

The Role of Pakistan's Indigenous Medicinal Flora in Combating Urinary Tract Infections: Exploring Botanical Heritage for Modern Healthcare

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Abstract

Urinary Tract Infections (UTIs) exist a major healthcare problem throughout the world, the growing trend worldwide and general public interest in traditional drugs contribute, in preventing a number of side effects and toxicities. "Diseases are afflicting people around the world, including in Pakistan, who are suffering from various ailments like UTIs and the overusage of antibiotics is making things worse." It is important to take advantage of the flora that may have potential to treat UTIs, which are easily accessible and inexpensive. Integrative medicine is a comprehensive approach to UTI care that includes traditional and complementary treatments. Particularly, botanical therapeutics have become promising adjuncts or alternatives because of their effectiveness, safety, and potential antimicrobial activity. Drawing upon literature from Pakistan, where traditional herbal medicine holds cultural significance, the native botanicals employed in treating UTIs are investigated. Botanical interventions such as , pumpkin seeds (*Cucurbita pepo*), Aloe vera (*Aloe barbadensis* miller), Niazbo (*Ocimum sanctum*), Bichu Booti (Nettle Root), Pomegranate (*Punica granatum*), Zahkm -e -hayat (*Bergenia ligulata*), Rupturewort (*Herniaria hirsute*), Beejband Surkh (*Abutilon indicum*) , Kharboza (*Cucumis melo*), Bhutta (*Stigma maydis*) have garnered global attention for their ability to hinder bacterial adhesion to urinary epithelial cells, modulate immune responses, and exhibit antimicrobial effects against uropathogens. These plant-based remedies might be better than antibiotics in some ways. They could lead to less drug resistance and have fewer side effects. People often make these remedies by boiling, steeping, or extracting them just like in old-time medicine. Using these plants shows how valuable herbal treatments can be. It also highlights why it's crucial to blend old knowledge with new healthcare approaches.

Keywords: Flora of Pakistan, Traditional medicine, Urinary tract infection, Herbal remedies

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Introduction

Urinary tract infections (UTIs), caused by the infiltration of bacteria into the urinary tract comprising the kidneys, bladder, or urethra, pose a significant health concern globally. In 2019 alone, an estimated 404.61 million cases of UTIs were recorded, resulting in 236,790 deaths and 520,200 Disability-Adjusted Life Years. Notably, there has been a concerning 2.4-fold increase in UTI-related deaths from 1990 to 2019, alongside a rise in the age-standardized mortality rate, escalating from 2.77 per 100,000 to 3.13 per 100,000. (Yang et al., 2022) These statistics underscore the pressing need for effective preventive measures and treatments to mitigate the escalating burden of UTIs, which afflict approximately 60% of women and 12% of men during their lifetimes and prompt over 8.1 million healthcare visits annually (Foxman, 2002). The financial burden of UTIs in the United States surpasses \$3.5 billion alone, with over half of prescribed anti-infection agents for suspected UTIs in older adults deemed unnecessary. Globally, approximately 150 million individuals endure UTIs annually, resulting in over \$6 billion in direct healthcare expenses. UTIs commonly afflict individuals with various chronic conditions such as diabetes, stroke, arthritis, obesity, alcohol use disorder, hypertension, HIV, liver cirrhosis, Hepatitis C, long-term care residents, those who are immunocompromised, pregnant women, individuals with a history of or current catheterization, spinal cord dysfunction, and certain cancers. (Mohiuddin & Nasirullah, 2019). Pakistan's diverse landscapes host a wealth of medicinal plants, offering remedies for various ailments. In Punjab's wetlands, herbs like *A. vesica* are revered for treating respiratory and digestive issues (Iqbal et al., 2021) Sindh's deserts boast resilient species like *Aloe vera* and *Ricinus communis*, used for digestive and skin problems (Iqbal et al., 2021) S The rough landscape of Balochistan is abundant in plants known for treating gastrointestinal and skin issues, with *Pinus gerardiana* being the dominant species. (HAQ et al., 2021) In Azad Kashmir's valleys, there is a diverse array of medicinal plants, particularly effective against digestive disorders (Amjad et al., 2020) This botanical diversity is a reflection of Pakistan's deep cultural connection with nature and its sustainable utilization over centuries. Throughout Pakistan's various regions, there exists a wealth of medicinal plants renowned for their effectiveness in treating a wide range of ailments. UTIs stand out as a major health issue across the country including multiple range of diseases related to urinary tract infections like enlarged prostate, kidney stones, and other conditions that can affect health. The medicinal plants grown and cultivated in different provinces of Pakistan including the agricultural of

