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Herbal Extracts Acting as Diuretics: A Comprehensive Review

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Abstract:

Diuretics are medications utilized to lower blood pressure by enhancing urine production and sodium expulsion. Nevertheless, various diuretics, including loop and thiazide diuretics, can lead to adverse effects such as imbalances in electrolytes. Consequently, there is a growing fascination in exploring the therapeutic attributes of herbs and botanicals. Natural remedies derived from plants are considered a viable option for treating specific conditions and providing protection against certain diseases. Scientific evidence is progressively supporting the diuretic properties of traditional medicinal plants. This article delves into the potential mechanisms underlying these diuretic effects and reviews research that identifies extracts promoting diuresis, measured through urine output, sodium, and potassium excretion. The review highlights various genera and species with well-documented diuretic effects.

***Keywords*:** herbal extract; diuresis; sodium, and potassium excretion

1. Introduction:

Diuretics play a vital role in managing conditions characterized by fluid overload, such as acute renal failure, hypercalciuria, and liver cirrhosis. They effectively reduce blood volume and venous return to the heart, thereby lessening cardiac workload, oxygen need, and blood pressure. As a result, diuretics are essential in the treatment of hypertension [1]. However, commonly used loop and thiazides diuretics bring about undesirable side effects, including electrolyte imbalances such as hypokalemia, hyperuricemia, and hyponatremia, as well as acid-base imbalance, metabolic abnormalities (hyperglycemia and hyperlipidemia), and acute hypovolemia [2]. Herbs have long been recognized for their perceived healing properties and are considered a wellspring of traditional knowledge. Across the globe, various medicinal plants have been employed to address diverse ailments, and fortunately, there is a rich diversity of wild plants growing in different regions. The significance of medicinal plants and traditional healing practices in tackling healthcare challenges is gaining swift acknowledgment. This increased interest has sparked a surge in global research focused on plants with medicinal value. In Ayurvedic medicine, numerous indigenous remedies are believed to possess diuretic effects [3].

This review article lists several medicinal herbs that have been shown to have diuretic impacts, explores the possible causes of these diuretic actions and summarizes studies that have found plant extracts that increase urine production, sodium, and potassium elimination.

2. Herbs Having Diuretic Effects:

Senna septemtrionalis (Viv.) (Fabaceae)

Originally native to the Americas, *S. septemtrionalis*, a shrub belongs to Fabaceae family, has now become widely distributed in tropical and subtropical regions, extending its presence to locations like India and South Africa [4]. A chemical analysis of ethanol extract of *S. septemtrionalis* using gas chromatography mass spectrometry technique (GC/MS) showed that the main component was D-pinitol (42.2%). The other detected components were fatty acids, including oleic acid, octadecanoic acid, hexadecenoic acid, and linoleic acid, and carboxylic

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acids, such as benzoic acid, oxalic acid, malic acid, and succinic acid. It was demonstrated that *S. septemtrionalis* (ethanol extract, 100 mg/kg), meaningfully amplified urine volume (2.67-fold) and the elimination of sodium (Na^+) and potassium (K^+) (5.60-fold and 7.2-fold respectively). The diuretic effects of *S. septemtrionalis* extract are likely linked to the involvement of prostaglandins and nitric oxide [5].

***Halosarcia indica* (Amaranthaceae)**

H. indica, an eatable plant utilized in traditional Indian traditional medicine, has demonstrated healing properties for skin infections. The plant's young shoots are consumed as salad greens. *H. indica* (aqueous extract, 400 mg/kg) was administered to rats, it exhibited diuretic action equivalent to the standard diuretic furosemide. The extract revealed a time-dependent rise in urine volume (Diuresis Index: 1.62 –1.96). *H. indica* extract is known to contain chlorogenic acid, sinapic acid, caffeic acid, ferulic acid, scopoletin, quercetin 3-O-β-D-glucoside, β-sitosterol-D-glucopyranoside, and phenylpropanoids [6]. The diuretic impact of the *Halosarcia indica* extract is likely credited to the existence of these phytochemical compounds [7].

***Lagopsis supina* (Steph) IK. Gal. (Lamiaceae)**

L. supina (Steph) IK. Gal. has been a traditional therapeutic plant in China for centuries, reputed for its believed benefits in enhancing blood circulation, alleviating blood stasis, and possessing anti-inflammatory and diuretic properties [8]. Ultra-high performance liquid chromatography-quadrupole time-of-flight mass spectrometric analysis (UHPLC-qTOF-MS/MS) of *L. supina* aqueous soluble fraction (LSB) identified various types of bioactive compounds including phenylpropanoids, flavonoids, mono-terpenoids, and diterpenoids with notable examples; caffeic acid, chlorogenic acid, acteoside, stachysoside A, rutin, luteolin and apigenin. LSB exhibits significant acute and prolonged diuretic effects. This is accomplished via inhibiting the renin-angiotensin-aldosterone system (RAAS) pathway and downregulating the serum levels, Messenger RNA (mRNA) expressions, and protein levels of Aquaporins (AQP-1, AQP-2, and AQP-3) in rats subjected to saline loading [9]. Aquaporins are specialized channel proteins for water transport, facilitating rapid and passive movement across secretory epithelia in the body and playing a pivotal role in water balance regulation. These proteins are present in many tissues, including the kidneys, lungs, liver, and brain [10]. The activity of AQP-1, 2, and 3 channels plays a crucial role in regulating water balance. Down-regulating these channels enhances water excretion, while up-regulating them promotes water retention, ultimately impacting urine volume [11]. It is reported that while ethanol extract of *L. supina* can influence urinary content of Na^+ and K^+, it does not disturb the pH of urine, serum, and urine Na^+-K^+-ATPase, tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) contents [12].

