IOSR Journal Of Pharmacy www.iosrphr.org
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 8, Issue 6 Version. II (June 2018), PP. 67-80

Arabian medicinal plants with antiurolithiatic and diuretic effects - plant based review (Part 1)

Prof Dr Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, University of Thi qar, Iraq.
Corresponding Author: Prof Dr Ali Esmail Al-Snafi

Abstract: Antiurolithiatic drugs are the drugs which dissolve or prevent the formation of urinary calculi, while diuretics are drugs which increase the volume of urine excreted. Several medicinal plants can inhibit urolithiasis by many mechanisms: maintains crystalloid-colloid balance by decreasing excretion of urinary calcium, oxalate, uric acid, phosphorus and protein in urolithiasis, improves the renal function by increasing the excretion of urea and creatinine, diuretic and ACE inhibition activity. On the other hand many drugs can produce diuretic effect via their effects on renal water channels, on renal carriers, on nitric oxide-cGMP pathway, on prostaglandin-cAMP pathway, on the renin-angiotensin-aldosterone system (RAAS), on the kinin–kallikrein system (KKS), s on carbonic anhydrase and osmotic effects on kidneys. The current review will discuss the medicinal plants with antiurolithiatic and diuretic effects and their potential in the treatment of urinary stone.

Keywords: Diuretic, Antiurolithiatic Medicinal Plants, Pharmacology

Date of Submission: 20-06-2018 Date of acceptance: 05-07-2018

I. INTRODUCTION:

Renal stones are a common worldwide health condition with considerable morbidity and recurrence. The development of the stones is related to decreased urine volume or increased excretion of stone-forming components such as calcium, oxalate, urate, cystine, xanthine, and phosphate [1-2]. Several medicinal plants can inhibit urolithiasis by many mechanisms included: maintains crystalloid-colloid balance by decreasing excretion of urinary calcium, oxalate, uric acid, phosphorus and protein in urolithiasis [3], improves the renal function by increasing the excretion of urea and creatinine [4], potential antioxidant activity reduces renal tubular epithelial cell injury when exposed to oxalate and/or CaOx, so the loss of membrane integrity subsequently facilitates the retention of calcium oxalate crystals and growth of stones in renal tubules [4-7], and diuretic and ACE inhibition activity[8-9].

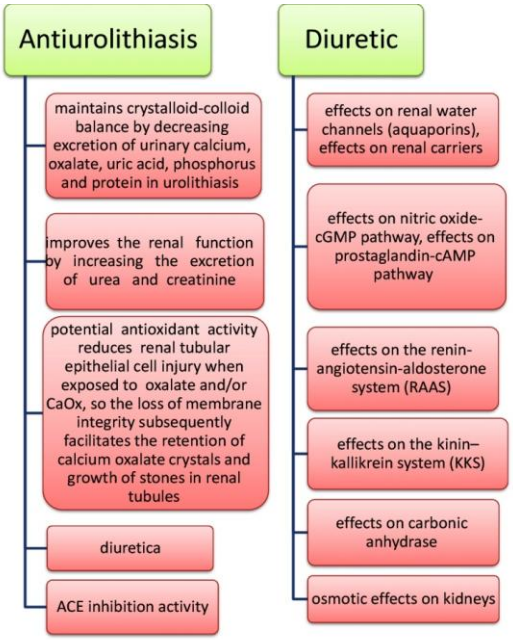

Fig 1: Mechanisms of antiurolithiasis and diuretic effects of medicinal plants

I-Medicinal plants with antiurolithiatic effects:

Adiantum capillus-veneris

The hydro alcoholic extract of *A. capillus-veneris* Linn. on calcium oxalate crystallisation was evaluated by *in vitro* study. Crystallization was induced by addition of 50 µl of 0.1 M sodium oxalate in whole urine in the absence and the presence of extract at different concentrations (0.50 mg, 0.75 mg and 1 mg). The nucleation and aggregation rates were followed at 620 nm after mixing calcium chloride and sodium oxalate solution and in a buffered solution containing calcium oxalate monohydrate crystals, respectively. The rate was evaluated by comparing the slope of turbidity in the presence of extract with that of control using the spectrophotometer. Crystals in the urine were also analysed by light microscopy. Extract of the test drug inhibited the crystallization in solution; less and smaller particles were observed in the presence of extract. These results were further confirmed in the nucleation assay, though the rate of nucleation was not inhibited but number of crystals was found to be decreased. The extracts also inhibited crystal aggregation[10-11].

The result of significant in vitro inhibitory effects on crystallization and aggregation was further confirmed by *in vivo* study against ethylene glycol (0.75%) and ammonium chloride (1%) induced urolithiasis in male Sprague Dawley rats. Urine microscopy showed significant reduction ($p<0.001$) in the number of crystals. Serum levels of calcium, phosphorous, and blood urea were found to be decreased significantly. Serum creatinine level was found to be similar to plain control. The animals treated with test drug showed much improvement in body weight. Histopathology of kidney showed almost normal kidney architecture in treated groups [12-13].

Adonis aestivalis

In lithiasis induced by feeding the rats with 0.75% ethylene glycolated water for 28 days. Ethylene glycol treatment raised the urinary calcium, phosphate, oxalate and protein levels significantly ($p< 0.05$) in the lithiatic group, where magnesium level showed a significant decrease. However, after the treatment with *Adonis aestivalis* (divided doses of extract of 60 mg/kg of body weight daily by gavages). *Adonis aestivalis* attenuated the elevated parameters and inhibit stone formation [14-15].

Agrimonia eupatoria

Significant uricolytic activity has been documented for agrimony infusions and decoctions (15% w/v), following their oral administration to male rats at a dose of 20 ml/kg body weight (equivalent to 3 g dry plant powder)[16-17].

However, Grase*et al.,* found that *Agropyron repens* L. exerted no effect on urolithiasis risk factors when given to the rats in combination with different diets (standard, high glucidic and high protein) [18].

Althaea rosea

In both preventive and curative protocols, treatment of rats with hydroalcoholic extract of *Althaea rosea* roots significantly reduced the kidney calcium oxalate deposits compared to ethylene glycol group. Administration of *Althaea rosea* extract also reduced the elevated urinary oxalate due to ethylene glycol [19-20].

Ammannia baccifera

Prasad *et al* tested the antiurolithic activity of *A. baccifera* in male albino rats. Urinary stones were induced by implantation of zinc discs in the urinary bladder. They found that the ethanolic extract of *A. baccifera* (2g/kg/day, po) was effective in reducing the formation of stone and also in dissolving the pre-formed one. There was a significant increase in the urinary excretion of calcium, magnesium and oxalate, four weeks after implantation of zinc discs. Treatment with *A. baccifera* has significantly reduced calcium and magnesium levels in the prophylactic group while it has reversed the levels of these ions to normal values in the curative group [21-22].

Ammi visnaga

Ammi visnaga was investigated for the preventive effect of kidney stone formation. In cell culture experiments, it was found that *Ammi visnaga* and its compounds (khellin and visnagin) protected cell damage from calcium oxalyate crystals. In addition, *Ammi visnaga* and its compounds prevented calcium oxalyate crystals formation in stone forming rats by increasing the urinary pH and citrate concentration along with a decrease of urinary oxalate. The calcium oxalyate crystals deposition in the rat kidneys was significantly decreased in the group of rats receiving *Ammi visnaga* and its compounds [23-24].

The oral administration of an aqueous extract prepared from the fruits of *A. visnaga* as well as two major constituents khellin and visnagin prevent crystal deposition in stone-forming rats. Hyperoxaluria was induced in male Sprague-Dawley rats by giving 0.75% ethylene glycol and 1% ammonium chloride via the drinking water. The Khella extract (KE; 125, 250 or 500 mg/kg) was orally administered for 14 days. The histopathological examination of the kidneys revealed that KE significantly reduced the incidence of calcium oxalate (CaOx) crystal deposition. In addition, KE significantly increased urinary excretion of citrate along with a decrease of oxalate excretion. Comparable to the extract, khellin and visnagin significantly reduced the

incidence of CaOx deposition in the kidneys. However, both compounds did not affect urinary citrate or oxalate excretion indicating a mechanism of action that differs from that of the extract. For KE, a reasonably good correlation was observed between the incidence of crystal deposition, the increase in citrate excretion and urine pH suggesting a mechanisms that may interfere with citrate reabsorption [25]. The prophylactic effects of *Ammi visnaga* may be attributed to its diuretic activity to maintain the oxalate, below the supersaturation to precipitate as Calcium oxalate [26]**.**

Apium graveolens

Tthe effect of Apium graveolens in reducing calcium deposits from renal parenchyma was studied in rabbit models with induced nephrocalcinosis by a large dose of oxalic acid, *Apium graveolens* significantly reduced blood urea nitrogen, serum creatinine and serum Na^+ levels in addition to non-significant reduction in serum K^+. It caused a significant reduction in calcium deposition in renal parenchyma after 10 days treatment. This effect was attributed to its diuretic effect [27-28].