Punjab, arid deserts of Sindh and Balochistan and in the valleys of Azad Kashmir are used for the medicinal purpose for alleviating UTI symptoms. These research analysis on natural remedies reflects Pakistan a rich cultural heritage which emphasize the importance of nature's healing properties for the treatment of various diseases and their symptoms.

***Cucurbita maxima* (Mitha Kaddu)**

Pumpkins, the members of the Cucurbitaceae family including species *Cucurbita maxima*, *Cucurbita pepo*, and *Cucurbita moschata*, are extensively grown and utilized globally. These plants are native to South America but now cultivated in Asia including Pakistan, India and Bangladesh. *Cucurbita maxima*, consists a range of medicinal compounds such as Polyphenols, Flavanoids, Carotenoids, and terpenoids, contributing to its antioxidant properties. These Phytoconstituents used to prevent cancer, bacteria, and inflammation .(Hussain, Kausar, Din, Murtaza, Jamil, Noreen, Rehman, et al., 2021). The utilization of *C.maxima* and *C. pepo* extracts has become increasingly popular for the treatment of renal tract symptoms caused by benign prostatic hyperplasia, amelioration of symptoms, enhancement in quality of life, and improvement in uroflowmetry parameters. (Damiano et al., 2016) The effectiveness of a blend comprising pumpkin seed extract, soy germ isoflavonoids, and cranberry was evaluated in addressing mild to moderate lower urinary tract symptoms in patients with benign prostatic hyperplasia in the current investigation. The results showed a significant enhancements in International Prostate Symptom Score and the urological quality of life index following a three-month regimen of this combined formulation. (Theil et al., 2022). It has been revealed that extracts originating from pumpkin seeds exhibit a greater inhibitory effect against *C. albicans* compared to extracts from pumpkin peel and flesh. This discovery underscores the potential effectiveness of pumpkin seed extracts as a natural solution for combating *C. albicans* infections in the urinary tract.

***Aloe barbadensis* (Gheegwar)**

Aloe vera, celebrated for its ancient healing properties, contains a gel rich in beneficial collenchyma and parenchyma cells, widely utilized in food, supplements, and Ayurvedic and Unani therapies. Research highlights its multifaceted benefits, ranging from anti-inflammatory and antibacterial properties to wound healing and immune modulation. Meanwhile, urinary tract infections (UTIs), typically instigated by bacterial infiltration from the skin or rectum into the urethra, primarily affect the bladder, with *Escherichia coli* serving as the predominant pathogen. Recent investigations delve into the potential of specific plant compounds, including those present in Aloe vera, as inhibitors of the 8BVD protein, presenting promising avenues for combating UTIs. (Gurisha et al., 2024). The antimicrobial properties of *Aloe vera* extracts showed a promising effect against resistant Gram-negative bacteria as well as targeting antibiotic –resistant bacteria that are responsible for the UTIs (Arsene et al., 2022, Gurisha, Rao, & Cherupally, 2024)