***Kalanchoe pinnata* (Lamk.) (Crassulaceae)**

K. pinnata, commonly recognized as 'saião-roxo,' 'leaf-of-fortune,' 'leaf of the coast,' 'yellow flower of fortune,' and 'para-tudo,' is a succulent herb in the Crassulaceae family. Originating from India, it thrives in parks and the uninhabited mounds of North-Western India. The leaves of *K. pinnata* encompass a diverse array of chemical compounds, including fatty acids, acyclic aromatic organic acids, amino acids, bufadienolides, α-β unsaturated acyclic ketones, fenantrenic derivatives, sterols, long-chain hydrocarbons, and triterpenoids. Investigations reveal that the ethyl acetate fraction derived from *K. pinnata* demonstrates diuretic effects in male Wistar rats. Meaningly increased sodium (Na^+) and potassium (K^+) elimination was observed (50 and 100 mg/kg), while only the 100 mg/kg dosage markedly elevated urine volume and chloride (Cl^-) excretion. The pronounced diuretic activity of the *K. pinnata* ethyl acetate fraction is likely attributed to its abundant content of flavonoids and polyphenols [13]. Chemical analysis of *K. pinnata* leaves reveals a variety of bioactive compounds with quercetin, kaempferol, apigenin, and epigallocatechin gallate as the major components. Other notable finds include luteolin-7-glucoside, myricetin, and genistin, each potentially contributing to the plant's therapeutic properties [14].

***Desmostachya bipinnata* (Poaceae)**

D. bipinnata, commonly referred to as "Halfa grass" or "Darbh," belongs to the Poaceae (Gramineae) family, which encompasses a diverse array of economically and medicinally significant plants, including cereals, bamboos, and sugarcane. Species within the Gramineae family are known for various therapeutic properties, such as astringent, wound-healing, anti-emetic, diuretic, and treatment of ailments related to eye [15]. Native to Northeast, West Tropical, and Northern Africa, as well as the Middle East, Temperate, and Tropical Asia, *D. bipinnata* is known as "Big cord grass," and "Salt reed-grass" in English [16]. In traditional practices, Darbh, the local name for *D. bipinnata*, is commonly employed in daily rituals. It is utilized for treating cuts, wounds, dysentery, and exhibits diuretic properties [17]. Previous chemical analyses of the plant have identified several known coumarins (such as scopoletin and umbelliferone), sugars, amino

acids, and carbohydrates. Additionally, the ethanolic extract of *D. bipinnata* revealed the isolation of five primary flavonoid glycosides, including kaempferol, quercetin, quercetin-3-glucoside, tricin and tricin-7-glucoside [18, 19]. Pharmacological investigations have demonstrated that *D. bipinnata* possesses anti-ulcerogenic, analgesic, antipyretic, and anti-inflammatory actions [19, 20]. The diuretic effect of a hydro-alcoholic extract of the entire plant was evaluated on rats at dosages of 250 and 500 mg/kg (orally), with frusemide (20 mg/kg) used as a standard. The hydro-alcoholic extract displayed noteworthy diuretic action, exhibiting the highest potency at 500 mg/kg in increasing urinary output compared to the standard frusemide. Moreover, the extract proved the most active in elevating urinary electrolyte contents (Na^+, K^+, and Cl^-) at the tested doses. Preliminary phytochemical examination identified the existence of alkaloids, carbohydrates, proteins, tannins, phenolic compounds, flavonoids, triterpenoids, and glycosides in *D. bipinnata* extract, suggesting that the diuretic activity could be attributed to these phytochemical constituents [21].

***Petroselinum crispum* (Parsley) (Apiaceae)**

P. crispum, frequently recognized as Parsley or Baqdunis, is a vibrant green biennial herb belonging to the Apiaceae family. It has a rich history of medicinal use across European, Mediterranean, and Asian regions for centuries [22]. Originally native to Spain, Italy, Greece, Malta, Algeria, Tunisia, and Morocco, *P. crispum* is not only valued for its culinary contributions but is also utilized in foodstuffs as a natural additive and a scent in beauty products and fragrances. The volatile oil resulting from parsley displays antimicrobial, diuretic, and mild antioxidant properties. Analysis of essential oil of parsley reveals a complex blend of compounds with 1,3,8-p-menthatriene, apiole, and myristicin as the main components. Other notable constituents include β-phellandrene, α, p-dimethyl styrene, myrcene, and various pinene isomers. Parsley leaves contain flavonoids, with apiin glucoside as the predominant component. Luteolin-7-apiosylglucoside, apigenin-7-glucoside, 6″ -acetyl-apiin, isorhamnetin-3,7-diglucoside and chrysoeriol-7-apiosylglucoside also contribute to the leaves chemical profile [23]. Beyond being a popular garnish for soups, salads, meats, vegetables, sauces, and spice blends, parsley plays a significant role in herbal medicine [24]. Its versatility has resulted in its incorporation into various industries, including food, pharmaceuticals, perfumes, and cosmetics [25]. With a wide array of established pharmacological activities, parsley serves as a remedial plant with effects such as antioxidant, hepatoprotective, neuroprotective, anti-diabetic, analgesic, spasmolytic, immunosuppressant, anti-coagulant, antiulcer, laxative, estrogenic, diuretic, hypotensive, antibacterial, and antifungal properties [26]. Particularly noteworthy are parsley's diuretic qualities, aiding in the elimination of toxins from bodily tissues [27]. It stands out as a rich source of minerals such as iron, calcium, phosphorus, manganese, and zinc, along with starch, vitamins B, C, A, and E, β-carotene, and antioxidants [24]. Tannins, flavonoids, sterols, and triterpenes were proved to be present in parsley leaves (ethanolic extract) [28]. Additionally, parsley provides nutritional value and exhibits antioxidant and neutralizing activities [29]. Experimental studies indicate that animals administered parsley seed extract showed significant diuretic activity, excreting a notably greater volume of urine over 24 hours compared to those receiving only water. The diuretic effect of parsley is believed to involve the prevention of the Na^+–K^+ pump, leading to reduced reabsorption of sodium and potassium ions, promoting osmotic water flow into the lumen, and inducing diuresis [27].

