Alleviates liver, bladder and kidney stones	1 teacup twice daily for two weeks	49	0.515	105	1.1	60
<i>Asparagus racemosus</i> Willd. (Liliaceae), HUP-0005	Shahghandal	Leaves	Decoction	Expel stones from the urinary tract	1 teacup twice daily for 8-12 days	25	0.263	45	0.47	80
<i>Bergenia ciliata</i> L. (Saxifragaceae), HUP-0006	Butpai	Rhizome	Powder	Release kidney stones	10 g daily for one week	36	0.378	70	0.73	100
<i>Bergenia stracheyi</i> Engl. (Saxifragaceae), HUP-0028	Butpai	Rhizome	Powder	Release kidney stone	10 g daily for one week	22	0.231	30	0.31	100
<i>Bryophyllum pinnatum</i> (Lam.) Oken. (Crassulaceae), HUP-0029	Pthar chat.	Leaves	Extract	Break the kidney stone	2 teaspoons twice daily for 5 to 8 days	32	0.336	65	0.68	90
<i>Celtis australis</i> L. (Urticaceae), HUP-0007	Batkalar	Fruits	Decoction	Remove stones from the UT, with frequent urination	1 teacup twice daily for two weeks	41	0.431	92	0.96	70
<i>Cichorium intybus</i> L. (Asteraceae), HUP-0008	Kasni	Roots	Decoction	Control inflammation/pain of kidney and urinary tract	2 teacup thrice daily for one week	36	0.378	87	0.91	50
<i>Citrus sinensis</i> (L.) Osbeck. (Rutaceae), HUP-0030		Fruits	Juice	Reduce kidney stone and support kidney functions	40 ml daily for two weeks	20	0.210	45	0.47	70
<i>Citrullus lanatus</i> (Thunb.) Matsumura. (Cucurbitaceae), HUP-0031	Tarbooz	Seeds	Powder	Control kidney and urinary tract pain	3 g orally for 4-8 days	25	0.263	68	0.71	90
<i>Conyza canadensis</i> L. (Asteraceae), HUP-0009	Not Known	Whole plant	Decoction	Gravel and kidney disorders.	1 teacup per day for 9-13 days	35	0.368	88	0.92	30
<i>Cyperus rotundus</i> L. (Cyperaceae), HUP-0010	Muther	Rhizome	Decoction	Dissolve stones	Taken orally	19	0.2	59	0.62	60
<i>Dioscorea deltoidea</i> Wall. (Dioscoreaceae), HUP-0011	Karins	Rhizome	Cooked	Kidney disorders.	Taken orally	31	0.326	76	0.8	70
<i>Eclipta alba</i> Hassak. (Asteraceae), HUP-0012	Not Known	Leaves	Juice	Remove stones from the gallbladder	25-50 ml before breakfast daily for one week	45	0.473	98	1.03	40
<i>Equisetum ramosissimum</i> Desf. (Equisetaceae), HUP-0013	Not Known	Whole plant	Juice	Urine burning and expel kidney stones.	30-50 ml every morning for 6-10 days	39	0.410	100	1.05	90
<i>Eryngium maritimum</i> L. (Apiaceae), HUP-0014	Kandiari	Roots	Decoction	Cystitis and urethritis and also alleviate kidney stones.	1 teacup daily for two weeks	26	0.273	62	0.65	40
<i>Euphorbia prostrata</i> L. (Euphorbiaceae), HUP-0032	Doadal	Whole plant	Powder	Kidney stones.	3-5 g twice daily for 9-12 days	15	0.157	33	0.34	50
<i>Ficus carica</i> L. (Moraceae), HUP-0033	Angir	Fruits	Decoction	Destroy urinary and gall stones	Half of the teacup before breakfast for 5-10 days	19	0.2	79	0.83	70
<i>Flemingia grahamiana</i> Wight and Arn. (Fabaceae), HUP-0034	Kamaila	Leaves	Extract	Diuretics and cure painful urination	Two spoons daily for half a month	27	0.284	82	0.86	60
<i>Micromeria biflora</i> (Buch.-Ham. ex D. Don.) (Labiatae), HUP-0035		Whole plant	Decoction	Remove kidney stones	1 teacup twice daily for two weeks	18	0.189	49	0.51	50