***Ocimum tenuiflorum* (Niazbo)**

Niazbo or *Ocimum tenuiflorum* (Lamiaceae family), mostly it grown in tropical and warm temperate regions with approximately 160 species, the genus is widely dispersed across warm regions globally including Pakistan, India (Nahak et al., 2011). Its significance in complementary and alternative is remarkable, it serves as a remedy for a number of diseases ailments including upper respiratory tract infections, GI disorders, headaches, dermatological diseases, pneumonia, as well as cough, fever, and conjunctivitis. Phytochemical analysis of *Ocimum* indicates a diverse profile, encompassing the phenolic compounds, glycosides, flavonoids, tannins, and saponins comprising Oleanolic acid, Ursolic acid, Rosmarinic acid, Eugenol, Carvacrol, Linalool, and β -caryophyllene. The plant also reported for its antibacterial activity against various antibiotic resistant microorganisms (Panchal & Parvez, 2019). The pharmacological activities such anti-diabetic and anti-neoplastic effects has been reported in previous studies(Eid et al., 2023). Due to the presecnce of high content of essential oil and aromatic compounds, Niazbo serves both as a cooking purpose and an appealing ornamental plant. Compounds within the *Ocimum* genus, to which *ocimum* belongs, demonstrate a myriad of beneficial actions including antioxidant, antibacterial, antifungal, antifertility, anticancer, antidiabetic, antimicrobial, hepatoprotective, cardioprotective, antiemetic, antispasmodic, analgesic, adaptogenic, and diaphoretic properties (Panchal & Parvez, 2019)and radioprotective properties, aiding in lipid peroxidation reduction and superoxide dismutase activity enhancement. Moreover, the plant exhibits promising potential in the treatment of central nervous system disorders like depression. With a minimum inhibitory concentration (MIC) of 20 mg/ml against bacteria such as *E. coli*, *Vibrio cholerae*, and *Salmonella typhi*, *O. tenuiflorum* demonstrates substantial antibacterial activity.. (Kumar et al.) Niazbo's or *Ocimum* kidney-strengthening properties are notable, particularly in addressing kidney stones. Consuming a mixture of basil leaf juice and honey consistently over six months has been shown to aid in stone expulsion. Additionally, the plant detoxifying attributes help lower uric acid levels, a common contributor to kidney stone formation(Suneetha et al., 2021)

***Punica granatum* (Anaar)**

The Punicaceae family is limited to just two species, with *Punica protopunica* found solely on the island of Socotra. Originating in Iran, these plants spread to the Himalayas and the Mediterranean region of Europe in ancient times. *Punica granatum*, commonly known as pomegranate, thrives in countries like Iran, Pakistan, India, Egypt, Afghanistan, Iraq, China, Bangladesh, Saudi Arabia, and Burma. Believed to have originated in the Middle East, it spread to the Mediterranean, India, China, America, Mexico, and California. In Pakistan, *P. granatum* is found in native forests, particularly in northern regions at altitudes of 1000 to 2000 meters. It's also prevalent in Khyber Pakhtunkhwa, Baluchistan, south-Waziristan, and parts of Kashmir and Hazara.(Ali et al., 2017)

Pomegranate has been cherished for centuries for its remarkable nutritional profile and health benefits. The phytoconstituents such as phenolic compounds including proanthocyanidins, ellagitannins, and flavonoids showed significant antioxidant and anti-inflammatory properties. The pharmacological activities reported by *P.grantum* includes anti-aging, anti-cancer, anti-diabetic, cardio-protective, and neuroprotective effects against conditions like Alzheimer's and Parkinson's disease. It shows promising effect in the treatment of liver fibrosis, it also exhibits anthelmintic and antifungal activities against pathogenic fungal strains.