***Cola nitida* (Kolanut) (Sterculiaceae)**

C. nitida, frequently known as Kolanut in the Sterculiaceae family, is frequently utilized in tropical Africa for addressing various health issues such as migraines, morning sickness, and metabolic disorders. Theobromine and caffeine are the main active ingredients found in kolanuts [30]. *Cola nitida* leaf has been reported to contain active phytochemicals including alkaloids, flavonoids, tannins and phenolics. Its medicinal efficacy arises from a diverse range of secondary metabolites, making it effective in the treatment of conditions like cough, asthma, and malaria [31]. A study explored the diuretic, natriuretic, and kaliuretic actions of *C. nitida* (methanolic extract) in male Wistar rats, administered in doses ranging from 100 to 600 mg/kg over a 14-day period, with furosemide as a standard drug. The findings showed that treatment with the mentioned doses of *C. nitida* pointedly enhanced body weight gain and water intake compared to the control group, whereas food intake remained unaffected. There were notable rises in urine volume and urinary electrolytes (Na^+, K^+, and Cl^-), accompanied by a reduction in plasma/renal alanine transaminase (ALT) and aspartate transaminase (AST) effects, as well as plasma creatinine and urea concentrations. Importantly, there were no observed changes in plasma electrolytes when related to the control and groups treated with furosemide [32]. The diuretic activity of *C. nitida* is attributed to its caffeine content, with doses of 300-600 mg/kg showing a more substantial increase in urine production equated to the furosemide-treated group, suggesting higher potency at these doses. Caffeine, at an effective dose of 250 mg, has been demonstrated to enhance urine volume and sodium excretion [33]. Additionally,

theophylline, another potent constituent of *C. nitida*, has shown the ability to rise glomerular filtration rate (GFR) or renal blood flow [34], potentially reducing tubular reabsorption of water and sodium, leading to diuresis and natriuresis [33].

***Cicer arietinum* L. (Fabaceae)**

C. arietinum L. (Chickpea) is a significant legume crop cultivated and consumed widely worldwide, particularly in Afro-Asian countries. In recent decades, there has been notable interest in chickpea due to its diverse mineral components and isoflavone content. Notably, isoflavonoids, including formononetin (4′-O-methyl ether of daidzein), biochanin A (4′-O-methyl ether of genistein), ononin (formononetin glucoside), sissotrin (biochanin A glucoside), genistein, trifolirhizin, vigradiatain, and 2′-Hydroxydaidzin, have been identified as the principal bioactive constituents in chickpea seeds. [35]. Beyond its nutritional significance, chickpea is gaining attention for its nutraceutical and prebiotic potential. New studies explore its potential function in mitigating long-lasting ailments like diabetes, hypertension, overweightness, and cancer, given its composition of various bioactive compounds with potential health benefits in humans [36]. An assessment of the diuretic effects of methanol extracts from two chickpea varieties (black or Desi and white or Kabuli) (200 and 400 mg/kg) revealed that there was no significant diuretic effect until 120 minutes. However, a highly significant diuretic effect was observed at the 12^{th} and 24^{th} hours, comparable to the reference drug furosemide (20 mg/kg) [37]. Some herbs excite the thirst center in the hypothalamus, leading to increased fluid consumption and subsequent diuresis, while others cause diuresis owing to having elevated salt concentration [38]. Furosemide, a conventional diuretic, works by increasing urine volume and the removal of sodium and potassium, inhibiting electrolyte reabsorption in the loop of Henle [39]. The diuretic effect of chickpea extracts is proposed to be linked to a reduction in water and electrolyte reabsorption. The regulation of sodium and water reabsorption involves hormonal and non-hormonal factors, such as the renal-angiotensin-aldosterone system and prostaglandins [40]. The compounds present in the extracts are believed to exert diuretic effects by increasing urine output, possibly acting synergistically or individually to induce vasodilation. The observed diuretic effect is likely a result of the cumulative influence of multiple substances or the presence of secondary active metabolites [39].

