A REVIEW ON ANTI-UROLITHIATIC ACTIVITY OF MEDICINAL PLANTS

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INTRODUCTION

Urinary system:

The Urinary System is a group of organs in the body concerned with filtering out excess fluid and other substances from the bloodstream. The Urinary system includes the following:

- Two kidneys responsible for formation of urine.
- Two ureters responsible for the transport of urine to urinary bladder from kidney.
- Urinary bladder temporary store-house of urine and urethra.

The Urinary system works with the other systems of the body to maintain homeostasis. The kidneys are the main organs of homeostasis because they maintain the acid base balance and the water salt balance of the blood [1].

Kidneys:

The paired kidneys are reddish, bean-shaped organs located just above the waist between the peritoneum and the posterior wall of abdomen. Because their position is posterior to the peritoneum of the abdomen cavity, they are said to be retroperitoneal organs. The kidneys are located between the levels of the last thoracic and third lumbar vertebrae, a position where they are partially protected by the eleventh and twelfth pairs of ribs.

- **External anatomy of kidney:**

Each kidney is 10-12 cm (4-5 in.) long, 5-7 cm (2-3 in.) wide, and 3 cm (1 in.) thick. The lateral surface of the kidney is convex. The medial surface is concave and has a vertical cleft called the renal hilum. The ureters, renal
blood vessels, lymphatic, and nerves all join each kidney at the hilum. A top each kidney is an adrenal (or suprarenal) gland, an endocrine gland that is functionally unrelated to the kidney.

Three layers of supportive tissue was surrounded to each kidney, they are:

1. The deep layer, the renal capsule, is a smooth, transparent sheet of dense irregular connective tissue. It serves as a barrier against trauma and helps to maintain the shape of the kidney.
2. The middle layer, the adipose capsule, is a mass of fatty tissue surrounding the renal capsule. It protects the kidney from trauma and holds it firmly in place within the abdominal cavity.
3. The superficial layer, the renal fascia, is another thin layer of dense irregular connective tissue that anchors the kidney to the surrounding structures and to the abdominal wall. On the anterior surface of kidneys, the renal fascia is deep to the peritoneum.

Renal Vein

The renal veins are veins that drain the kidney. They connect the kidney to the inferior vena cava. Because the inferior vena cava is on the right half of the body, the left renal vein is generally the longer of the two. Unlike the right renal vein, the left renal vein often receives the left gonadal vein (left testicular vein in males, left ovarian vein in females). It frequently receives the left suprarenal vein as well.

Renal Artery

The renal arteries normally arise off the abdominal aorta and supply the kidneys with blood. The arterial supplies of the kidneys are variable and there may be one or more renal arteries supplying each kidney. Due to the position of the aorta, the inferior vena cava and the kidneys in the body, the right renal artery is normally longer than the left renal artery. The right renal artery normally crosses posterior to the inferior vena cava. The renal arteries carry a large portion of the total blood flow to the kidneys. Up to a third of the total cardiac output can pass through the renal arteries to be filtered by the kidneys.

Ureters

The ureters are two tubes that drain urine from the kidneys to the bladder. Each ureter is a muscular tube about 10 inches (25 cm) long. Muscles in the walls of the ureters send the urine in small spurts into the bladder (a collapsible sac found on the forward part of the cavity of the bony pelvis that allows temporary storage of urine). After the urine enters the bladder from the ureters, small folds in the bladder mucosa act like valves preventing backward flow of the urine [2].
A renal lobe consists of a renal pyramid, its overlying area of renal cortex, and one-half of each adjacent renal column. Together, the renal cortex and renal pyramids of the renal medulla constitute the parenchyma (functional portion) of the kidney. Within the parenchyma, the functional units of the kidney, about 1 million microscopic structures called nephrons are present. Urine formed by the nephrons drains into large papillary ducts, which extend through the renal papillae of the pyramids. The papillary ducts drain into cup like structures called minor and major calyces. Each kidney has 8 to 18 minor calyces and 2 or 3 major calyces. A minor calyx receives urine from the papillary ducts of one renal papilla and delivers it to a major calyx. From the major calyces, urine drains into a single large cavity called the renal pelvis and then out through the ureters to the urinary bladder. The hilum expands into a cavity within the kidney called the renal sinus, which contains part of the renal pelvis, the calyces and branches of the renal blood vessels and nerves. Adipose tissue helps stabilize the position of these structures in the renal sinus.