<i>Phyllanthus niruri</i> L. (Euphorbiaceae), HUP-0036		Whole plant	Extract	Stone breaker	1 teacup daily for one month	56	0.589	94	0.98	90
<i>Polygonum aviculare</i> L. (Polygonaceae), HUP-0016	Tarubra.	Leaves	Decoction	Dissolve and expel kidney stones	1 teacup daily for 12-17 days	34	0.357	66	0.69	60
<i>Rumex acetosa</i> L. (Polygonaceae), HUP-0017	Khatri	Roots	Powder	Dissolve kidney and bladder stones	5-8 g daily for 6-10 days	60	0.631	109	1.147	80
<i>Polygonatum multiflorum</i> Allioni. (Liliaceae), HUP-0018	Adbis	Roots	Decoction	Dissolves kidney stones and promote kidney functions	1 teacup daily for 5-8 days	24	0.252	42	0.442	50
<i>Tamarindus indica</i> L. (Caesalpiniaceae), HUP-0019	Imli	Fruits	Decoction	Eliminate calculi/stones	1 teacup twice daily for 10 days	17	0.178	39	0.410	70
<i>Trachyspermum ammi</i> (L.) Sprague. (Apiaceae), HUP-0020	Ajwain	Seeds	Cooked	Remove kidney stones	10 g seeds soaked in water overnight, taking before breakfast daily	29	0.305	78	0.821	57
<i>Tribulus terrestris</i> L. (Zygophyllaceae), HUP-0021	Gokhru	Seeds	Powder	Promotes urine discharge and removes painful urine	4-7 g twice daily for 11-15 days	31	0.326	93	0.97	90
<i>Trianthema portulacastrum</i> L. (Aizoaceae), HUP-0037	kandiari	Leaves	Decoction	Diuretic and break the kidney and bladder stones	1 teacup daily for 5-8 days	20	0.21	75	0.78	80
<i>Trichodesma indicum</i> (L.) R. Br. (Boraginaceae), HUP-0038		Leaves	Extract	Stone breaker	1 spoon thrice daily for 9-13 days	22	0.231	69	0.72	60
<i>Solidago virga-aurea</i> L. (Asteraceae), HUP-0022	Not Known	Leaves	Decoction	Promote urination/flush out kidney and bladder stones.	1 teacup thrice daily for one week	36	0.378	85	0.89	23
<i>Urtica dioica</i> L. (Urticaceae), HUP-0023	Bichubooti	Leaves	Decoction, Cooked	Dissolves calcium oxalate/renal stones	Taken orally/1 teacup twice daily for 15-30 days	12	0.126	46	0.48	40
<i>Verbena officinalis</i> L. (Verbenaceae), HUP-0024	Not Known	Whole plant	Decoction	Remove kidney stones/disorders	2 teacup twice daily for 7-11 days	11	0.115	38	0.4	25
<i>Withania somnifera</i> Dunal. (Solanaceae), HUP-0025	Askand	Roots	Decoction	Prevent and treat kidney damage	1 teacup daily for 7-11 days	13	0.136	67	0.70	32
<i>Xanthium strumarium</i> L. (Asteraceae), HUP-0026	Kandiari	Leaves	Decoction	Treat bladder infections	1 teacup twice daily for two weeks	40	0.421	92	0.96	60

FC, Frequency citation; RFC, Relative frequency of citation; \sum Ui, Sum of all uses mentioned by each informant for a species; UV, Use values; FL%, Fidelity level percentage.

Preparations of herbal remedies

The local communities used the native diversity of medicinal plants for treating urolithiasis disease by following several administrative ways; decoction was the popular and dominant way of preparation

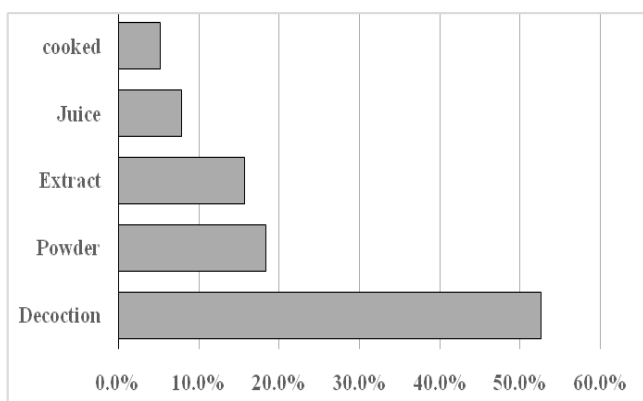


Fig. 4. Types of preparations used against urolithiasis in the study area.