Alismatis rhizoma* (AR) (*Alismataceae)

Alismatis rhizoma (*Alisma orientale*), referred to as AR, is a dried rhizome utilized as a traditional Chinese medicinal herb. Broadly nurtured in China, Japan, Korea, India, and Europe, AR has been employed for over a millennium in treating various conditions, including dysuria, edema, urinary tract infections, fluid and phlegm retention, nephropathy, hyperlipidemia, diabetes, and vertigo. Recognized for its diuretic, antitumoral, and damp-heat clearing properties, AR has stood the test of time in traditional medicine. AR is rich in chemical compounds, predominantly triterpenoids, sesquiterpenoids (alismol, alismoxide, orientalol A, orientanone), diterpenoids and essential oil in which δ-elemene, β-elemene, spathulenol, γ -cadinol, and γ - eudesmol are the key contributing aroma-active compounds. Notably, the alisols (alisol A, alisol B, alisol E, alisol A 24-acetate, and alisol B 23-acetate), a class of protostane-type triterpenoids, have garnered considerable attention due to their distinctive chemical structures and diverse biological effects. It was proved that ethanol extract possesses substantial diuretic properties, seemingly linked to the sodium-chloride co-transporter in the distal convoluted tubule of the kidney. Initial pharmacological studies indicate that the diuretic impact of alisol A 24-acetate in AR closely resembles that of neoflumen, a conventional thiazide diuretic that hinders the sodium-chloride transporter in the distal tubule [41,42]. Recent study uncovered the main triterpenoids in AR and a total of forty-four triterpenoids were detected [43].

***Opuntia ficus-indica* (L.) Mill. (Cactaceae)**

O. ficus-indica (L.) Mill., frequently recognized as prickly pear, is a plant indigenous to America and widely spread across Africa, Asia, and Australia. Mexico is particularly abundant in wild Opuntia species, with *O. ficus-indica* being the most extensively cultivated and domesticated variant. This plant is notably enriched with biologically active constituents, encompassing pigments (carotenoids, betalains, and betacyanins), vitamins (E, A, C, B1, B2, B3), fatty acids (palmitic, oleic, linoleic, and linolenic acids), flavonoids (isorhamnetin, kaempferol, quercetin, lutein, and rutin), and phenolic compounds (ferulic, coumaric, and gallic acids) [44]. *O. ficus-indica* has a longstanding history of traditional medicinal usage in addressing several ailments. As a member in the Cactaceae family, it is cultivated as a tropical or subtropical plant, and its fruits are globally imported, and consumed. In Mexico, the plant is referred to as nopal, and the fruit is known as tuna. Traditional uses in Mexico include the treatment of skin diseases, inflammation, and ulcerations [45]. The flattened

stems of *O. ficus-indica*, referred to as cladodes (cladophylls or phylloclades), are armed with spines and multicellular hairs or trichomes. Devoid of leaves, these cladodes are rich in water content and contain substantial amounts of protein, dietary fiber, carbohydrates, antioxidants, flavonoids, minerals, and vitamins [46]. Studies have delved into the diuretic effect of *O. ficus-indica* in rats and rabbits. In rats, both the cladode gel and aqueous extract, administered orally, were found to enhance urine volume, creatinine clearance, and urinary excretion of sodium and potassium. Notably, these effects were observed without significant alterations in serum creatinine or blood urea. A comparative study with furosemide, a conventional diuretic, revealed similar impacts on plasma potassium levels. In rabbits, intravenous administration of the plant aqueous extract or cladode gel through single and repeated doses, exhibited diuretic activity [47]. These findings suggest that the plant extracts may emulate the actions of loop diuretics, like furosemide, by enhancing the urinary elimination of potassium and sodium. The presence of flavonoids in *O. ficus-indica*, particularly isorhamnetin glycosides [48], aligns with the known diuretic properties of flavonoids [7]. Consequently, the diuretic impact of the plant is probably attributable to its abundant content of flavonoids [47].

***Nigella sativa* L. (Ranunculaceae)**

N. sativa L., commonly known as black cumin or black seed, is gaining recognition as a remarkable herb in the Ranunculaceae family, boasting a rich historical and religious significance. Extensive research has unveiled its broad range of pharmacological potential. Indigenous to Southern Europe, North Africa, and Southwest Asia, *N. sativa* is cultivated in numerous countries worldwide, including the Middle Eastern Mediterranean region, South Europe, India, Pakistan, Syria, Turkey, and Saudi Arabia. Various active compounds have been identified in different varieties of black seeds. Volatile oil, a crucial component of seeds, is mainly composed of thymoquinone, with other constituents such as thymohydroquinone, dithymoquinone, p-cymene, carvacrol, 4-terpineol, t-anethol, longifolene, α-pinene, and thymol. *N. sativa* seeds also contain two types of alkaloids: isoquinoline alkaloids (e.g., nigellicimine) and pyrazol alkaloids (nigellidine and nigellicine) and additionally, alpha-hederin, a water-soluble pentacyclic triterpene saponin. Thymoquinone is primarily responsible for most of the pharmacological properties attributed to *N. sativa*. The nutritional composition of *N. sativa* seeds includes protein (26.7%), fat (28.5%), carbohydrates (24.9%), and crude fiber (8.4%). Moreover, the seeds contain a variety of vitamins and minerals, such as copper (Cu), phosphorus (P), zinc (Zn), and iron (Fe). The fatty oil extracted from the seeds is rich in unsaturated fatty acids, particularly linoleic, oleic, and eicodadienoic acids. Saturated fatty acids (palmitic, stearic acid), α-sitosterol, and stigmasterol are also present in the seeds [49]. A study delved into the diuretic activities of *N. sativa* aqueous extract in rats indicated that intraperitoneal administration of the crude extract (10, 30, and 50 mg/kg), demonstrated noteworthy diuretic, kaliuretic, and natriuretic actions in a dose-dependent way. Despite these effects, urinary pH stayed consistent throughout the study. The diuretic index values indicated robust diuretic action, and the Lipschitz values, which relate the response of the test compound to the response of the standard, revealed that; 50 mg/kg dose exhibited 46% diuretic activity compared to furosemide. Preliminary phytochemical analysis of *N. sativa* identified alkaloids, anthraquinones, flavonoids, saponins, and tannins, known inducers of diuresis. The study suggests that *N. sativa* crude extract holds strong potential as a diuretic agent and may emerge as a promising candidate for treating hypertension associated with renal disorders [50].