Each nephron consists of the following Parts:
- Glomerulus
- Bowman’s capsule
- Proximal tubule
- Loop of henle
- Distal tubule
- Collecting duct

Nephrons

A nephron is the basic structural and functional unit of the kidney. The chief function is to regulate water and soluble substances by filtering the blood, reabsorbing what needed and excreting the rest as urine. Nephrons eliminate wastes from the body, regulate blood volume and pressure, control levels of electrolytes and metabolites, and regulate blood pH. Its functions are vital to life and are regulated by the endocrine system by hormones such as anti diuretic hormone, aldosterone, and parathyroid hormone [2].

Functions of Kidney:
- Regulation of blood ionic composition - The kidneys helps to regulate the blood levels of several ions, most importantly sodium ions, potassium ions, calcium ions chloride ions and phosphate ions.
- Regulation of blood pH - The kidneys excretes a variable amount of hydrogen ions into the urine and conserves bicarbonate ions, which are an important buffer of pH in the blood. Both of these activities help to regulate blood PH.
- Regulation of blood volume - The kidneys adjusts blood volume by conserving or eliminating water in the urine.
- Regulation of blood pressure - The kidneys also helps to regulate blood pressure by secreting the enzyme rennin, which activates the rennin-angiotensin-aldosterone pathway Increased renin causes an increase in blood pressure.
- Maintenance of blood osmolarity - By separately regulating loss of water and loss of solutes in the urine, the kidneys maintain a relatively constant blood osmolarity close to 300 milliosmoles per litre (mOsm/liter).
- Production of hormones - The kidneys produces two hormones. Calcitriol, the active form of vitamin D, helps to regulate calcium homeostasis, and erythropoietin which stimulates the production of red blood cell.
Formation of Urine [3]:

Urine is formed in three steps: Filtration, Reabsorption, and Secretion.

Filtration: It is a largely passive process where a portion of the blood passes from the glomerular bed into the glomerular capsule. The filtrate then enters the proximal convoluted tubule, where tubular reabsorption and secretion begin.

Tubular reabsorption: It occurs when the filtrate components move through the tubule cells and return to the blood in the peritubular capillaries. Some of the reabsorption is passive, but the reabsorption of most substances depends on active transport processes.

Tubular secretion: It is the reverse process of tubular reabsorption. This process is important for the disposal of substances not already in the filtrate (drug metabolites, etc) and as a way for controlling blood pH.

General characteristics of urine (http://www.ivyrose.co.uk):

Volume: The average, normal volume is approximately 1000 ml to 2000 ml per day.

Physical characteristics of urine

Colour: yellow or amber but can vary considerably with diet

Turbidity: transparent when freshly voided but becomes turbid (cloudy) upon standing

pH: Range from 4.6-8.0, and varies considerably with the diet

Specific gravity: 1.001 to 1.035

Chemical composition of urine

Urine is approximately 95% of water and the other components of normal urine are the solutes that are dissolved in the water component of the urine. These solutes can be divided into two categories according to their chemical structure (e.g. size and electrical charge).

Organic molecules

These are electrically neutral and can be relatively large

These include:

Urea - Urea is an organic (i.e. carbon-based) compound. It is also known as carbamide. Urea is derived from ammonia and produced by the deamination of amino acids. The amount of urea in urine is related to quantity of dietary protein.

Creatinine - Creatinine is a normal (healthy) constituent of blood. It is produced mainly as a result of the breakdown of creatinine phosphate in muscle tissue. It is usually produced by the body at a fairly constant rate (which depends on the muscle mass of the body).