Not only the seeds and juice the peel of the pomegranate holds valuable potential. The extract of the rind are used in various medicinal and cosmeceutical products due to its significant antioxidant properties. The extract used in alleviating hepatic and renal damage induced by specific toxins. Pomegranate occupies a significant place in folk medicine from parasitic infections to respiratory pathologies. (El Bohi et al., 2021), (Viuda-Martos et al., 2010), (Boozari & Hosseinzadeh, 2017). All the parts of the fruit including the peel, arils, and seeds, have been subjected to extraction in various solvents such as water, ethanol, methanol, and ethyl acetate to yield antibacterial compounds such as hydrolyzable tannins (punicalagin, penicillins, ellagic acid, and gallic acid), flavonols (myricetin, quercetin) and anthocyanins (cyanidin-3-glucose, pelargonidin-3-galactose). It has been reported that extracts from pomegranate seeds exhibit activity against various strains of *E. coli* isolated from urinary tract infections, suggesting a potential role in preventing bacterial adhesion. Key polyphenols like ellagitannins and anthocyanins, concentrated in the peel and kernels, exhibit antimicrobial, antioxidant, and anti-inflammatory properties. Recent research has highlighted the antimicrobial and antioxidant effects of aqueous pomegranate peel extract against uropathogenic *E. coli* (Tache et al., 2022).

***Bergenia ligulata* (Zahkm -e -hayat)**

The *Bergenia* genus consists of six species and is found across the temperate Himalayan region stretching from Kashmir to Nepal, as well as in Central and East Asia, and Pakistan. Typically, it thrives in rocky terrain at elevations ranging from 1200 to 2700 meters above mean sea level (Nissar et al., 2024). Pashanbhed (*Bergenia ligulata* Wall), commonly referred to as the stone breaker, holds a significant place in traditional Indian medicine, particularly in the treatment of kidney stones. With Ayurvedic principles advocating the continual evolution of medical science, the present moment offers an opportune time for fruitful research in diseases where Ayurveda demonstrates potential superiority. Among urinary disorders, Ashmari, or kidney stones, stands out as a prevalent and distressing condition. In ancient times, the diagnosis of Ashmari relied solely on Lakshanas, or clinical features. *Bergenia ligulata* exists in three varieties: *B. ligulata*, *B. ciliata*, and *B. stracheyi*, with bergenin as its principal chemical constituent. Extensive phytochemical studies have unveiled numerous secondary metabolites in the plant, including coumarins, flavonoids, benzenoids, lactone, fructose, tannins, phenols, and sterols. Research has highlighted an array of pharmacological activities associated with *Bergenia ligulata*, including anti-urolithic, antiviral, hepatoprotective, diuretic, anti-inflammatory, and cardio-protective effects. Compounds like bergenin, (+) afzelechin, (+) catechin, and β -sitosterol have been identified in its phytochemistry, contributing to its diverse therapeutic potential. As modern facilities lead to biological imbalances, the exploration of traditional remedies like Pashanbhed holds promise in addressing contemporary health challenges (Haritha et al., 2021; Das et al., 2022).

***Herniaria hirsute* (Rupturewort)**

Distribution in Belgium; France; Spain; Portugal; Italy; Switzerland; Austria; Germany; Czechoslovakia; Poland; Hungary; Yugoslavia; Greece; Turkey; Cyprus; Lebanon; Palestine; Iran; Afghanistan; India; Kashmir; Morocco; Algeria; Ethiopia. Plant parts contain saponin glycoside herniarin and an alkaloid paronychin. It is used as fodder for cattle and camels. Among the constituents, herniariasaponin has been identified as the most abundant saponin, alongside others such as saponins, flavonoids, and coumarins (Peeters, 2022). Several research studies have highlighted calcium oxalate as the predominant constituent of kidney stones, comprising approximately 80% of cases. These stones exhibit a high recurrence rate, ranging from 70 to 81% in men and 47 to 60% in women. *Hirsuta*, a plant widely distributed throughout the Maghreb region, typically thrives in sandy soils along pathways, uncultivated areas, dry grasslands, pastures, olive groves, and frequented spots resilient to foot traffic. Traditionally, this botanical species has been recommended for conditions such as fluid retention, edema, reduced urine output (oliguria), kidney stone formation (renal lithiasis), inflammation of the bladder (catarrh), and situations necessitating renal function stimulation to enhance water elimination (Ammor et al., 2020). The methanol extract derived from *Herniaria hirsuta* underwent fractionation to elucidate the compound responsible for its therapeutic efficacy in preventing and treating urolithiasis. The fractions were subsequently evaluated for their impact on calcium oxalate crystallization using both in vitro and in vivo models. Within human urine, only the fraction eluted with ethanol/water demonstrated an association with the formation of smaller crystals primarily composed of calcium oxalate dihydrate, mirroring the effects observed with the aqueous extract. Administered at a dosage of 5 mg/day, this fraction notably decreased crystal deposition in rats with lithiasis. Initial analysis of the fraction revealed the presence of saponins, which may account for the beneficial properties of *Herniaria hirsuta* in managing kidney stones (Al-Snafi, 2018).