***Thymus serrulatus* Hochst. ex Benth. (Lamiaceae)**

T. serrulatus, a plant indigenous to Ethiopia, holds a significant place in folk medicine owing to its recognized diuretic, anti-inflammatory, and antioxidant properties. Beyond its medicinal use, it also serves as a culinary herb and flavoring agent. Thymus species, in general, are widely employed in Ethiopian traditional medicine to treat a spectrum of ailments, ranging from infectious diseases to chronic ailments. *T. serrulatus*, specifically, finds application in treating conditions like cough, headache, hypertension, stomach-ache, earache, liver ailment, and gonorrhoea [51]. In the context of protecting against cadmium-induced renal toxicity, *T. serrulatus* essential oil (TSA oil) demonstrated notable efficacy. It significantly improved serum kidney function markers, non-enzymatic antioxidants, and lipid peroxidation. Furthermore, it downregulated the amplified expression of NF-κB p65 (Nuclear factor kappa-light-chain-enhancer of activated B cells), iNOS (inducible nitric oxide synthase), and SMAD2 **(**mothers against decapentaplegic homolog 2) in Cd-intoxicated rats. These results propose that the nephroprotective action of TSA oil is possibly credited to its antioxidant and anti-inflammatory properties [52]. In another study evaluating diuretic activity, *T. serrulatus* leaves (total aqueous extract, and the n-butanol fraction), showed substantial effects in saline-loaded Swiss albino mice. The total aqueous extract exhibited significant diuretic, natriuretic, and kaliuretic effects, while the n-butanol fraction, particularly at a dose of 1,000 mg/kg, demonstrated the highest diuretic impact comparable to the reference drug. These findings highlight the

diuretic potential of *T. serrulatus* leaves (total aqueous extract and the n-butanol fraction), showcasing significant impacts on urinary electrolytes [53]. The aqueous extract of *T. serrulatus* was subjected to LC-MS analysis, leading to the identification of phenolic compounds, specifically derivatives of caffeic acid and salvianolic acids. Additionally, flavones such as isoscutellarein, luteolin, and apigenin glycosides were observed in the extract. Essential oil extracted from *T. serrulatus*, is predominantly consisted of thymol (as the major component), along with carvacrol, p-cymene, γ-terpinene, carvacrol methyl ether, and β-myrcene [54]. Further, a phytochemical investigation of crushed dried *T. serrulatus* leaves indicated the presence of alkaloids, tannins, saponins, and phytosterols. The enhanced diuretic action of the n-butanol fraction compared to the total extract is likely due to the existence of phenolic compounds, secondary metabolites known for their diuretic activity [55].

***Moringa stenopetala* (Baker f.) Cufodontis (Moringaceae)**

M. stenopetala, a member of Moringaceae family is commonly found in southern Ethiopia, typically thrives at altitudes ranging from 5 to 10 meters. The cooked leaves *of M. stenopetala* serve as a staple food for local societies, and the plant's parts, as; leaves, seeds, and roots, are traditionally employed in folk medicine to address diverse disorders such as hypertension, stomach pain, high blood sugar, leishmaniasis, and infertility [56, 57]. Rutin was identified as the principal constituent of the leaves of *M. stenopetala* along with a very small amount of neochlorogenic acid [58]. In a study aimed at exploring the diuretic action of *M. stenopetala*, a hydro-ethanolic extract of its leaves was administered using an *in-vivo* mice model of diuresis. Different doses (150, 250, 350, 500, and 1000 mg/kg) of the extract were utilized, with furosemide (10 mg/kg) serving as a standard drug. The results indicated a substantial rise in urine production for all extract doses compared to the control group at 0.5 and 1 hour. By 2.5 hours, the 500 mg/kg dose demonstrated the highest urine output, surpassing both the control group and the other extract doses. Moreover, sodium (Na+) and chloride (Cl^-) excretion meaningly increased at the 250 and 350 mg/kg doses compared to the control group. At the 500 and 1000 mg/kg doses, Na^+ and Cl^- elimination remained comparable, and there was a noteworthy increase in potassium (K^+) excretion compared to the reference drug and control group, respectively. These findings suggest that *M. stenopetala* may induce its diuretic effect by hindering the $Na^+/K^+/Cl^-$ co-transporter at the thick ascending loop of Henle, akin to the mechanism of action observed in the loop diuretic furosemide. This proposed mechanism could elucidate the observed potassium loss at higher extract doses and the substantial urine output, characteristic features of loop diuretics. However, further research is essential to fully comprehend the diuretic mechanism of *M. stenopetala* [59].