Uric acid - Uric acid is an organic (i.e. carbon-based) compound. Due to its insolubility, uric acid has a tendency to crystallize, and is a common part of kidney stones.

Other substances/molecules

Example of other substances that may be found in small amounts in normal urine include carbohydrates, enzymes, fatty acids, hormones, pigments, and mucins (a group of large, heavily glycosylated proteins found in the body).

Individual elements: These include,

Sodium (Na⁺) and Potassium - Amount in urine arise with diet and the amount of aldosterone (a steroid hormone) in the body.

Chloride (Cl⁻) - Amount in urine varies with dietary intake (chloride is a part of common salt, NaCl).

Magnesium - Amount in urine varies with the diet and the parathyroid hormone in the body. (Parathyroid hormone increases the reabsorption of magnesium in the body which therefore decrease the quantity of magnesium in urine).

Calcium (Ca²⁺) – amount in urine varies with diet and the amount of parathyroid hormone in the body (parathyroid hormone increases the reabsorption of calcium in the body which therefore decrease the quantity of calcium in urine).

Small groups formed from a few different elements:

Ammonium (NH₄⁺) – the amount of ammonium produced by the kidneys may vary according to the pH of the blood and tissues in the body.

Sulphates (SO₄²⁻) – the quantity of sulphates excreted in urine varies according to the quantity and type of protein in the person’s diet.
Phosphates ($\text{PO}_4^{3-}$) – amount in urine varies with the amount of parathyroid hormone in the body (parathyroid hormone increases the quantity of phosphates in urine).

Abnormal Constituents of Urine:

**Glucose** - Recent intake of sugary foods, diabetes mellitus

**Protein** - Physical exertion, high protein; hypertension, glomerulonephritis

**Ketone bodies** - Starvation, untreated diabetes mellitus

**Haemoglobin** - Haemolytic anaemia, severe burns

**Bile pigments** - Hepatitis, cirrhosis, bile obstruction

**Erythrocytes** - Bleeding due to trauma, kidney stones, infection, cancer

**Leucocytes** - Urinary tract infection

d. Diseases or disorder of kidney:

**Cystitis**: Inflammation of the urinary bladder caused by bacteria

**Diabetes insipidus**: It is the excessive urination of water due to lack of anti diuretic hormone (ADH)

**Glomerulonephritis**: Inflammation of the glomeruli, is caused by a bacterial infection

**Incontinence**: It is the ability to control urination. It may be caused by aging, pregnancies, or prostate surgery.

**Kidney stones**: These are developed in the renal pelvis or calyces. Predisposing factors for kidney stones include dehydration, infection, obstruction, and genetics.

**Renal failure**: It is the sudden interruption of kidney function due to obstruction, reduced circulation, or kidney disease.

**Urinary tract infections**: include cystitis and urethritis, caused by bacteria.

**Kidney stones formation (Urolithiasis)**:

Kidney stones (renal lithiasis) are small, hard deposits of mineral and acid salts on the inner surfaces of the kidney. These stones are polycrystalline aggregates composed of crystalloid and organic matrix. These occur when three specific mechanisms are at work:

- There is an excess of salt in urine that cannot be dissolved and eliminated. So the urine is over saturated with this insoluble substance and crystals begin to form. Under normal circumstances, these crystals would have dispersed and been eliminated in urine.

- More crystals begin to form that cannot be excreted. They join together and form a strong bond that develops into a stone.

- The body is unable to inhibit the crystallization of these substances in the urine and the stones continue to form.

Common sites of formation are renal pelvis, calyces and in the bladder. Often many stones are found in kidney [4]. Many times urolithiasis is idiopathic; some risk factors including dehydration, genetics, and excessive intake of calcium, oxalate, or protein are the main cause of urolithiasis. When urinary calculi are quite tiny, they may pass unnoticed with the urine. Often calculi grow too large to pass easily through the urinary tract as well as some stones have rough or sharp edges, it can be quite painful when they pass through the urinary tract.