Asparagus racemosus

The antiurolithiatic effect of ethanolic extract of *Asparagus racemosus* was evaluated in urolithiasis in rats (using the model of Ethylene glycol 0.75% and ammonium chloride 2% in drinking water). The rats treated with ethanolic extract of A. racemosus at doses 800 and 1600 mg/ kg showed significant ($P < 0.05$) reduction of serum concentrations of calcium, phosphorus, urea, and creatinine. Histopathology of the kidneys revealed less tissue damage and were almost similar to control rats[29].

Benincasa hispida

Benincasa hispida fruit rind extract (outer thick pericarp) was also significantly increased ($p<0.001$) urine volume, sodium and chloride levels, and significant decrease ($p<0.001$) potassium excretion in rats when used orally in a dose of 100mg/kg bw [60]. When 0.75% v/v ethylene glycol was given to the rats in drinking water to induce chronic hyperoxaluria, with simultaneous *Benincasa hispida* extract at the dose of 250 and 500 mg/kg bw, orally for 35 days. The supplementation with *Benincasa hispida* extract significantly lowered the urinary excretion and kidney retention levels of oxalate, protein and calcium. Moreover, elevated serum levels of sodium, creatinine, calcium and phosphorus were significantly reduced by the extracts [9, 30-31].

Carthmus tinctorius

The effects of Floscarthami (FC) (600 and 1200 mg/day, by gastric gavages), was evaluated on calcium oxalate (CaOx) formation in ethylene glycol (EG)-fed rats. 24-h urine and blood samples were analyzed at the beginning and end of the experiment. Kidney tissue was histopathologically examined using a polarized light microscope, and crystal deposits were evaluated by a semi-quantitative scoring method; these scores were significantly lower in the FC groups (600 and 1200 mg/day) than in the placebo group[32-33].

Cicer arietinum

The diuretic and anti-nephrolithiasis activities of *Cicer arietinum* ethanolic seed extract were evaluated in albino rats. The activity was studied by using ethylene glycol induced nephrolithiasis model. Cystone was used as standard drug. Two test doses of *Cicer arietinum* ethanolic seed extract were used. The total duration of evaluation was 28 days. Urine volume, urine analysis, serum analysis were used to assess the efficacy of test drug. The results revealed that the extract decreased urinary stones in the kidney with good diuretic property[34-35].

Clerodendrum inerm

The diuretic activity of chloroform and ethanolic extract of leaves of *Clerodendrum inerm* was investigated in rats. The effect of 200 and 400mg/kg of both extracts were evaluated on urine volume and electrolyte concentration. Both extracts showed good diuretic activity after 24 hr[36-37].

Clitoria ternatea

Clitoria ternatea roots or their extract in 95% alcohol showed no significant diuretic or natriuretic effect in dogs when administered orally in non-toxic dose. Intravenous doses of the extract led to a moderate increase in the excretion of sodium and potassium in the urine, but at the same time, it showed signs of kidney damage[38-39].

Convolvulus arvensis

The diuretic effect of the *Convolvulus arvensis* root extracts were assessed in rats with the using furosemide as standard diuretic drug. The parameters studied were included body weight before and after test period, total urine volume, urine concentration of Na^+, K^+ , $HCO_3^-$and Cl^-. The water and ethanol extracts (50 and 100 mg/kg) of the root extract of *Convolvulus arvensis* produced time dependent increase in urine output. Electrolyte excretion was also significantly affected by the extracts. The water extract increased the urine excretion of Na^+, K^+ and HCO_3^-. In contrast, the ethanol extract increased the excretion of HCO_3^-, decreased the loss of K^+ and had little effect on renal removal of Na^+. The high-ceiling diuretic, furosemide, increased the renal excretion of Na^+ and Cl^-; but had no effect on K^+ and HCO_3^- loss[40-41].

Coriandrum sativum

The acute diuretic activity of aqueous extract of the seed of *Coriandrum sativum* was evaluated in rats. The aqueous extract of coriander seed was administered by continuous intravenous infusion (120 min) at two doses (40 and 100mg/kg) to anesthetized Wistar rats. Furosemide (10mg/kg), a standard diuretic was used as the reference drug. Excretion of water and electrolytes (sodium, potassium and chloride) in urine, and glomerular filtration rate (equal to creatinine clearance) were determined. The crude aqueous extract of coriander seeds increased diuresis, excretion of electrolytes, and glomerular filtration rate in a dose-dependent way. Furosemide was more potent as a diuretic and saluretic. The authors concluded that the mechanism of action of the plant extract appears to be similar to that of furosemide[42-43].

Crocus sativus

The diuretic activity of aqueous extract of dried saffron (stigma of *Crocus sativus*) was studied in rat. Aqueous extracts of saffron were administered to experimental rats orally as 60, 120 and 240 mg/kg bw and compared with hydrochlorothiazide (10 mg/kg bw, intraperitoneally), as positive control and normal saline solution as placebo. The measured parameters for diuretic activity were total urine volume, urine electrolytes concentration such as sodium and potassium, creatinine and urea concentration. The treated rats with aqueous extract of saffron of 120 and 240 mg/kg bw showed higher urine output when compared to the control group. Also, the extract possessed significant dose-dependent increase in the excretion of electrolytes when compared to the control group[44-45].

Cynodon dactylon

The diuretic activity of aqueous extract of *Cynodon dactylon* was evaluated in rats. Aqueous extract of *Cynodon dactylon* at a dose of 100, 250, 500mg, 750 mg/kg bw orally, showed diuretic activity. Rats received aqueous extract at the dose of 750mg/kg/body weight excreted nearly four folds urine as compared to the control group. The excretion of sodium, potassium and chloride ions were also increased[46-47].

The diuretic potential and effect on urinary electrolytes of aqueous *Cynodon dactylon* L. (Poaceae) rhizomes extract was studied in rats. Different concentrations of plants extract (0.125, 0.250, and 0.500 g/kg of body weight) or the reference drug furosemide (0.015 g/kg) were administrated orally to hydrated male Wistar rats and their urine output was measured at several interval of time after a single dose administration. The results showed that furosemide induced significant diuresis and electrolytes excretion during the first hours. Plant extracts increased significantly urinary output and electrolytes excretion at the dose of 0.500 g/kg. This diuretic effect seems to be not related to K^+ plant content. Urinary pH remained mostly unchanged during the course of the study . No lethality was observed among animals[48].

The diuretic activity of *Cynodon dactylon* was evaluated in rats and in Guinea pigs in comparison with hydrochlorothiazide. Crude extract of plant was administered to rats orally at a dose of 1.25 and 2.5ml/kg. The diuretic activity of extract was evaluated by estimation of urine volume, sodium, potassium and chloride content. The plant administered group showed significant increase in urine output, urinary electrolyte excretion compared to control group. High dose of *Cynodon dactylon* extract group produced results comparable to standard drug[49-50].

Desmostachia bipinnata

The diuretic effect of hydro-alcoholic extract of *D. bipinnata* whole plant was studied in rats. Frusemide (20 mg/kg) was served as positive control for diuretic activity. The hydro-alcoholic extract showed significant diuretic activity and was found to be the most potent in increasing the urinary output at 500 mg/kg when the effect was compared with that of the standard frusemide ($P<0.01$). Moreover, this extract was found to be most effective in increasing urinary electrolyte concentration (Na^+, K^+, and Cl^-) at both doses tested[51-52].

Dolichos lablab

Antilithiatic study revealed that the methanolic extract of White & Black seeds of *Dolichos lablab* possessed antilithiatic activity, but less than that recorded for the extract of leaves and bulbs of *Nymphaea odorata*[53-54].

Equisetum arvense

The diuretic effect of EADE was assessed clinically by monitoring the volunteers' water balance over a 24 h period. The dried extract of Equisetum arvense (EADE, 900mg/day) produced a diuretic effect that was stronger than that of the negative control and was equivalent to that of hydrochlorothiazide without causing significant changes in the elimination of electrolytes. Only rare minor adverse events were reported[55-56].