***Abutilon indicum* (Beejband Surkh)**

The Malvaceae family encompasses diverse plant forms, widely distributed throughout the tropical and subtropical regions of both the New and Old Worlds. In Pakistan, it is prevalent in the provinces of Sindh and Punjab, though sightings are infrequent in the Khyberpakhtoonkhwa. *Abutilon*, a large genus within this family, comprises approximately 150 species, ranging from herbs to shrubs and small trees, native to tropical and subtropical regions. Genus *Abutilon* is rich in various phytochemical constituents. *Abutilon indicum* (Linn.) (Malvaceae) contains lactones, sesquiterpenes, flavonoid aglycones, steroids, carbohydrates, phenols, tannins, alkaloids, flavonoid glycosides, proteins, alkaline sulfates, and amino acids. Notably, ethanolic extract contains a high concentration of quercetin, particularly in flowers. Roots contain asparagine, Gallic acid, and fixed oil, while fruits contain flavonoids and alkaloids (Patel & Rajput, 2013). *Abutilon indicum* (Linn.) Sweet (Malvaceae), generally called as "*Atibala*" is a plant of high medicinal importance. The plant possesses several beneficial effects such as cooling, laxative, digestive, analgesic, anti-inflammatory, astringent, diuretic, expectorant, antihelmintic, aphrodisiac, and demulcent (Bolleddu et al., 2021). Evaluation of the ethanolic extract of *A. indicum* revealed its significant preventive and curative effects against calcium oxalate-induced urolithiasis, demonstrating reductions in stone deposition, kidney weights, and serum biochemical markers, supported by histopathological evidence of renal protection (Gomaa et al., 2018). The study concluded that *Abutilon Indicum* extract has a significant positive effect on reducing kidney damage induced by heat stress in rats, as evidenced by improvements in biochemical parameters and histological features (Mshary et al., 2023).

***Cucumis melo* (Kharboza)**

The Cucurbitaceae family or cucurbits, are mainly found in subtropical and tropical climates, particularly in West Africa, Southeast Asia, Mexico, and Madagascar. They include edible plants like watermelons, cucumbers, luffas, pumpkins, courgettes, zucchinis, and summer squash, which can be grown on all continents. There are about 800 species and 130 genera of cucurbits worldwide. The 24 genera of this plant are found in West Africa while Pakistan flora contains 33 species including domesticated and wild species. *Coccinia*, *Lagenaria*, *Luffa*, *Momordica*, and *Zehneria*, and cultivated ones include *Citrullus*, *Cucumis*, *Cucurbita*, *Cucumeropsis*, *Lagenaria*, *Telfairia*, and *Trichosanthes* all are belong to the wild genera. *C. melo* fruit extract contains highest concentration of gallic acid and rutin which shows its anti oxidant activities. The seeds of this fruit also contained elevated level of polyphenol (Zhang et al., 2020). It has been reported that the sequential extraction of *C. melo* seed kernels revealed the presence of stigmaterol, rutin, kaempferol, quercetin, apigenin, and luteolin. (Wahid et al., 2022). In complementary and alternative medicines, *Cucumis melo* locally known as Kharbuzah, has upheld a longstanding reputation for its therapeutic virtues to treat various renal diseases, including the dissolution of kidney and bladder stones, and easing symptoms such as painful and burning urination, urinary tract ulcers, and urine retention. It also been employed to alleviate conditions like cough, bilious disorders, hepatitis, bile obstruction, eczema, and other related ailments (Fahamiya et al., 2016).