Kidney stones may contain various combinations of chemicals. The vast majority (75-80%) of the stones from urolithiasis are made from calcium oxalate or calcium phosphate. The rest are made up of uric acid (possibly resulting from gout), struvite (magnesium ammonium phosphate), and cystine (uncommon and most likely a genetic defect) (NIH Publication no.08-2495).

Epidemiology [5]:

The epidemiology of urolithiasis differs according to geographical area in term of prevalence and incidence, age and sex distribution, stone composition and stone location. Such differences have been explained in terms of race, diet and climate factors. Epidemiological surveys have been previously reviewed showing that in economically developed countries the prevalence rate ranged between 4% and 20%. Bladder stones constitute 10–15% of the stone burden in adult and 15–30% in paediatric stone-formers. As living standard increase, particularly in the urban areas of the more affluent developing countries, the incidence of upper urinary tract stones is increasing.
Classification of Kidney Stones [6]:

Kidney stones are broadly classified into calcareous (calcium containing) stones, which are radio-opaque, and non-calcareous stones. On the basis of their composition, stone are classified as shown in the table.

### Classification of Kidney stones

| Composition                    | Causative factors       |
|-------------------------------|-------------------------|
| calcium oxalate, phosphate,   | Metabolic abnormality   |
| or both                       | Idiopathic              |
| Struvite (triple phosphate)   | Infection               |
| Uric acid                    | Hyperuricaemia          |
| Cystine                      | Hyperuricosuria         |
| Other (Xanthine, indinavir)   | --                      |

Calcareous Stones (Calcium Containing Stones):

Calcareous stones are mainly responsible for all urinary calculi. Calcium containing calculi can occur as pure calcium oxalates or calcium phosphate but more often the mixture of two.

**Calcium oxalate stones:**

Calcium oxalate stones are the most common type of urinary calculi and can exist in monohydrate and dehydrate forms, with or without of phosphate. Calcium oxalate stone are radio opaque and usually visible on plain film radiography or non contrast CT [6, 7].

**Hyperoxaluria:** Approximately 80-90% of oxalate is synthesized in the liver. An additional 10% to 20% is related to the dietary consumption of oxalate or vitamin C [6, 7, 8]. Hyperoxaluria causes oxalate crystal formation, which combines with urinary calcium to form calcium oxalate stones [7]. There are several causes of hyperoxaluria

- Primary hyperoxaluria, Type 1 - it is caused by deficiency of the enzyme alanine:glyoxalate amino transferase in the liver.
- Primary hyperoxaluria, Type 2 - it is caused by deficiencies of hepatic enzyme D-glycerates dehydrogenase and glyoxylate reductase, which cause increase in urinary oxalate and glycerate excretion.
- Enteric hyperoxaluria occurs in patients with short bowel syndrome or malabsorption.

**Hypocitriuria:** Citrate is most common and abundant organic anion in human urine, and is a well-recognized inhibitor of stone formation. Hypocitriuria is defined as urinary citrate excretion of less than 320 mg. It is well known risk factor for calcium nephrolithiasis, and has been identified in 20% to 60% of calcium stone formers. Hypocitraturia is seen in 15% to 63% of patients with urolithiasis [7].

**Hyperuricosuria:** Hyperuricosuria is defined as urinary uric acid excretion of > 600 mg daily. The most common cause of hyperuricosuria is increased dietary purine intake, because uric acid is the end product of purine metabolism. Chronic metabolic acidosis can result in protein metabolism and thus increased excretion of urate and formation of kidney stones [7].

Calcium phosphate stones:

Calcium phosphate is commonly found in association with oxalate in stones. Calcium phosphate stones occur only when the chemical pressure for crystallization is high, and thus they are usually seen in very active stones disease. Pure calcium phosphate stones always associated with renal tubular acidification defects. When the kidney lose some of their ability to lower urinary pH, the resulting higher pH increases the divalent and trivalent forms of phosphate, which causes calcium phosphate super saturation [6].