Euphorbia hirta

The diuretic effect of the E. hirta leaf extracts was evaluated in rats. The water and ethanol extracts (50 and 100 mg/kg) of the plant produced time-dependent increase in urine output. The water extract increased the urine excretion of Na^+, K^+ and $HCO3^-$. while, the ethanol extract increased the excretion of $HCO3^-$, decreased the loss of K^+ and had little effect on renal removal of Na^+[57-58].

Foeniculum vulgare

The ethanolic fruit extract (500 mg/kg dose) showed, statistically, a highly significant diuretic effect in rats, that was evident both after 5 ($P<0.0l$) and 24 ($P<0.05$) h of its administration. The plant-induced diuresis

comparable to that of urea (960 mg/kg) and was almost double that of the control animal's urine output. The diuresis was not associated with changes in sodium and/or potassium excretion[59].

The diuretic activity of aqueous and 80% methanol extracts of *Foeniculum vulgare* Mill. (Apiaceae) leaf was evaluated in rats using different doses of aqueous or 80% methanol extract (100, 200 and 400 mg/kg) orally. Rats treated with 200 and 400 mg/kg doses of aqueous and 80% methanol extract of *Foeniculum vulgare* showed an increased urine volume ($p<0.001$). However, 100 mg/kg dose of both extracts failed to produce significant increase in 24 h urine volume compared to control groups. Both extracts increased natriuresis, kaliuresis and chloriuresis ($p<0.001$) at the middle and higher doses[60].

Glossostemon bruguieri

Glossostemon bruguieri powder and its alcoholic extract together with four of the purified compounds (takakin 7-0-glucoside, isosctullarien, its 7-0 –glucoside and takakin 8-0-glucoside) were shown to increase urine volume but not sodium on albino rats, being more pronounced and equipotent with that of the standard drug, furosemide [61].

***Gossypium* species**

The diuretic activity of ethyl acetate and alcohol extract of *Gossypium herbaceum* Linn leaves (100 and200 mg/kg body weight) was investigated in male wistar albino rats. The total urine volumes of the both extracts (200mg/kg) treated rats were elevated nearly two folds compared with the control. Excretion of sodium, potassium and chloride ions were increased significantly compared with control group. The diuretic effect was comparable with that of the standard drug Frusemide, however, alcoholic extract showed more significant diuretic activity compared with the ethyl acetate extract as a diuretic. The increase of sodium and potassium in the urine of the group treated with both extracts was dose dependent[62].

Herniaria hirsuta

Herniaria hirsuta was evaluated in nephrolithiasis in rats as a preventive agent against the development of kidney stones. The experiment was conducted in normal and calcium oxalate (CaOx) nephrolithiasic rats during 3 weeks. The results showed that water intake and urinary volume increased in nephrolithiasic rats, but their urinary pH decreased especially in the third week of treatment. Urinary oxalate increased significantly during the second week in untreated rats and remained constant in rats treated with Herniaria decoction. However, urinary calcium decreased significantly in week 2 in untreated rats and remained constant in the treated rats. Qualitative analysis of crystalluria showed that untreated rats excreted large CaOx monohydrate and few dihydrate crystals while treated animals excreted small CaOx dihydrate crystals mostly. The examination of kidney sections revealed that CaOx deposition was decreased in the treated compared to untreated rats[63-64].

The effects of Herniaria hirsuta L. (Carryophyllaceae) and Agropyron repens L. (Gramineae), as herb infusion, combined with different diets (standard, high glucidic, high protein) on the calcium oxalate urolithiasis were studied in rats. The results revealed that the antilithiasic effects of the H. hirsuta infusion clearly depends on the diet. Thus, a clear increase in the citraturia was only detected when such infusion was administered with the high protein diet[65].

The effectiveness of an extract of Herniaria hirsuta on calcium oxalate crystallization was studied in vitro. Crystallization was induced in whole normal human urine samples in the absence or presence of the extract. Crystals generated in the urine were harvested and analysed by scanning electron microscopy. The nucleation and aggregation of calcium oxalate crystals were measured separately using spectrophotometric methods. The herb extract promoted the precipitation of calcium oxalate particles in whole urine. The results showed the extract of H. hirsuta promoted the nucleation of calcium oxalate crystals, increasing their number but decreasing their size. It also promoted the formation of calcium oxalate dihydrate crystals, despite the presence of calcium oxalate monohydrate particles. The extract may contain substances that inhibit calcium oxalate crystal aggregation[66].

The prophylactic effect of oral administration of *Herniaria hirsute* decoction was investigated in experimentally induced calcium oxalate (CaOx) nephrolithiasis in rats. *H. hirsuta* has an impressive prophylactic effect on CaOx stones in nephrolithic rats, the effect which did not mediated by biochemical or diuretic changes[67].

Cystine stones represent 1% of urinary calculi in adults and 10% in children and are especially recurrent and resistant. In Morocco, various plants, *Herniaria hirsuta*, Opuntia ficus-indica, Zea mays and Ammi visnaga were used against nephrolithiasis. The effect of plant extracts on the disolution of cystine stones was studied in vitro. The results revealed that the studied herbal extracts were efficient for dissolving cystine stones, probably by formation of complexes between cystine and polyhydroxylated molecules present in the extracts[68].

The interaction of calcium oxalate crystals with renal epithelial cells is a critical event in kidney stone formation. The effect of aqueous extract from Herniaria hirsuta on the adhesion of calcium oxalate monohydrate (COM) crystals to cultured renal cells was investigated. Calcium oxalate monohydrate crystal binding to cells was inhibited by extract in a concentration dependent manner. It was suggested that the extract may coats the crystals and inhibits their attachment to cells[69].

The methanol extract of Herniaria hirsuta was fractionated determine the nature of compound responsible for the beneficial effect of Herniaria hirsuta in prevention and cure of urolithiasis. The fractions were then assayed on calcium oxalate crystallization in *in vitro* and *in vivo* models. In the whole human urine, only the fraction eluted with ethanol/water was associated to formation of smaller crystals composed of calcium oxalate dihydrate, similarly to the aqueous extract. When tested at 5 mg/day, it reduced significantly crystal deposition in lithiasic rats. Preliminary identification of the fraction showed the presence of saponins which may be responsible for the beneficial effect of Herniaria hirsuta in the treatment of kidney stones[70].

Hibiscus rosa-sinensis

The aqueous extract of flowers of Hibiscus rosa-sinensis was evaluated for antilithatic potential in vitro. The presence of calcium oxalate crystals was evaluated immediately and after 24 hrs of stone induction. Crystal aggregation after 24 hrs was inhibited by Hibiscus rosa-sinensis extract. The extract interfered with early stages of stone formation and may represent an alternative form of treatment and or prevention for urolithiasis[71].

Hibiscus sabdariffa

The diuretic activity of Hibiscus sabdariffa aqueous extract was evaluated on in vivo and in situ models. The aqueous extract was administrated in increasing doses and the diuresis produced and disposal of electrolytes were evaluated. The renal filtration rate with plant extract, furosemide and amiloride were evaluated in isolated kidney. The diuretic and natriuretic effect of Hibiscus sabdariffa aqueous extract showed a dose-dependent behavior. The pharmacological constants of natriuretic effect was ED_{50} = 86 mg/kg and Emax = 0.9 mEq/100 g/5 h. In the in vitro model, renal filtration was increased 48% with the aqueous extract of Hibiscus sabdariffa and an additive effect was recorded when Hibiscus sabdariffa aqueous extract was perfused with furosemide[72].

The diuretic, natriuretic, and potassium sparing effects of Hibiscus sabdariffa are due in part to the modulation of aldosterone activity by the presence of compounds potentially responsible for this modulation, as anthocyanins, flavonoids, and chlorogenic acid[73].

Juniperus communis

A 10% aqueous infusion of juniper, 0.1% aqueous solution of juniper oil (with 0.2% of Tween 20 solubilizer) and 0.01% aqueous solution of terpinen-4-ol were orally administered to rats at 5ml/100g bw to determine the effect on urine output. Compared to water, the 10% aqueous infusion of juniper and the 0.1% aqueous solution of juniper oil caused reductions of only 6% in diuresis over a 24-hour period, equivalent to the effect of 0.004 IU/100g of ADH, while the 0.01% solution of terpinen-4-ol caused a reduction of 30% in diuresis ($p<0.01$), equivalent to 0.4 IU/100g intraperitoneal of ADH. Continued daily administration at the same daily dose level, the two juniper preparations and terpinen-4-ol stimulated diuresis on days two and three, although only the 10% aqueous infusion of juniper exerted significant diuretic activity (+ 43% on day two; +44% on day three; $p<0.05$), suggesting that the diuretic effect is partly due to the essential oil and partly to hydrophilic constituents[74-75].