(52.6%), followed by powder (18.4%), extracts (15.7%), juice (7.8%) and cooked (5.2%) (Fig. 4). Mostly used medicinal plants demonstrate that approximately 650 species are utilized as mono- or polyherbal remedies and are used in the form of decoction and acts as diuretic substances (31). The preparation of polyherbal remedies is considered less toxic, safe and effective by traditional medicinal systems and is inexpensive than allopathic therapy (2). In traditional therapies, plant parts used, their preparation and the route of administration may have a significant role in the pharmacological action of medicinally used plant taxa.

Important ethnomedicinal species

The UV of plant species determines the relative importance of plants in the study area. The highest UV was recorded for *Rumex acetosa* L. (1.14), *Agrimonia eupatoria* L. (1.1), *Equisetum ramosissimum* Desf. (1.05), *Aerva lanata* L. (1.04), *Eclipta alba* Hassak. (1.03), *Phyllanthus niruri* L. (0.98), *Tribulus terrestris* L. (0.97), *Xanthium*

strumarium L. and *Celtis australis* L. (0.96 each), *Cichorium intybus* L. (0.91), *Conyza canadensis* L. (0.92), and the other recorded plant species were <0.90 use-values. RFC values can be used to identify the most known medicinal plants species among the local peoples. In this study, the high RFC value was recorded for *Rumex acetosa* L. (0.63), *Phyllanthus niruri* L. (0.58), *Aerva lanata* L. (0.57), *Agrimonia eupatoria* L. (0.51), *Eclipta alba* Hassak. (0.47), *Celtis australis* L. (0.43), *Achyranthes aspera* L. and *Xanthium strumarium* L. (0.42 each), *Equisetum ramosissimum* Desf. (0.41), and the other recorded plant species were <0.4 RFC value. Use value and RFC value are dynamic as it changes with the area and depends on the local people's traditional knowledge, so the UV and RFC value may vary within the same area or area to area and community to community (35). Correlation analysis between RFC and UV was significant at the 0.01 level (0.803**), indicating that the local people have significant traditional knowledge of the cited species (Table 3).

Table 3. Correlation between RFC, UV and FL% of the recorded medicinal plants

Variables	N	Descriptive		Correlation		
		Mean	SD	RFC	UV	FL%
RFC	38	0.3147	0.13278	1	0.803**	0.128
UV	38	0.7471	0.24125	0.803**	1	0.091
FL	38	61.8947	22.28536	0.128	0.091	1

** represents that correlation is significant at the 0.01 level (2-tailed)

Fidelity Level percentage shows the importance of each species for specific urolithiasis disease in this study (Table 2). Those species with above 50 FL% in the study area were considered for further literature search, parts used, pharmacological properties and chemical constituents against urolithiasis. The similarity of traditionally used/reported species was also evaluated against the phytoconstituents assessed in preclinical models of urolithiasis (Table 4). An *in-vitro* experiment (33) found that phenolic compounds (ethyl acetate extracts) from the *Bergenia ciliata* leaves effectively dissolved calcium phosphate and oxalate stones, where cystone was more effective than phenolic compound against urolithiasis. The leaf extracts of *Bryophyllum pinnatum* and their chemical constituents are useful for preventing kidney stones formation and decreasing urinary calcium levels.