The causes of calcium stones are as follows;

**Idiopathic hypercalciuria:** Hypercalciuria in the presence of normal serum calcium is termed as idiopathic hypercalciuria. Hypercalciuria is defined as a urinary output of greater than 200 mg of calcium in 24-hour period [8, 18].
Non-Calcareous Stones:

**Struvite stones [7]:**
Struvite stones are composed of magnesium, ammonium and phosphate mixed with carbonate. These stones are formed in urine with a pH of greater than 7.2. These stones can grow very rapidly to form a complete stone cast within the drainage system of the kidney. They are usually associated with urinary tract infections, which change the urinary environment to permit rapid stone growth. Consequently, the stone formed can become very large in size. If left untreated they can cause chronic infection, destroy the kidney, and may result in death.

![Fig No.7 Struvite Stones](image)

**Uric acid stones:**
Usually, uric acid stones are found between 5 to 10% of all stones analyzed in a stone clinic. Uric acid is an end product of metabolism. Generally, these stones are associated with urine pH less than 5.5. Uric acid stones are spherical with a smooth yellow-orange surface and nearly radio graphically transparent unless mixed with calcium crystals or struvite. Approximately 25% of patients with uric acid stone have gout problem. There are three major factors for the development of uric acid stones i.e. Low urine volume, acidic urine pH, and hyperuricosuria. There are many reasons for this build up: genetics, certain medications, obesity, and a diet rich in foods such as organ meats [9, 10].

![Fig No.8 Uric Acid Stones](image)

**Cystine stones:**
These are rare stones occurring 1% of stone patients due to an inherited defect in amino acid transport within the kidney. Cystine is a building block for muscles, nerves and other parts of the body. But in some people who inherit a rare, metabolic condition, called cystinuria, it is also the source of the least common of all kidney calculi i.e. cystine stones.

Consequently, cystine stones occur because the kidneys do not reabsorb cystine properly. Excess cystine crystals are found in the urine of affected patients which clumps together to form stones. Patients who are affected tend to be young and develop recurrent kidney stones throughout life [7].

**Miscellaneous Stones:**
There are some stones which are rarely found in kidneys or urinary tract which are
- Ammonium uric acid calculi
- Dihydroxyadenine stones
- Matrix calculi
- Triamterene stones
- Xanthine stones

Dihydroxylidine and Xanthine stones occur due to deficiency of the enzyme adenine phospho ribosyl transferase and xanthene oxidase. Xanthine stones also occur due to the intake of larger dose of allopurinol. Triamterine stones occur in the patients who are treated with triamterine (potassium-sparing diuretics). Ammonium uric acid stones occur due to urealetic infection which increased urinary uric acid and decreased fluid intake. Matrix stones are rare stones formed heavily infected urinary tract.

**SIGNS AND SYMPTOMS:**
- Oliguria (reduced urinary volume) caused by obstruction of the bladder or urethra by a stone or rarely simultaneous obstruction of both ureters by two separate stones.
- Postternal azotemia and hydronephrosis (distension and dilation of the renal pelvis and calyces) can be observed following the obstruction of urine flow through one or both ureters [11].
- Renal Colic- renal colic is caused by peristaltic contractions of the ureter as it attempts to expel the stones. It typically begins in the flank or lower back, often radiating to the groin or in men, to the testes. Pain caused by kidney stones, referred to as renal colic, is often described as one of the strongest pain sensation felt by humans [12].
- Hematuria, pyuria, and dysuria [6].
- Other symptoms include blood in urine, nausea and vomiting, shivers, sweating and fever if there is accompanying infection.
Pathophysiology of Urinary Calculi:

The physical process of stone formation is a complex cascade of events. Kidney stones result from the growth of crystals into stones [13]. The process of stone formation depends on urinary volume; concentrations of calcium, phosphate, oxalate and sodium ions, concentrations of natural calculus inhibitors and urinary pH [14]. High ion levels, low urinary volume, low pH, and low citrate levels favor the formation of urinary calculi.