However, oral administration of lyophilized aqueous extract of juniper at 1000mg/kg bw to rats, it didnt increase urine volume or excretion of Na^+, K^+ or Cl^- ions over a six-hour period compared to the effect of the same volume of water[76].

***Quercus* Spp**

Ninty seven patients suffering from urolithiasis were treated with Litiax. 82 of them presented ureteral stones and the other 15 kidney stones. The product was administered in doses of 1350 mg/ day. The treatment lasted between 8 and 225 days, the average duration being 58 days. It was revealed from the results obtained that the product tested has an inhibiting effect on the growth of the stone, antiinflammatory and diuretic. It also seems to inhibit the bacteria proliferation to a certain extent. The product is easily tolerated [77].

Plantago major

The *in vitro* effect of *Plantago major* extract on calcium oxalate crystals was investigated. The concentrations of *Plantago major* extract used were from 100ppm to 350ppm. Extract of *Plantago major* has inhibitory effect on the number of crystals but it was not significant. However, extract of*Plantago major* was better than allopurinol and potassium citrate in inhibiting the size of the calcium oxalate crystal *in-vitro*[78].

Portulaca oleracea

The antiurolithiasis activity of the ethanolic extract of aerial parts of *Portulaca oleracea* Linn was studied using the ethylene glycol (0.75% v/v) and ammonium chloride (2% w/v) induced urolithiasis model in albino rats. Several parameters were used including urinary volume, urine pH, urine and serum parameters to assess the

activity. The ethanolic extract of *Portulaca oleracea* was administered in doses of 100, 200 and 400 mg/kg body weight orally for 15 days. Standard drug used was cystone. Treatment with the extract restored all the elevated biochemical parameters including serum and urine (calcium, creatinine, urea, BUN), restored the urine pH to normal and increased the urine volume significantly ($P < 0.05$) when compared to disease control group. The histopathological studies confirmed the induction of lithiasis as microcrystal deposition was observed in section of kidney from animals treated with ethylene glycol and ammonium chloride. This was reduced, after treatment with the extract [79].

Punica granatum

Animals model of calcium oxalate urolithiasis was was used to evaluate the anti-urolithiatic effect of Punica granatum. Chloroform extract (PGCE) and methanol extract (PGME) were given orally at 100, 200 and 400mg/kg, along with ethylene glycol for 28 days. On 28 day, 24h urine was collected from individual rats and used for estimation of urine calcium, phosphate and oxalate. The serum creatinine, urea and uric acid levels were estimated for each animal. The kidney homogenate was used for the estimation of renal oxalate contents. The paraffin kidney sections were prepared to observe the CaOx deposits. The ethylene glycol control caused significant ($P<0.001$ vs. normal) increase in levels of urine oxalate, calcium and phosphate, serum creatinine, urea and uric acid and renal tissues oxalates, as compared to normal. The paraffin kidney sections show significant histopathological changes. The treatment of PGCE and PGME at 100, 200 and 400mg/kg doses, significantly ($P<0.001$ vs. control) decreased the urine oxalate, calcium and phosphate, renal tissue oxalates and serum creatinine, urea and uric acid after 28 days [80].

Terminalia chebula

The antiurolithiatic property of aqueous extract of fruit of *Terminalia chebula* in Wistar albino rats. The protective effect of aqueous extract of *Terminali achebula* fruit was evaluated at two dose levels (100 and 200mg/kg body weight) using ethylene glycol induced calcium oxalate urolithiasis model in rats. The results indicate that ethylene glycol treatment decreases calcium level in urine and increased it in the kidney tissue homogenate, which were prevented in animal receiving simultaneous treatment of extract. Extract treatment decreased the elevated levels of oxalate and phosphate in urine as well as kidney tissue homogenate. The extract supplementation also prevented the elevation of serum levels creatinine, uric acid and blood urea nitrogen. Histopathological study revealed that extract reduced histological changes and retained the normal architecture of kidney tissue [81].

Trigonella foenum-graecum

The therapeutic efficacy of standardized fenugreek seed extract with trigonelline as marker (SFSE-T) was evaluated in experimental urolithiasis in rats. Effects of subacute oral treatments of SFSE-T (30 and 60 mg/kg) and reference anti-urolithiasis drug, Cystone (750 mg/kg) were evaluated against 0.75% ethylene glycol (EG) and 1 % w/v ammonium chloride (AC) induced urolithiasis in rats. The biochemical (urinary and serum) and histopathological parameters were investigated. Subacute oral treatment of SFSE-T (60 mg/kg) showed reversal of EG+AC induced changes in urine (decreased 24-h urine output, pH, excretion of creatinine, citrate, and chloride and increased uric acid and oxalate excretion) and serum (increased creatine, uric acid and blood urea nitrogen) parameters and decreased creatine clearance. Histopathology examination of the kidneys sections from SFSE-T (60 mg/kg) treated rats showed lowered number of crystals, cell damage and tubulointerstitial damage index as compared with EG+AC control rats [82].

II-Medicinal plants possessed diuretic effects:

Several medicinal plants possessed diuretic effects. Diuretic effects of medicinal plants are mediated by their effects on renal water channels (aquaporins), effects on renal carriers, effects on nitric oxide-cGMP pathway, effects on prostaglandin-cAMP pathway, effects on the renin-angiotensin-aldosterone system (RAAS), effects on the kinin–kallikrein system (KKS), effects on carbonic anhydrase and osmotic effects on kidneys[83].

Agropyron repens

The sugar mannitol present in large quantities in this herb, and is known as a standard osmotic diuretic, that is, it is absorbed whole from the gut and excreted largely by the kidney tubules. Its presence in the tubules means that extra water has to be retained in order to maintain osmotic pressure. The saponins and vanillin, also have diuretic properties. Because of Couch grass diuretic and antimicrobial effects, it was used to flush out the urinary tract during infections [84].

Benincasa hispida

Benincasa hispida fruit rind extract (outer thick pericarp) was also significantly increased ($p<0.001$) urine volume, sodium and chloride levels, and significant decrease ($p<0.001$) potassium excretion in rats when used orally in a dose of 100mg/kg bw [85].

Cicer arietinum

The diuretic activities of *Cicer arietinum* ethanolic seed extract were evaluated in albino rats. The total duration of evaluation was 28 days. Urine volume, urine analysis, serum analysis were used to assess the efficacy of test drug. The results revealed that the extract possessed good diuretic property[86].

Citrus species

It was recorded that when women drank 1/2 liter of orange juice daily, their urinary pH value and citric acid excretion increased thereby diminishing the risk of forming calcium oxalate stones significantly[87-88].

Clerodendrum inerm

The diuretic activity of chloroform and ethanolic extract of leaves of *Clerodendrum inerm* was investigated in rats. The effect of 200 and 400mg/kg of both extracts were evaluated on urine volume and electrolyte concentration. Both extracts showed good diuretic activity after 24 hr[89].

Clitoria ternatea

Clitoria ternatea roots or their extract in 95% alcohol showed no significant diuretic or natriuretic effect in dogs when administered orally in non-toxic dose. Intravenous doses of the extract led to a moderate increase in the excretion of sodium and potassium in the urine, but at the same time, it showed signs of kidney damage[90].

Convolvulus arvensis

The diuretic effect of the *Convolvulus arvensis* root extracts were assessed in rats with the using furosemide as standard diuretic drug. The parameters studied were included body weight before and after test period, total urine volume, urine concentration of Na^+, K^+ , $HCO_3^-$and Cl^-. The water and ethanol extracts (50 and 100 mg/kg) of the root extract of *Convolvulus arvensis* produced time dependent increase in urine output. Electrolyte excretion was also significantly affected by the extracts. The water extract increased the urine excretion of Na^+, K^+ and HCO_3^-. In contrast, the ethanol extract increased the excretion of HCO_3^-, decreased the loss of K^+ and had little effect on renal removal of Na^+. The high-ceiling diuretic, furosemide, increased the renal excretion of Na^+ and Cl^-; but had no effect on K^+ and HCO_3^- loss[91].

Coriandrum sativum

The acute diuretic activity of aqueous extract of the seed of *Coriandrum sativum* was evaluated in rats. The aqueous extract of coriander seed was administered by continuous intravenous infusion (120 min) at two doses (40 and 100mg/kg) to anesthetized Wistar rats. Furosemide (10mg/kg), a standard diuretic was used as the reference drug. Excretion of water and electrolytes (sodium, potassium and chloride) in urine, and glomerular filtration rate (equal to creatinine clearance) were determined. The crude aqueous extract of coriander seeds increased diuresis, excretion of electrolytes, and glomerular filtration rate in a dose-dependent way. Furosemide was more potent as a diuretic and saluretic. The authors concluded that the mechanism of action of the plant extract appears to be similar to that of furosemide[92].