***Biophytum sensitivum* (Linn.) DC. (Oxalidaceae)**

B. sensitivum, also recognized as "Viparitalajjalu," is a petite herb belonging to Oxalidaceae family, characterized by its paripinnate leaves forming a rosette at the base with 3-12 pairs of leaflets. The plant features yellow flowers in terminal racemes and produces elliptic shining capsules having numerous transversely tubercled seeds. Widely distributed as a weed through India, the flower of *B. sensitivum* holds special significance in the tradition and culture of Kerala, India, as one of the 10 sacred plants. The aerial parts of *B. sensitivum* yielded two biflavones, cupressuflavone, and amentoflavone, along with three flavonoids, namely luteolin-7-methyl ether, isoorientin, and 3`-methoxyluteolin 7-O-glucoside. Additionally, 4-caffeoylquinic acid was also isolated from the plant. It has been reported that *B. sensitivum* exhibits diverse pharmacological activities, including chemoprotective, hypoglycemic, immunomodulatory, antitumor, antifertility, anti-metastatic, anti-inflammatory, antipyretic, analgesic, and antioxidant properties [60,61]. To assess the diuretic activity of *B. sensitivum*, a study in rats measured urine production and content of sodium (Na^+), potassium (K^+), and chloride (Cl^-) ions in the urine. It was indicated that *B. sensitivum* (methanol extract) meaningly enhanced urine production and the elimination of Na^+ and K^+ related to the control group. The aqueous extract also demonstrated a substantial rise in urine output and K^+ ions, while the chloroform extract exhibited no noteworthy action on urine productivity or electrolyte content. It is hypothesized that the diuretic effect of *B. sensitivum* may involve mechanisms such as enhancing renal blood flow and subsequently elevating glomerular filtration rate. phytochemical analysis of the plant indicated the existence of alkaloids, carbohydrates, flavonoids, tannins, and phenolic constituents. The detected diuretic action could be attributed to the separate or collective effects of these chemical ingredients existing in the plant. These findings substantiate the traditional claims of *B. sensitivum* as a diuretic agent [62].

***Panicum repens* (Poaceae)**

P. repens L. grass is a perennial grass characterized by the formation of dense colonies and extensive,

creeping rhizomes belonging to the Poaceae family. Typically considered a weed, it thrives in moist, coastal, sandy soils but can also grow in heavier upland soils. In Egypt, it is referred to as "Nigeel farisi." The ethanolic extract derived from the roots and rhizomes of *P. repens* has demonstrated hypolipidemic activity. High-performance liquid chromatography (HPLC) identified the presence of gallic acid, chlorogenic acid, chicoric acid, primulic acid, rutin, apigenin-7-glucoside, and quercetin [63]. A study investigated the diuretic action of *P. repens* L. (ethanolic extract) in rats. Rats were administered *P. repens* extract (500 mg/kg) orally, with frusemide serving as a reference drug. After 24 hours, urine volume and the content of sodium and potassium were determined. Both the *P. repens* extract and frusemide treatment resulted in a meaningful rise in the assessed parameters compared to their respective control groups [64]. The observed increase in urinary potassium and sodium excretion, like the action of frusemide, suggests that the plant extract may act similarly to loop diuretics. Loop diuretics, like frusemide, are known to enhance urinary flow rate and electrolyte elimination, including sodium, potassium, and chloride [65]. This indicates the inference that the diuretic activity of *P. repens* L. resembles that of loop diuretics such as frusemide.

***Tribulus alatus* Del. (Zygophyllaceae)**

Tribulus, a genus encompassing approximately 25 species of flowering plants within the Zygophyllaceae family. Among them is *T. alatus* Del., an annual or biennial prostrate herb thriving in dry sandy soil alongside roads in warm-temperate areas and it is notably widespread in all Egyptian deserts. The fruits of this plant are used in Pakistan for the treatment of urinary disorders and cough [66]. Research has demonstrated that *T. alatus* exhibits the ability to enhance sperm count and motility levels following a 30-day treatment period with the observed increase in testosterone levels promoting protein synthesis. The elevated testosterone levels serve as a positive nitrogen balancer, facilitating rapid recovery from muscular stress [67]. Additionally, *T. alatus* has been found to possess diuretic activity according to a study that revealed that alcoholic extracts of its aerial parts without fruit, fruits, and total aerial parts all led to a noteworthy rise in urine volume, sodium, and potassium concentrations [68]. The isolation of six flavonol [isorhamnetin 3-O-(6``-E-p-coumaroyl)- β - D-glucopyrano-side , kaempferol 3-O-(3``,6``-di-O-E-p-coumaroyl)- β - D-glucopyranoside, kaempferol 3-O-(3``-E-p-coumaroyl)- β - D-glucopyranoside , tribuloside , quercetin 3-O- β - D-gluco-pyranoside, and kaempferol 3-O- β -D -glucopyranoside] and saponin glycosides from the aerial parts indicates that these compounds may be accountable for the diuretic action [66]. Considering the action of loop diuretics, which chiefly involve hindering the $Na^+/K^+/Cl^-$ co-transporter in the thick ascending limb of Henle's loop, the administration of alcoholic extracts of *T. alatus* resulted in increased urinary water and electrolyte excretion. This strongly suggests that the plant extracts operate as loop diuretics [65].

***Citrullus lanatus* (watermelon) (Cucurbitaceae)**

Research indicates that watermelon supplementation may contribute to lowering blood pressure; however, further investigation with larger sample sizes is necessary to validate these findings, particularly among individuals with hypertension or prehypertension [69]. Traditionally, watermelon has been employed for treating kidney diseases and promoting urination. The diuretic effects of watermelon pulp extract were observed in rats, indicating a decrease in serum chloride concentrations and a rise in urinary sodium and chloride content. GC–MS examination of the ethanolic extract from the pulp revealed the presence of steroids, with (3β)-9,19-Cyclolanost-24-en-3-ol being the most abundant, and alkanes (specifically isomers of heptacosane) as the main components. Additionally, the plant contains various nutritionally valuable constituents, including vitamins such as A, B series, and C; minerals like potassium, magnesium, calcium, phosphorus, and sodium; as well as carotenoids, including lycopene, beta-carotene, phytofluene, lutein, phytoene, and neurosporene. Watermelon is also rich in carbohydrates, both essential and unessential amino acids, healthy unsaturated fatty acids [70]. Prior studies have proved that steroidal compounds from medicinal plants possess anti-urolithiasis and natriuretic actions [71], aligning with the findings of the study shown by Siddiqui et al. [70].