The current reported medicinal plants activities against urolithiasis may be due to the presence of bioactive compounds in the plant parts used traditionally and some of these parts of the plants have been investigated for their bioactive compounds against urolithiasis, while some are still unknown. Previous studies found the effectiveness of the chemical constituents against urolithiasis derived from plant parts that were practiced in the present study, such as *Citrullus lanatus* and *Tribulus terrestris* (seed) (34, 36), *Equisetum ramosissimum*, *Oxalis corniculata* and *Phyllanthus niruri* (whole plant) (37–39), *Zea mays* (stem) (40), *Asparagus racemosus*, *Agrimonia eupatoria*, *Polygonum aviculare*, *Trichodesma indicum*, *Xanthium strumarium* and *Trianthema portulacastrum* (leaves) (29, 41–44),

Rumex acetosa (root) (45), *Celtis australis*, *Tamarindus indica*, *Ficus carica* and *Citrus sinensis* (fruit) (46–48), *Dioscorea deltoidea* and *Cyperus rotundus* (rhizome) (49, 50). The present study demonstrated that the chemical compounds from plant parts in the modern health systems and their utilization (51) may have been practiced earlier by the ancient traditional medicine systems in their own way and may have been transferred from generation after generation.

Previous studies demonstrated that *Bergenia stracheyi* had been widely used by traditional Indian, Nepalese and Chinese medicine systems for the treatment of bladder and kidney stones and several other diseases (52–54). Similarly, the present study recorded *Bergenia stracheyi* with cent fidelity level, used against kidney stones that release stones from the kidney, yet no medical therapy has been performed. Another plant species *Flemingia grahamiana* was continuously reported in the study area, but it has not been well explored as anti-urolithiasis in pre-clinical trials. Therefore, further clinical trials are required, especially of these two species, to record their efficacy against urolithiasis.

Cultural significance

The WHO promotes and advises the documentation of traditionally used medicinal plants for the treatment of various diseases around the world (55). Various clinical trials have been conducted to evaluate the efficacy and safety of various traditional medicinal plants. About 75% of drugs currently used directly or indirectly came from traditional medicinal plants (56). Listing of high value ethnomedicinal plants is essential and has a significant value in determining human-plant relationships (57). It is important to involve the local communities in developing useful drugs plants that can socio-economically uplift them. The present study found that only older people and traditional healers have more knowledge of these useful medicinal plants, which may transfer generation after generation. Hence, proper documentation of ethnomedicinal knowledge of valuable medicinal plants in the country is necessary and should be analyzed using modern research techniques to find useful compounds and molecules, and then should be further evaluated in the preclinical and clinical models for the treatment of various diseases. There is a dire need to find better alternative drugs due to the adverse effects of conventional medicines and herbal medicine can be a possible solution for that purpose only after passing through vigorous chemical and biological screening procedures (58). It is also important that new crops are introduced to ethnobotanists and anthropologists, who can gather and document the traditional knowledge and significance of those plants, which will help to conserve the biodiversity and lead to sustainable utilization of these useful plant resources. The currently collected information will help to drive the research work forward and can help in the scientific evaluation of the safety and efficacy of the traditional herbal remedies used by the tribes, especially the less familiar remedies (59, 60). Consequently, people can be informed and guided about the scientifically proven efficacious drug treatments for various diseases, which will improve their health conditions.

Table 4. Major reported species, phytoconstituents and their pharmacological activities against urolithiasis (evidence from literature)