Crocus sativus

The diuretic activity of aqueous extract of dried saffron (stigma of *Crocus sativus*) was studied in rat. Aqueous extracts of saffron were administered to experimental rats orally as 60, 120 and 240 mg/kg bw and compared with hydrochlorothiazide (10 mg/kg bw, intraperitoneally), as positive control and normal saline solution as placebo. The measured parameters for diuretic activity were total urine volume, urine electrolytes concentration such as sodium and potassium, creatinine and urea concentration. The treated rats with aqueous extract of saffron of 120 and 240 mg/kg bw showed higher urine output when compared to the control group. Also, the extract possessed significant dose-dependent increase in the excretion of electrolytes when compared to the control group[93].

Cynodon dactylon

The diuretic activity of aqueous extract of *Cynodon dactylon* was evaluated in rats. Aqueous extract of *Cynodon dactylon* at a dose of 100, 250, 500mg, 750 mg/kg bw orally, showed diuretic activity. Rats received aqueous extract at the dose of 750mg/kg/body weight excreted nearly four folds urine as compared to the control group. The excretion of sodium, potassium and chloride ions were also increased[94].

The diuretic potential and effect on urinary electrolytes of aqueous *Cynodon dactylon* L. (Poaceae) rhizomes extract was studied in rats. Different concentrations of plants extract (0.125, 0.250, and 0.500 g/kg of body weight) or the reference drug furosemide (0.015 g/kg) were administrated orally to hydrated male Wistar rats and their urine output was measured at several interval of time after a single dose administration. The results showed that furosemide induced significant diuresis and electrolytes excretion during the first hours. Plant extracts increased significantly urinary output and electrolytes excretion at the dose of 0.500 g/kg. This

diuretic effect seems to be not related to K^+ plant content. Urinary pH remained mostly unchanged during the course of the study . No lethality was observed among animals[95].

The diuretic activity of *Cynodon dactylon* was evaluated in rats and in Guinea pigs in comparison with hydrochlorothiazide. Crude extract of plant was administered to rats orally at a dose of 1.25 and 2.5ml/kg. The diuretic activity of extract was evaluated by estimation of urine volume, sodium, potassium and chloride content. The plant administered group showed significant increase in urine output, urinary electrolyte excretion compared to control group. High dose of *Cynodon dactylon* extract group produced results comparable to standard drug[96-97].

Desmostachia bipinnata

The diuretic effect of hydro-alcoholic extract of *D. bipinnata* whole plant was studied in rats. Frusemide (20 mg/kg) was served as positive control for diuretic activity. The hydro-alcoholic extract showed significant diuretic activity and was found to be the most potent in increasing the urinary output at 500 mg/kg when the effect was compared with that of the standard frusemide ($P<0.01$). Moreover, this extract was found to be most effective in increasing urinary electrolyte concentration (Na^+, K^+, and Cl^-) at both doses tested[98].

Equisetum arvense

The diuretic effect of EADE was assessed clinically by monitoring the volunteers' water balance over a 24 h period. The dried extract of Equisetum arvense (EADE, 900mg/day) produced a diuretic effect that was stronger than that of the negative control and was equivalent to that of hydrochlorothiazide without causing significant changes in the elimination of electrolytes. Only rare minor adverse events were reported[55].

Euphorbia hirta

The diuretic effect of the E. hirta leaf extracts was evaluated in rats. The water and ethanol extracts (50 and 100 mg/kg) of the plant produced time-dependent increase in urine output. The water extract increased the urine excretion of Na^+, K^+ and $HCO3^-$. while, the ethanol extract increased the excretion of $HCO3^-$, decreased the loss of K^+ and had little effect on renal removal of Na^+[99].

Foeniculum vulgare

The ethanolic fruit extract (500 mg/kg dose) showed, statistically, a highly significant diuretic effect in rats, that was evident both after 5 ($P<0.0l$) and 24 ($P<0.05$) h of its administration. The plant-induced diuresis comparable to that of urea (960 mg/kg) and was almost double that of the control animal's urine output. The diuresis was not associated with changes in sodium and/or potassium excretion[100].

The diuretic activity of aqueous and 80% methanol extracts of *Foeniculum vulgare* Mill. (Apiaceae) leaf was evaluated in rats using different doses of aqueous or 80% methanol extract (100, 200 and 400 mg/kg) orally. Rats treated with 200 and 400 mg/kg doses of aqueous and 80% methanol extract of *Foeniculum vulgare* showed an increased urine volume ($p<0.001$). However, 100 mg/kg dose of both extracts failed to produce significant increase in 24 h urine volume compared to control groups. Both extracts increased natriuresis, kaliuresis and chloriuresis ($p<0.001$) at the middle and higher doses[101-102].

Glossostemon bruguieri

Glossostemon bruguieri powder and its alcoholic extract together with four of the purified compounds (takakin 7-0-glucoside, isosctullarien, its 7-0 –glucoside and takakin 8-0-glucoside) were shown to increase urine volume but not sodium on albino rats, being more pronounced and equipotent with that of the standard drug, furosemide [103].

***Gossypium* species**

The diuretic activity of ethyl acetate and alcohol extract of *Gossypium herbaceum* Linn leaves (100 and200 mg/kg body weight) was investigated in male wistar albino rats. The total urine volumes of the both extracts (200mg/kg) treated rats were elevated nearly two folds compared with the control. Excretion of sodium, potassium and chloride ions were increased significantly compared with control group. The diuretic effect was comparable with that of the standard drug Frusemide, however, alcoholic extract showed more significant diuretic activity compared with the ethyl acetate extract as a diuretic. The increase of sodium and potassium in the urine of the group treated with both extracts was dose dependent[104-105].

Hibiscus rosa-sinensis

The effect of aqueous extract of *Hibiscus rosa-sinensis* on urinary volume and electrolyte extraction was studied in albino rats. Aqueous extract was administered in100, 200, 400 and 600 mg/kg doses orally. Urinary volume, total Na^+ , K^+ , Cl^- concentrations were estimated at 5^{th} & 24^{th} hr and compared with control group. Aqueous extract of *Hibiscus rosa-sinensis* increased the urinary volume of the 5^{th} and 24^{th} hr samples. Na^+ and Cl^- excretion were also significantly increased in 200 and 400 mg/kg doses[106].

Hibiscus sabdariffa

The diuretic activity of Hibiscus sabdariffa aqueous extract was evaluated on in vivo and in situ models. The aqueous extract was administrated in increasing doses and the diuresis produced and disposal of electrolytes

were evaluated. The renal filtration rate with plant extract, furosemide and amiloride were evaluated in isolated kidney. The diuretic and natriuretic effect of Hibiscus sabdariffa aqueous extract showed a dose-dependent behavior. The pharmacological constants of natriuretic effect was ED_{50} = 86 mg/kg and Emax = 0.9 mEq/100 g/5 h. In the in vitro model, renal filtration was increased 48% with the aqueous extract of Hibiscus sabdariffa and an additive effect was recorded when Hibiscus sabdariffa aqueous extract was perfused with furosemide[107].

The diuretic, natriuretic, and potassium sparing effects of Hibiscus sabdariffa are due in part to the modulation of aldosterone activity by the presence of compounds potentially responsible for this modulation, as anthocyanins, flavonoids, and chlorogenic acid[108].

Juniperus communis

A 10% aqueous infusion of juniper, 0.1% aqueous solution of juniper oil (with 0.2% of Tween 20 solubilizer) and 0.01% aqueous solution of terpinen-4-ol were orally administered to rats at 5ml/100g bw to determine the effect on urine output. Compared to water, the 10% aqueous infusion of juniper and the 0.1% aqueous solution of juniper oil caused reductions of only 6% in diuresis over a 24-hour period, equivalent to the effect of 0.004 IU/100g of ADH, while the 0.01% solution of terpinen-4-ol caused a reduction of 30% in diuresis ($p<0.01$), equivalent to 0.4 IU/100g intraperitoneal of ADH. Continued daily administration at the same daily dose level, the two juniper preparations and terpinen-4-ol stimulated diuresis on days two and three, although only the 10% aqueous infusion of juniper exerted significant diuretic activity (+ 43% on day two; +44% on day three; $p<0.05$), suggesting that the diuretic effect is partly due to the essential oil and partly to hydrophilic constituents[109].