***Vepris heterophylla* (Rutaceae)**

V. heterophylla, a remedial plant deeply rooted in African folk medicine, has been historically utilized to control diverse ailments, particularly edematous disorders, and hypertension. In the northern region of Cameroon, traditional healers have harnessed the potential of *V. heterophylla* (aqueous extract) to manage arterial hypertension. The presence of fatty acids, anthraquinones, volatile oils, glycosides, saponins, tannins, coumarins, triterpenes, phenolic compounds, flavonoids, alkaloids, and sterols were recognized in *V. heterophylla*. A dedicated study planned to evaluate the diuretic effects of the aqueous extract of *V. heterophylla*, administered at doses of 50, 100, 150, 200, and 250 mg/kg (orally), in rats. The findings illustrated that the aqueous extract significantly elevated urinary water and electrolyte excretion in normal rats in a dose-dependent way, with the most pronounced effects observed at doses

ranging from 150 to 250 mg/kg. This extract facilitated the efficient elimination of excess fluid and notably reduced urinary osmolarity compared to control groups. Across various doses, the administration of the extract (orally) gave significant diuresis and a modest rise in electrolyte (Na^+, K^+, and Cl^-) elimination, with the dose of 250 mg/kg exhibiting the most prominent effects [72]. GC-MS analysis of the essential oil of *Vepris heterophylla* leaves revealed the detection of geijerene and pregeijerene as the main constituents, sabinene, elemol, α-cadinol, δ-cadinene, (E)-ocimene, and terpinen-4-o1 were also identified [73]. The observed increase in natriuresis following acute treatment with the aqueous extract of *V. heterophylla* leaves provides insight into the heightened diuresis [74]. Moreover, *V. heterophylla* was found to induce urine acidification and significantly reduce urinary osmolarity in treated rats. These findings suggest that *V. heterophylla* may interfere with the basal secretion of ADH (antidiuretic hormone) and diminish the receptiveness of uriniferous tubules to ADH action, leading to polyuria characterized by low osmolarity [75]. Furthermore, the study proposes that *V. heterophylla* may function as a loop diuretic by impeding the $Na^+/K^+/Cl^-$ co-transporter system in the thick ascending loop of the nephron. This mechanism results in increased natriuresis and kaliuresis, contributing to the observed diuretic effects of *V. heterophylla* [72].

***Ficus glumosa* Del. (Moraceae)**

F. glumosa, a plant featured in the pharmacopeias of Cameroon, Senegal, and East Africa, is traditionally employed for treating conditions like edema, hemorrhoids, and cardiovascular diseases, particularly hypertension. Native to Ethiopia, it grows well in various regions of tropical Africa, typically in dry areas within meadows and wooded bushes. *F. glumosa* is known to flourish on rocky outcrops, often aiding in the splitting of rocks. It attains its maximum size, reaching up to 10 meters, particularly in valley areas [76]. A study investigated the diuretic properties of *F. glumosa* aqueous extract (225, 300, and 375 mg/kg) in rats. Results displayed a noteworthy hastening in the removal of excess fluid, a decrease in urinary osmolarity, and increased urine volume 24 hours next to administration, particularly at the 375 mg/kg dose. This extract induced alkalinization of urine, elevated Na^+, K^+, and Cl^- levels, and exhibited robust inhibitory effects on carbonic anhydrase and saluretic activity [77]. Earlier research highlighted the significant presence of crude protein, essential amino acids, and essential minerals in the leaves and stem bark of *F. glumosa*, potentially aiding in addressing protein malnutrition in developing countries [78]. The biological activities of *Ficus glumosa* to its secondary metabolites profile, which is composed of alkaloids, flavonoids, saponins, triterpenoids, tannins, phenolic acids, steroids, and coumarins. Quantitative analysis revealed high levels of total flavonoids/phenolics in the ethyl acetate (EA) and n-butanol fractions of the stem bark. The EA fraction exhibited potent antioxidant and anti-proliferative properties, attributed to the identified compounds including gallic acid, protocatechuic acid caffeoylquinic acid isomer, epi-catechin, and catechin using HPLC-ESI-MS/MS analysis [79].

Clinical trials

Equisetum arvense L (Equisetaceae) is among the most recommended medicinal plants. Widely distributed across the Americas, Europe, Northern Africa, and Asia, it has a traditional application as a diuretic and is valued for its remineralization, antiedematous, and anti-inflammatory properties. The aerial components of *E. arvense* encompass flavonoids, saponins, caffeic acid, phenolic compounds, alkaloids, sterols, and minerals, with silicon and potassium salts being predominant. The significant presence of flavonoids, phenolic compounds, and mineral salts suggests the plant's efficacy as a mild diuretic in herbal medicine. A study investigated the diuretic effects of *E. arvense* extract compared to hydrochlorothiazide and placebo in thirty-six healthy male volunteers. Results indicated that *E. arvense* extract demonstrated a stronger diuretic action than the placebo and comparable to hydrochlorothiazide, without significant electrolyte changes or increased catabolite elimination. The extract was well-tolerated with minor adverse events [80]. The phenolic components of *E. arvense* was assessed through HPLC analysis, revealing the presence of quercetin 3-O-glucoside (isoquercitrin), apigenin 5-O-glucoside, kaempferol 3-O-glycoside, and di-E-caffeoyl-meso-tartaric acid [81].