***Stigma maydis* (Catania et al.)**

Zee mays or Corn, belonging to the Poaceae family, is native plant of North America, particularly Mexico. Now it is cultivated all over the world notably across regions in Africa and Asia. The corn silks have gained importance for their effectiveness in treating urinary tract infections including chronic nephritis and cystitis. People all over the world utilize corn silk to regulate blood pressure and for the treatment of many diseases such as fever, gout, and bacterial infections (Odelola et al., 2023). Since ancient times corn silk has been employed for the healing of many renal diseases. The diuretic properties of corn silk facilitate smooth muscle contractions, resulting in increased urine production. As the (UTIs) are triggered by various factors including poor hygiene, pregnancy, and kidney stones, it has been reported that the phytochemicals in the corn silk extract such as flavonoids, tannins, terpenoids, and alkaloids showed alleviation of inflamed tissues, reducing the discomfort associated with urination within 5 to 20 days (Vijitha & Saranya, 2017; Parihar et al., 2022). Not only the extract but the tea of corn silk also aids in increasing diuresis, thereby promoting urine flow and assisting in the breakdown of stones, easing their passage. In chronic kidney disorders the corn silk in tea form, reported to decrease fluid retention and lower serum creatinine levels. It has been found effective in reducing potassium levels when consumed alongside other medications. A study conducted on rat model of kidney failure revealed that it help in treating nephrotoxicity studies, the extracts of binhong leaves and corn silk can enhance kidney function and aid in detoxification (Sepehri et al., 2011). The aqueous extract of corn silk has been observed to enhance the removal of toxins such as urea, potassium, and creatinine, leading to improved renal function. A research has been conducted that shows significant reduction in symptoms among patients with urinary tract infections (UTIs), along with decreased levels of pus cells, red blood cells (RBCs), and crystals. Notably, no adverse effects have been reported, highlighting both its effectiveness and safety (Sahib et al., 1970). Extensive research has been undertaken on the biological activity of corn silk components for treating various conditions including gout, edema, nephritis, cystitis, kidney stones, and prostatitis. Corn silk is deemed completely safe for human consumption and does not pose any side effects (Yamani & Zoughbi, 2022).

***Coriandrum sativum* (Dhania)**

Coriander is cultivated across various regions globally, spanning from Europe and Asia to the Americas and Oceania, with some cultivation even observed in the United Kingdom and the United States. Coriander green leaves have high moisture content, with significant proportions of carbohydrates, proteins, minerals, and fats. Dehydrated coriander seeds contain moisture, essential oil, fatty oil, protein, fat, crude fiber, and ash content. The seed oil of coriander typically contains around 60 to 70% linalool and approximately 20% hydrocarbons. However, oil extracted from the herbal portion differs from that of the seeds. Essential oil ingredients include β -pinene, α -thujene, sabinene, camphor, limonene, myrcene, α - β -ocimene, γ -terpinene, terpinolene, cumin aldehyde, and citronellal. Coriander oil is rich in phytonutrients such as linalool, geraniol, carvone, borneol, limonene, and camphor. Aqueous coriander extracts have been observed to enhance diuresis and urinary flow, along with sodium, potassium, chloride excretion, and glomerular filtration rate in Wistar rats when administered at doses of 0.04 and 0.10 grams per kilogram via arterial distillation. The action of diuretic activity of coriander seemed alike to that of furosemide (Naeem et al., 2022; Chettri et al., 2024).

Conclusion

It has been concluded that Pakistan flora is rich in medicinal plant species that are traditionally used to treat life threatening diseases including urinary tract infections in all over the world. The phytoconstituents such as alkaloids, flavonoids, glycosides, tannin, saponin in the plants provides various therapeutic effect and antimicrobial activities against various ailments. More over the plants are the source of antioxidant activities that are the source for the prevention of chronic diseases. For the future perspective there is need to explore the flora of Pakistan for the novel plant that are helpful for eliminating such diseases with less adverse effects.

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