However, oral administration of lyophilized aqueous extract of juniper at 1000mg/kg bw to rats, it didnt increase urine volume or excretion of Na^+, K^+ or Cl^- ions over a six-hour period compared to the effect of the same volume of water[110].

II. CONCLUSION:

The current review discussed the medicinal plants with antiurolithiatic and diuretic effects as promising herbal drugs because of their safety and effectiveness.

REFERENCES:

[1]. Smith DR, Tanagho EA and McAninch JW. Smith's general urology. Lange Medical Books/McGraw-Hill 2008.

[2]. Shukla AK. et al. A review on anti-urolithiatic activity of herbal folk plants. Asian Journal of Biomaterial Research 2017; 3(2):1-11.

[3]. Karadi RV, Gadgeb NB, Alagawadi KR and Savadi RV. Effect of *Moringa oleifera* L. root-wood on ethylene glycol induced urolithiasis in rats. J Ethnopharmacol 2006; 105: 306-311.

[4]. Divakar K, Pawar AT, Chandrasekhar SB, Dighe SB and Divakar G; Protective effect of the hydro-alcoholic extract of *Rubia cordifolia* roots against ethylene glycol induced urolithiasis in rats. Food Chem Toxicol 2010; 1013-1018.

[5]. Selvam R, Kalaiselvi P, Govindaraj A, Murugan VM and Satish Kumar AS, Effect of *A. lanata* leaf extract and *Vediuppu chunnam* on the urinary risk factors of calcium oxalate urolithiasis during experimental hyperoxaluria. Pharmacology Res 2001; 43: 89-93.

[6]. Aggarwal S, Tandon S, Singla SK and Tandon C. Reduction of oxalate induced renal tubular epithelial cell (NRK-52) injury and inhibition of calcium oxalate crystallization in vitro by aqueous extract of *Achyrenthes aspera*. Int J Green Pharm 2010; 4:159-164.

[7]. Bahuguna YM, Rawat MSM, Juyal V and Gusain K. Evaluation of Pyracantha crenulata Roem for antiurolithogenic activity in albino rats. Afr J Urol 2010; 15: 159-166.

[8]. Toblli JE, Ferder L, Stella I, De Cavanagh MVE, Angerosa M and Inserra F. Effects of angiotensin II subtype 1 receptor blockade by losartan on tubulointerstitial lesions caused by hyperoxaluria. J. Urol., 2002; 168: 1550-1555.

[9]. Patel RK, Patel SB and Shah JG. Anti-urolithiatic activity of ethanolic extract of seeds of *Benincasa hispida* (Thumb). Pharmacologyonline 2011; 3: 586-591.

[10]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Adiantum capillus-veneris* - A review. Asian Journal of Pharmaceutical Science and Technology 2015; 5(2): 106-111.

[11]. Ahmed A, Jahan N, WadudA, Bilal A and HajeraS. In vitro effect of hydro alcoholic extract of *Adiantum capillus-veneris* Linn. on calcium oxalate crystallization. International journal of Green Pharmacy 2013; 7(2): 106-110.

[12]. Ahmed SA. Antilithiasic activity of parsiaoshan in experimental models (dissertation). National Institute of Unani Medicine Rguhs, Bangalore, 2012.

[13]. Ahmed A, Wadud A, Jahan N, Bilal A and Hajera S. Efficacy of *Adiantum capillus veneris* Linn in chemically induced urolithiasis in rats. J Ethnopharmacol 2013; 146(1): 411-416.
[14]. Parameshwar P, RaoY N, Naik, V and Reddy S H. Evaluation of antilithiatic activity of *Adonis aestivalis* Linn. In male Wister rats. Der Pharmacia Lettre 2011; 3(2): 104-107
[15]. Al-Snafi AE. *Adonis aestivalis*: pharmacological and toxicological activities- A review. Asian Journal of Pharmaceutical Science & Technology 2016; 6(2): 96-102.
[16]. Giachetti D, Taddei E and Taddei I.Ricerchesull' attivitadiureticae duricosurica di *Agrimonia eupatoria*. Boll SocItal BiolSper 1986; 62: 705-711.
[17]. Al-Snafi AE. The pharmacological and therapeutic importance of *Agrimonia eupatoria*- A review. Asian Journal of Pharmaceutical Science and Technology 2015; 5(2): 112-117.
[18]. Grases F, Ramis M, Costa-Bauza A and March JC. Effect of *Herniaria hirsute* and *Agropyron repens* on calcium oxalateurolithiasis risk in rat. *Journal* Ethnopharmacology 1995; 45: 211-214.
[19]. Ahmadi M, Rad AK, Rajaei Z, Hadjzadeh M, Mohammadian N, and Tabasi NS. *Alcea rosea* root extract as a preventive and curative agent in ethylene glycol-induced urolithiasis in rats. Indian Journal of Pharmacology 2012; 44(3): 304-307.
[20]. Al-Snafi AE. The Pharmaceutical importance of *Althaea officinalis* and *Althaea rosea*: A Review. Int J Pharm Tech Res 2013; 5(3):1387-1385.
[21]. Prasad K V, Bharathi K and Srinivasan K K. Evaluation of *Ammannia baccifera* Linn. for antiurolithic activity in albino rats. Indian J Exp Biol 1994; 32(5): 311-313.
[22]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Ammannia baccifera* - A review. International Journal of Pharmacy 2015; 5(1): 28-32.
[23]. Vanachayangkul P. *Ammi visnaga* L. for prevention of urolithiasis. PhD Thesis, Florida University, 2008.
[24]. Al-Snafi AE. Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review. International Journal of Pharmacy and Industrial Research 2013; 3(3):257-265.
[25]. Vanachayangkul P, Chow N, Khan SR and Butterweck V. Prevention of renal crystal deposition by an extract of *Ammi visnaga* L. and its constituents khellin and visnagin in hyperoxaluric rats. Urol Res 2011; 39(3): 189-195.
[26]. Khan ZA, Assiri, AM, Al-Afghani HMA and Maghrabi JMA Inhibition of oxalate nephrolithiasis with Ammi visnaga (Al-Khillah) Int. Urol Nephrol 2001; 33: 605-608.
[27]. Al-Jawad FH, Al-Razzuqi RA and Al-Jeboori AA. *Apium graveolens* accentuates urinary Ca^{+2} excretions in experimental model of nephrocalcinosis. International Journal of Green Pharmacy 2011; 5(2):100-102.
[28]. Al-Snafi AE. The Pharmacology of *Apium graveolens*- A review. International Journal for Pharmaceutical Research Scholars 2014; 3(1-1): 671-677.
[29]. Jagannath N, Chikkannasetty SS, Govindadas D and Devasankaraiah G. Study of antiurolithiatic activity of Asparagus racemosus on albino rats. Indian J Pharmacol 2012;44(5):576-579.
[30]. Jayasree T, Kishore KK, Vinay M, Vasavi P, Dixit R, Rajanikanth M and Manohar V S. Diuretic effect of the chloroform extract of the *Benincasa hispida* rind (Pericarp) extract in Sprague-Dawley rats. International Journal of Applied Biology and Pharmaceutical Technology 2011; 2(2): 94-99.
[31]. Al-Snafi AE. The Pharmacological Importance of *Benincasa hispida*. A review. Int Journal of Pharma Sciences and Research 2013; 4(12): 165-170.
[32]. Lin WC, Lai MT, Chen HY, Ho CY, Man KM, Shen JL, Lee YJ, Tsai FJ, Chen YH and Chen WC. Protective effect of Flos carthami extract against ethylene glycol-induced urolithiasis in rats. Urol Res 2011; 40(6): 655-661.
[33]. Al-Snafi AE. The chemical constituents and pharmacological importance of *Carthamus tinctorius* - An overview. Journal of Pharmaceutical Biology 2015; 5(3): 143-166.
[34]. Divya S and Banda T. Evaluation of anti-diuretic and anti-nephrolithiatic activities of ethanolic seeds extract of *Cicer arietinum* in experimental rats. IJPRD 2014; 5(12): 9-12.
[35]. Al-Snafi AE. The medical Importance of *Cicer arietinum* - A review. IOSR Journal of Pharmacy 2016; 6(3): 29-40.
[36]. Upmanyu G, Tanu M, GuptaM,Gupta AK, Sushma A, and Dhakar RC. Acute toxicity and diuretic studies of leaves of *Clerodendrum inerme.* Journal of Pharmacy Research 2011; 4(5):1431-1432.
[37]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Clerodendrum inerme*- A review. SMU Medical Journal 2016; 3(1): 129-153.
[38]. Piala JJ, Madissoo H and Rubin B. Diuretic activity of roots of *Clitoria ternatea* L. in dogs. Experientia 1962; 18(2): 89.
[39]. Al-Snafi AE. Pharmacological importance of *Clitoria ternatea* – A review. IOSR Journal of Pharmacy 2016; 6(3): 68-83.