Taraxacum officinale (L.) Weber, belonging to the Asteraceae family and commonly referred to as dandelion, Herba Taraxaci, or Taraxacum herba, is a prevalent component in many U.S. and European herbal remedies. Widely utilized as a remedy for various conditions, dandelion has been identified to contain ascorbic acid, caffeic acid, chlorogenic acid, isoquercitrin, and luteolin. A pilot study explored the diuretic effect of a fresh leaf hydroethanolic extract of *T. officinale* in volunteers. Participants experienced a significant increase in urination frequency after the first and second doses, suggesting the potential diuretic efficacy of *T. officinale* hydroethanolic extract [82]. The major effects of the different herbal extracts discussed in the present review article were illustrated in **Table (1)**

Table (1): The Major Effects of The Different Herbal Extracts Discussed in The Present Review Article.

Plant	Major Effects	References
***Senna septemtrionalis* (Viv.)**	- Increasing urine output, sodium, and potassium excretion through modulation of prostaglandin E2 and nitric oxide production, as nitric oxide has been shown to induce natriuresis and diuresis and hindering fluid reabsorption in the renal tubules.	[5]
Halosarcia indica	- Increasing urine output, suggesting a strong diuretic effect, that is likely due to the presence of flavonoids and phenolic acids, which are known for their diuretic properties that influence kidney function by regulating water and ion transport.	[6,7]
***Lagopsis supina* (Steph) IK. Gal.**	- Inhibition of the renin-angiotensin-aldosterone system (RAAS), leading to increasing urine output. Also, the modulation of Aquaporins (AQP-1, 2, and 3) protein expression. Suppression of the RAAS can reduce sodium reabsorption and manifest a diuretic effect.	[9,10]
***Kalanchoe pinnata* (Lamk.)**	-The diuretic effect is associated with its rich content of flavonoids and polyphenols.	[13]
Desmostacha bipinnata	-Increasing the urinary output, urinary electrolyte concentration (Na^+, K^+, and Cl^-) that may be credited to phytochemical constituents like, phenolic compounds, flavonoids, triterpenoids, and tannins.	[21]
***Peteroselinum crispsum* (Parsley)**	- Inhibition of the Na^+–K^+ pump, leading to reduced absorption of Na^+ and K^+ and inducing osmotic water flow into the lumen, resulting in diuresis.	[27]
***Cola nitida* (Kolanut)**	- Enhancement of renal blood flow and the glomerular filtration rate associated with the caffeine and theophylline content.	[32]
***Cicer arietinum* L.**	- Reduction in water and electrolytes reabsorption.	[37]
***Alismatis rhizoma* (*Alisma orientale* Sam.)**	- Triterpenes played a primary role in mediating the diuretic action.	[41,42]
Opuntia ficus-indica	- Promotes the elimination of electrolytes such as sodium, potassium, and chloride, functioning akin to a loop diuretic. The diuretic characteristics of the extracts could be ascribed to the existence of flavonoids.	[47]
Nigella sativa	- The constituents proven to induce diuretic effects encompass alkaloids, anthraquinones, flavonoids, saponins, and tannins.	[50]
Thymus serrulatus	- Phenolic compounds (e.g. thymol) are acknowledged for their significant diuretic properties.	[53]
***Moringa stenopetala* (Baker f.) Cufodontis**	- Preventing the Na+/K+/Cl^- co-transporter at the thick ascending loop of Henle, as a loop diuretic (furosemide).	[59]
***Biophytum sensitivum* (L.) DC.**	- Increasing renal blood flow, resulting in an improved glomerular filtration rate, which is probably due to the combined or separate influence of the plant's constituents, as; alkaloids, flavonoids, tannins, and phenolic compounds.	[62]
***Panicum repens* L.**	- Elevation of urine volume and concentrations of sodium and potassium. The plant is proposed to act similarly to loop diuretics (furosemide).	[64, 65]

***Tribulus alatus* Del. nom. nud.**	- The presence of flavonoids and saponin glycosides is suggested to contribute to the observed diuretic effect.	[66,68]
***Citrullus lanatus* (Watermelon)**	- The diuretic impact is likely attributable to its main compounds, steroids, and alkanes, that are associated with natriuretic properties.	[70,71]
Vepris heterophylla (Engl.)	- Increasing in natriuresis, hindering basal secretion of ADH and lessen the tubules' reactivity to action of ADH in the urine which results in polyurea also, stopping the $Na^+/K^+/Cl^-$ co-transporter mechanism, hence elevating kaliuresis and natriuresis.	[72,75]
***Ficus glumosa* (Moraceae)**	- Enhancement of diuresis and mild natriuretic action. Moreover, the alkaline urine resulted from the elevated levels of Na^+, K^+, and Cl^-, suggesting a potent saluretic effect and inhibition of carbonic anhydrase activity.	[77]
Equisetum arvense	- The diuretic activity was comparable to the hydrochlorothiazide (reference drug) without causing significant changes in electrolyte excretion.	[80]
***Taraxacum officinale* L. (dandelion)**	- Enhancing the rate of urination.	[82]

3. Conclusion:

This review suggests that various herbal extracts and their fractions exhibit notable diuretic effects in test animals. Extra investigation is crucial to clarify the mechanisms of action and identify responsible phytochemicals. Clinical investigations are warranted to understand how these phytochemicals operate in human bodies.

4. Conflicts of interest:

The authors did not report any potential conflict of interest.

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6. References:

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