Botanical Name	Pharmacological Activities	Chemical groups	Constituents/extracts	STU	References
<i>Agrimonia eupatoria</i> L.	Antioxidant, antiasthmatic diuretic, astringent and gall bladder disorders	Flavonoids, terpenoids, tannins, carbohydrates glycosides, organic acids and oils	Ursolic acid, silicic, α -myrin and thiamine	Yes	(42)
<i>Asparagus racemosus</i> Willd.	Antioxidant, antibacterial and Diuretic	Flavonoids, terpenoids and saponinins	quercetin-3-glucuronide/leaves) and ethanolic extract	Yes	(29, 61)
<i>Bergenia ciliata</i> L.	Anti-inflammatory, antioxidant, antibacterial and analgesic	Phenolics and flavonoid	Alcoholic, butanol, ethyl acetate and hydro-methanol extracts	Yes	(33, 62, 63)
<i>Bergenia stracheyi</i> Engl.	antibacterial, antiviral, antifungal, cytoprotective and antioxidant	Tannins, flavonoids, benzanoids, steroids, coumarins, quinoids and lactone	Not well explored for kidney diseases	Not well explored for kidney diseases	(52, 53)
<i>Bryophyllum pinnatum</i> (Lam.) Oken.	Anti-inflammatory, antioxidant, antibacterial, analgesics and nephroprotective	Saponins, tannins, alkaloids and phenolic compounds	P.ether, chloroform, ethanol, acetone and aqueous extracts	Yes	(32)
<i>Celtis australis</i> L.	Antioxidant, cytotoxic, antibacterial and diuretic	Glycosides, steroids, saponins, terpenoids, tannins, alkaloids and phenolic compounds	Methanol, aqueous and ethyl acetate extracts	Yes	(48)
<i>Citrus sinensis</i> (L.) Osbeck.	Anti-inflammatory, antihypertensive, antidiabetic and diuretic	Phenolics, glycosides, tannins and saponins	Peel, Ethanolic and aqueous extracts	Yes	(47)
<i>Citrullus lanatus</i> (Thunb.) Matsumura	Antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, anti-plasmodial, antiangiardial and antiulcerogenic	Steroids and alkanes	Cycloartenyl acetate, octadecane, Heptacosane (1 st , 2 nd , 3 rd and 4 th isomers)	Partial	(34)
<i>Cyperus rotundus</i> L.	Analgesic, antioxidant, anti-inflammatory, antispasmodic, antiplatelet, antiallergic, antimicrobial and wound healing.	Flavonoids, tannins, glycosides, alkaloids, saponins, terpenoids, oils, carbohydrates and proteins	Hydroalcoholic extracts, glycerol, myristic acids, sitosterols and linoleic acid	Partial	(49, 64)
<i>Dioscorea deltoidea</i> Wall.	Antioxidant, contraceptive, antiarthritic, anti-rheumatic, anti-constipation, antimicrobial and diuretic	Phenolics, alkaloids and saponins	Aqueous extracts	Partial	(50)
<i>Equisetum ramosissimum</i> Desf.	Antibacterial, antiseptic and astringent, antiurolithiatic, analgesic, antidiabetic, diuretic and anti-hemorrhagic	Flavonoids and alkaloids	Quercetin-3-O-glucoside, kaempferol 3-O-glycoside, apigenin and 5-O-glucoside	Partial	(38)
<i>Ficus carica</i> L.	Anti-inflammatory, litholytic, astringent, antioxidant, demulcent and diuretic	Polyphenols, carbohydrates, minerals and vitamins	Gallic acid, chlorogenic acid, syringic acid, (+) - catechin and methanolic extracts	Yes	(46)
<i>Flemingia grahamiana</i> Wight & Arn.	Antioxidant, antimicrobial, anti-inflammatory, cytotoxic and antifungal	Alkaloids, terpenoids, quinones flavonoids, coumarins and phenols	Methanol and ethanolic extracts	Not well explored for kidney diseases	(65)
<i>Oxalis corniculata</i> L.	Antibacterial, anthelmintic, astringent, diuretic, antiarthritits, antiphlogistic and lithontripic	Phytosterols, tannins, flavonoids and glycosides	B-sitosterol, ethyl gallate, betulin, Oxalic acid and vitamin C	Yes	(66, 67)
<i>Phyllanthus niruri</i> L.	Diuretic, anti-inflammatory, antioxidant, antibacterial, analgesics and spasmolytic	Tannins, lignans, glycosides, flavonoids, alkaloids and phenylpropanoids	The aqueous extract of the whole plant and ellagitannins.	Yes	(39)
<i>Polygonum aviculare</i> L.	Diuretic, antihypertensive, antibacterial and antioxidant	Phenols, carboxylic acids and glycosides	Bryophillin A, hydroxycinnamic acid, bersaldegenin-3-acetate and bryophillin C	Yes	(43, 68)
<i>Rumex acetosa</i> L.	Anti-inflammatory, antihypertensive, antidiabetic and diuretic	Polyphenols, anthraquinones and tannins	Emodin, palmatin, and sennosides A and B	Yes	(45)
<i>Tamarindus indica</i> L.	Antibiotic and antilithiatic	Alkaloids, tannins, flavonoids, terpenoids and steroids	Caffeic acid, ferulic acid, chloramphenicol, myricetin and quercetin.	Yes	(46, 69)
<i>Tribulus terrestris</i> L.	Spasmolytic, diuretic, analgesics, anti-inflammatory and antibacterial	Saponin, flavonoids and alkaloid	n-Butanol, glycolate oxidase, quercetin.	Yes	(36)
<i>Trianthema portulacastrum</i> L.	Anti-inflammatory, antioxidant, antibacterial, analgesic, diuretic and spasmolytic	Saponins, flavonoids, tannins, alkaloids and phenolic compounds	β -Cyanin, 5,2'-dihydroxy7-methoxy-6,8-dimethyl flavones (Cmethylflavone), leptorumol, β -sitosterol, β -glucopyranosides.	Yes	(41, 70)