[40]. Sharma V and Verma P. *Convolvulus arvensis* L. root extracts increase urine output and electrolytes in rats. International Journal of Pharmaceutical Research & Development 2011; 3(3): 193-197.
[41]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia*- A review. IOSR Journal of Pharmacy 2016; 6(6): 64-75.
[42]. Aissaoui A, El-Hilaly J, Israili ZH and Lyoussi B. Acute diuretic effect of continuous intravenous infusion of an aqueous extract of *Coriandrum sativum* L. in anesthetized rats. J Ethnopharmacol 2008; 115(1): 89-95.
[43]. Al-Snafi AE. A review on chemical constituents and pharmacological activities of *Coriandrum sativum*. IOSR Journal of Pharmacy 2016; 6(7): 17-42.
[44]. Shariatifar N, Shoeibi S, Sani MJ, Jamshidi AH, Zarei A, Mehdizade A and Dadgarnejad M. Study on diuretic activity of saffron (stigma of *Crocus sativus* L.) aqueous extract in rat. J Adv Pharm Technol Res 2014; 5(1): 17-20.
[45]. Al-Snafi AE. The pharmacology of *Crocus sativus*- A review. IOSR Journal of Pharmacy 2016; 6(6): 8-38.
[46]. Shivalinge Gowda KP, Satish S, Mahesh CM and Kumar V. Study on the diuretic activity of *Cynodon dactylon* root stalk extract in albino rats. Research J Pharm and Tech 2009; 2(2): 338-340.
[47]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Cynodon dactylon*- A review. IOSR Journal of Pharmacy 2016; 6(7): 17-31.
[48]. Sadki C, Hacht B, Souliman A and Atmani F. Acute diuretic activity of aqueous *Erica multiflora* flowers and *Cynodon dactylon* rhizomes extracts in rats. J Ethnopharmacol 2010; 128(2): 352-356.
[49]. Aruna D, Chakarvarthy K and Sarath Babu K. Evaluation of diuretic activity of *Cynodon dactylon* in rats with comparison of hydrochlorothiazide. International Journal of Research in Pharmaceutical and Biomedical Sciences 2013; 4(2): 471-474.
[50]. Aruna D, Chakarvarthy K and Sarath Babu K. Diuretic efficacy of *Cynodon dactylon* on guinea pigs with comparison of medium efficacy. International Journal of Bioassays 2013; 2 (3): 500-502.
[51]. Golla U, Gajam PK and Bhimathati SS. Evaluation of diuretic and laxative activity of hydro-alcoholic extract of Desmostachya bipinnata (L.) Stapf in rats. Integr Med. 2014; 12(4): 372-378.
[52]. Al-Snafi AE. Pharmacological and therapeutic importance of *Desmostachya bipinnata*- A review. Indo Am J P Sci 2017; 4(01): 60-66.
[53]. Deoda RS, Pandya H, Patel M, Yadav KN, Kadam PV and Patil MJ. Antilithiatic activity of leaves, bulb and stem of *Nymphea odorata* and *Dolichos lablab* Beans. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2012; 3(1): 814-819.
[54]. Al-Snafi AE. The pharmacology and medical importance of *Dolichos lablab* (*Lablab purpureus*)- A review. IOSR Journal of Pharmacy 2017; 7(2): 22-30.
[55]. Carneiro DM, Freire RC, Honório TC, Zoghaib I, Cardoso FFS, Tresvenzol LMF, Paula JR, Sousa ALL, Jardim PCBV and Cunha LC. Randomized, double-blind clinical trial to assess the acute diuretic effect of *Equisetum arvense* (field horsetail) in healthy volunteers. Evidence-Based Complementary and Alternative Medicine 2014, http://dx.doi.org/10.1155/2014/760683
[56]. Al-Snafi AE. The pharmacology of Equisetum arvense- A review. IOSR Journal of Pharmacy 2017; 7(2): 31-42.
[57]. Johnson PB, Abdurahman EM, Tiam EA, Abdu-Aguye I and Hussaini IM. Euphorbia hirta leaf extracts increase urine output and electrolytes in rats. J Ethnopharmac 1999; 65(1): 63-69.
[58]. Al-Snafi AE. Pharmacology and therapeutic potential of *Euphorbia hirta* (Syn: *Euphorbia pilulifera*) - A review. IOSR Journal of Pharmacy 2017; 7(3): 7-20.
[59]. Tanira, MOM et al. Pharmacological and toxicological investigations on *Foeniculum vulgare* dried fruit extract in experimental animals. Phytother Res 1996; 10: 33-36.
[60]. Jemal A. Evaluation of the diuretic activity of aqueous and 80% methanol extracts of *Foeniculum vulgare* Mill (Apiaceae) leaf in rats. MSc Thesis, Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University, Ethiopia 2015.
[61]. El-Sayed NH, Awaad AS and Mabry TJ. Phytochemical studies and effect on urine volume of *Glossostemon bruguieri* Desf. constituents. Indian Journal of Experimental Biology 2004; 42: 186-189.
[62]. Narasimha DK, Reddy KR, Jayaveera KN, Bharathi T, Vrushabendra S and Rajkumar BM. Study on the diuretic activity of *Gossypium herbaceum* Linn leaves extract in albino rats. Pharmacologyonline 2008; 1: 78-81.
[63]. Atmani F, Slimani Y, Mimouni M, Aziz M, Hacht B and Ziyyat, A. Effect of aqueous extract from *Herniaria hirsuta* L. on experimentally nephrolithiasic rats. J Ethnopharmacol 2004; 95(1): 87-93.
[64]. Al-Snafi AE. Pharmacological importance of *Herniaria glabra* and *Herniaria hirsuta* - A review. Indo Am J P Sc 2018; 5 (4): 2167-2175.

[65]. Grases F, Ramis M, Costa-Bauzá A and March JG. Effect of Herniaria hirsuta and Agropyron repens on calcium oxalate urolithiasis risk in rats. J Ethnopharmacol 1995;45(3):211-214.
[66]. Atmani F and Khan SR. Effects of an extract from Herniaria hirsuta on calcium oxalate crystallization in vitro. BJU Int 2000;85(6):621-625.
[67]. Atmani F, Slimani Y, Mimouni M, Hacht B: Prophylaxis of calcium oxalate stones by Herniaria hirsuta on experimentally induced nephrolithiasis in rats. BJU Int 2003; 92: 137-140.
[68]. Meiouet F, El Kabbaj S and Daudon M. In vitro study of the litholytic effects of herbal extracts on cystine urinary calculi. Prog Urol 2011;21(1):40-47.
[69]. Atmani F, Farell G and Lieske JC. Extract from Herniaria hirsuta coats calcium oxalate monohydrate crystals and blocks their adhesion to renal epithelial cells. J Urol 2004;172(4 Pt 1):1510-1514.
[70]. Atmani F, Slimani Y, Mbark Addi N, Bnouham M and Ramdani A. In Vitro and in Vivo Antilithiasic Effect of Saponin Rich Fraction Isolated From Herniaria hirsuta . J Bras Nefrol 2006; 28(4):199-203.
[71]. Nirmaladevi R, Kalpana S, Kavitha D and Padma PR. Evaluation of antilithiatic potential of *Hibiscus rosa-sinensis* Linn, in vitro. Journal of Pharmacy Research 2012; 5(8): 4353-4356.
[72]. Alarcón-Alonso J, Zamilpa A, Aguilar FA, Herrera-Ruiz M, Tortoriello J and Jimenez-Ferrer E. Pharmacological characterization of the diuretic effect of Hibiscus sabdariffa Linn (Malvaceae) extract. Journal of Ethnopharmacology2011; 139(3}: 751-756.
[73]. Jiménez-Ferrer E, Alarcón-Alonso J, Aguilar-Rojas A, Zamilpa A, Jiménez-Ferrer C I, Tortoriello J and Herrera-Ruiz M. Diuretic effect of compounds from Hibiscus sabdariffa by modulation of the aldosterone activity. Planta Med 2012; 78(18): 1893-1898.
[74]. Stanic G, Samarzija I and Blazevic N. Time-dependent diuretic response in rats treated with juniper berry preparations. Phytother Res 1998; 12: 494-497.
[75]. Al-Snafi AE. Medical importance of *Juniperus communis* - A review. Indo Am J P Sc 2018; 5(3): 1979-1792.
[76]. Lasheras B et al. Etude pharmacologique preliminaire de Prunus spinosa L. Amelanchier ovalis Medikus, Juniperus communis L. et Urtica dioica L Plant Med Phytother 1986; 20:219-226.
[77]. Mandana Rodriguez A and GausaRull P. Therapeutic effects of *Quercus* extract in 78- Abdul Aziz S, See TL, Khuay LY, Osman K, and Abu Bakar MA. In Vitro effects of *Plantago major* extract on urolithiasis. Malays J Med Sci 2005; 12(2): 22–26.
[78]. Kishore DV, Moosavi F and Varma RK. Effect of ethanolic extract of *Portulaca oleracea* on ethylene glycol and ammonium induced urolithiasis. International Journal of Pharmacy and Pharmaceutical Sciences 2012; 5(2): 134-140.
[79]. Rathod NR, Biswas D, Chitme HR, Ratna S, Muchandi ISand Chandra R. Anti-urolithiatic effects of *Punica granatum* in male rats. J Ethnopharmacol 2012; 140(2): 234-238.
[80]. Pawar AT, Gaikwad GD, Metkari KS, Tijore KA, Ghodasara V and Kuchekar BS. Effect of *Terminalia chebula* fruit extract on ethylene glycol induced urolithiasis in rats. Biomedicine and Aging Pathology 2012; 2(3): 99-103.
[81]. KapaseCU ,Bodhankar SL, Mohan V and Thakurdesai PA. Therapeutic effects of standardized fenugreek seed extract on experimental urolithiasis in rats. Journal of Applied Pharmaceutical Science 2013; 3(9): 029-035.
[82]. Livero FA, Menetrier JV, Lourenco ELB and Junior AG. Cellular and molecular mechanisms of diuretic plants: an overview. Curr Pharm Des 2017;23(8):1247-1252.
[83]. Bermuda grass is evil,bermuda grass is bug. https://www.mdidea.com/products/ proper/proper079.html
[84]. Jayasree T, Kishore KK, Vinay M, Vasavi P, Dixit R, Rajanikanth M and Manohar V S. Diuretic effect of the chloroform extract of the *Benincasa hispida* rind (Pericarp) extract in Sprague-Dawley rats. International Journal of Applied Biology and Pharmaceutical Technology 2011; 2(2): 94-99.
[85]. Divya S and Banda T. Evaluation of anti-diuretic and anti-nephrolithiatic activities of ethanolic seeds extract of *Cicer arietinum* in experimental rats. IJPRD 2014; 5(12): 9-12.
[86]. Honow R, Laube N, Schneider A, Kessler T and Hesse A. Influence of grapefruit, orange, and apple-juice consumption on urinary variables and risk of crystallization. Br J Nutr 2003; 90: 295-300.
[87]. Al-Snafi AE. Nutritional value and pharmacological importance of citrus species grown in Iraq. IOSR Journal of Pharmacy 2016; 6(8): 76-108.
[88]. Upmanyu G, Tanu M, GuptaM,Gupta AK, Sushma A, and Dhakar RC. Acute toxicity and diuretic studies of leaves of *Clerodendrum inerme.* Journal of Pharmacy Research 2011; 4(5):1431-1432.
[89]. Piala JJ, Madissoo H and Rubin B. Diuretic activity of roots of *Clitoria ternatea* L. in dogs. Experientia 1962; 18(2): 89.
[90]. Sharma V and Verma P. *Convolvulus arvensis* L. root extracts increase urine output and electrolytes in rats. International Journal of Pharmaceutical Research & Development 2011; 3(3): 193-197.

[91]. Aissaoui A, El-Hilaly J, Israili ZH and Lyoussi B. Acute diuretic effect of continuous intravenous infusion of an aqueous extract of *Coriandrum sativum* L. in anesthetized rats. J Ethnopharmacol 2008; 115(1): 89-95.
[92]. Shariatifar N, Shoeibi S, Sani MJ, Jamshidi AH, Zarei A, Mehdizade A and Dadgarnejad M. Study on diuretic activity of saffron (stigma of *Crocus sativus* L.) aqueous extract in rat. J Adv Pharm Technol Res 2014; 5(1): 17-20.
[93]. Shivalinge Gowda KP, Satish S, Mahesh CM and Kumar V. Study on the diuretic activity of *Cynodon dactylon* root stalk extract in albino rats. Research J Pharm and Tech 2009; 2(2): 338-340.
[94]. Sadki C, Hacht B, Souliman A and Atmani F. Acute diuretic activity of aqueous *Erica multiflora* flowers and *Cynodon dactylon* rhizomes extracts in rats. J Ethnopharmacol 2010; 128(2): 352-356.
[95]. Aruna D, Chakarvarthy K and Sarath Babu K. Evaluation of diuretic activity of *Cynodon dactylon* in rats with comparison of hydrochlorothiazide. International Journal of Research in Pharmaceutical and Biomedical Sciences 2013; 4(2): 471-474.
[96]. Aruna D, Chakarvarthy K and Sarath Babu K. Diuretic efficacy of *Cynodon dactylon* on guinea pigs with comparison of medium efficacy. International Journal of Bioassays 2013; 2 (3): 500-502.
[97]. Golla U, Gajam PK and Bhimathati SS. Evaluation of diuretic and laxative activity of hydro-alcoholic extract of Desmostachya bipinnata (L.) Stapf in rats. Integr Med. 2014; 12(4): 372-378.
[98]. Johnson PB, Abdurahman EM, Tiam EA, Abdu-Aguye I and Hussaini IM. Euphorbia hirta leaf extracts increase urine output and electrolytes in rats. J Ethnopharmac 1999; 65(1): 63-69.
[99]. Tanira, MOM et al. Pharmacological and toxicological investigations on *Foeniculum vulgare* dried fruit extract in experimental animals. Phytother Res 1996; 10: 33-36.
[100]. Jemal A. Evaluation of the diuretic activity of aqueous and 80% methanol extracts of *Foeniculum vulgare* Mill (Apiaceae) leaf in rats. MSc Thesis, Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University, Ethiopia 2015.
[101]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Foeniculum vulgare* - A review. IOSR Journal of Pharmacy 2018; 8(5): 81-96.
[102]. El-Sayed NH, Awaad AS and Mabry TJ. Phytochemical studies and effect on urine volume of *Glossostemon bruguieri* Desf. constituents. Indian Journal of Experimental Biology 2004; 42: 186-189.
[103]. Narasimha DK, Reddy KR, Jayaveera KN, Bharathi T, Vrushabendra S and Rajkumar BM. Study on the diuretic activity of *Gossypium herbaceum* Linn leaves extract in albino rats. Pharmacologyonline 2008; 1: 78-81.
[104]. 105-Al-Snafi AE. Chemical constituents and pharmacological activities of *Gossypium herbaceum* and *Gossypium hirsutum* - A review. IOSR Journal of Pharmacy 2018; 8(5): 64-80.
[105]. Jena M, Mishra S and Mishra SS. Effect of aqueous extract of Hibiscus rosa-sinensis Linn on urinary volume and electrolyte extraction in albino rats. Int J Pharm Bio Sci 2013; 4(3): 304 – 309.
[106]. Alarcón-Alonso J, Zamilpa A, Aguilar FA, Herrera-Ruiz M, Tortoriello J and Jimenez-Ferrer E. Pharmacological characterization of the diuretic effect of Hibiscus sabdariffa Linn (Malvaceae) extract. Journal of Ethnopharmacology2011; 139(3}: 751-756.
[107]. Jiménez-Ferrer E, Alarcón-Alonso J, Aguilar-Rojas A, Zamilpa A, Jiménez-Ferrer C I, Tortoriello J and Herrera-Ruiz M. Diuretic effect of compounds from Hibiscus sabdariffa by modulation of the aldosterone activity. Planta Med 2012; 78(18): 1893-1898.
[108]. Stanic G, Samarzija I and Blazevic N. Time-dependent diuretic response in rats treated with juniper berry preparations. Phytother Res 1998; 12: 494-497.
[109]. Lasheras B et al. Etude pharmacologique preliminaire de Prunus spinosa L. Amelanchier ovalis Medikus, Juniperus communis L. et Urtica dioica L Plant Med Phytother 1986; 20:219-226.

Prof Dr Ali Esmail Al-Snafi " Arabian medicinal plants with antiurolithiatic and diuretic effects - plant based review (Part 1). ” IOSR Journal of Pharmacy (IOSRPHR), vol. 8, no. 06, 2018, pp. 67-80.