<i>Trichodesma indicum</i> (L.) R. Br.	Anti-inflammatory, Antioxidant, antimicrobial, antiviral and skin diseases	Phenols, glycosides, terpenoids, oils and tannins	Methanol and Ethanolic extracts	Yes	(71)
<i>Xanthium strumarium</i> L.	Antiulcerogenic, anti-proliferative, anti-inflammatory, analgesic, antidiabetic and hypoglycaemic, antiarthritic, diuretic and renoprotective, antimicrobial, antihelminthic and anti-plasmodial.	Terpenoids, steroids, coumarins, lignanoids, phenols, coumarins and glycosides	Deacetyl xanthumin, xanthostrumarin and xanthatin	Yes	(31, 44, 72)
<i>Zea mays</i> L.	Anti-inflammatory, antioxidant, diuretic and nephroprotective	Saponins, flavonoids, tannins and alkaloids	Corn silk extracts	Yes	(40, 73)

STU, Similarity with Traditional Utilization

Status of medicinal plants of Abbottabad region

The primary sources of medicinal plants in Pakistan are rangelands and forests, mainly utilized as traditional medicines (74–76). The biodiversity of medicinal plants in the region is under serious threat because of anthropogenic activities, overgrazing, deforestation, timber smuggling, ruthless and unscientific collection (22). These anthropogenic activities lead to the alteration in habitat, fragmentation and severe habitat destruction, which resulted in significant habitat loss. Furthermore, climate change and plant invasions are the other serious threats in this regard (77, 78). Both *in situ* and *ex situ* conservation measures are required to conserve the regional flora, such as massive reforestation, natural gas supply, community awareness, providing energy efficient cookstoves, and establishing botanical gardens and proper guiding training of medicinal-plant collectors, which may help in flora conservation. However, these efforts will only get results if they are cross-sectoral and promote cooperation and collaboration among the natural resource managers, government agencies, traditional medical practitioners and various other interest groups.

Conclusion

The current study reported that the local communities widely practice indigenous herbal-based medicines and its utilization remains to be a viable and better alternative therapeutic option for the rural and underprivileged sections of the communities. However, precise traditional knowledge about medicinal plants was found among few people (mostly older people) in the local communities. Therefore, proper exploration, documentation and preservation of traditional ethnomedicinal knowledge are required before it disappears forever and needs to be preserved for future generations. Our survey revealed that there are still some claims that warrant experimental investigations, implying that a lot can still be learned from exploring medicinal plants in the region, which may lead to finding valuable phytoconstituents in plants that are effective against urolithiasis and also other diseases. All these ethnomedicinal plants require a thorough scientific investigation for isolation, identification, biochemical assays, toxicities and evaluation of pharmacological activities of the phytoconstituents, especially of the high-fidelity level plants. This

study will help in preserving the useful and immensely important knowledge of traditionally used medicinal plants in the region and promote the importance of ancient healing practices in the coming generations. It also emphasizes the need for a holistic approach to engaging the local communities in the conservation of medicinal plants by sustained harvest and cultivation in their natural habitat due to the immense ecological and pharmacological importance.

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Authors' contributions

GMS: Conceptualization, methodology, investigation, formal analysis. NS: Conceptualization, writing, software, statistical analysis, writing and editing. A.N: Conceptualization, critical review and editing. MU, MH, SM and MS: Visualization, data curation. FUK, NJ and A: Funding acquisition.

Conflict of interests

Authors do not have any conflict of interests to declare.

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