The pathogenesis of urinary calculi formation is the end result of the following fundamental multi-step physicochemical processes.

Saturation → Super saturation → Nucleation → Crystal aggregation → Crystal growth → Crystal retention → Stone formation

Super saturation:

The central event in stone formation is super saturation. The term super saturation refers to a solution that contains more of the dissolved material than could be dissolved by the solvent under normal circumstances. Super saturation occurs when the concentration of substances forming urinary calculi increases in urine, or urine volume decreases, as well as the absence or reduction in urinary stone inhibitors occurs in urine.

Super saturation depends on urinary pH, ionic strength, solute concentration, and complexation. The level of super saturation of a salt is expressed as the ratio between the actual ion-activity product (AP salt) and the solubility product (SP salt). The point at which saturation of a solution is reached, and crystallization begins is commonly known as thermodynamic solubility product (K_sp).

Urine contains inhibitors of crystallization and can hold large concentrations of solute above the K_sp, a metastable state. If the concentration of solute increases further and a point is reached where it cannot be held in solution, this concentration is known as KF, which is the point of formation of product in urine. Thus, super saturation of the urine constitutes a driving force within the solution which can lead to crystallization and trigger a series of pathophysiologic events that include nucleation, crystal aggregation, growth, and attachment to epithelia.

Nucleation:

Urinary super saturation alone cannot explain the formation of urinary stones. Nucleation is the formation of a solid crystal phase in a solution. It is an essential step in the formation of urinary calculi [13] Nucleation involves the association of crystalloids in solution to form a sub microscopic particle. There are two types of nucleation; the homogeneous nucleation and the heterogeneous nucleation.

- The homogeneous nucleation results, when the process occurs spontaneously in a pure solution. Because impurities are always present in human urine, the homogeneous nucleation is unlikely to occur in vivo.
- Heterogeneous nucleation sites in urine can be epithelial cells, red blood cells, cell debris, urinary casts, other crystals and bacteria. The surfaces provided by the impurities can serve as a nidus in the nucleation process, leading to the heterogeneous nucleation. The heterogeneous nucleation will, generally, occur at a lower super saturation level than that required for the homogeneous nucleation [14]. The nucleation of crystalline components may occur in the lumens of renal tubules, in the basement membranes of tubule cells, or at both sites, perhaps depending on the type of stone.

Crystal Aggregation:

The process in which crystal nuclei bind to each other to form larger particles is called aggregation. The initial nuclei can grow by further addition of desired salts. Aggregation of particles in solution is determined by a balance of forces, some with aggregating effects and some with disaggregating effects. A small inter-particle distance increases the attractive force and favours particle aggregation. Crystal aggregation plays an important role in stone formation.

Crystal Growth: Crystal growth is the next major step of the formation of urinary calculi. In this process atoms or molecules from solution are added to the solid phase of growing crystal in a geometrically precise arrangement. The crystal growth process starts with the nucleation stage. Several atoms or molecules in a supersaturated liquid start forming clusters. Crystal growth is determined by the molecular size and shape, the physical properties of the material, the super saturation levels, the pH of solution, and the defects present in the structure of crystal. The combination of crystal aggregation and crystal growth can explain the genesis of urinary calculi.

Crystal Retention:

Another process that may lead to stone formation is crystal retention. None of the previously discussed elements, i.e. crystal precipitation, growth, and aggregation would results in urinary stone formation if the nucleated crystals were flushed out by urinary flow. Crystal retention is, therefore, a key factor. Crystal retention will result if the crystals grow large enough to be trapped in renal tubules.
Fig No.10 Pathophysiology of Urolithiasis
Role of Oxidative Stress in Urolithiasis:
Reactive oxygen and nitrogen species play significant regulatory roles. They normally occur at steady state levels and are generated when needed. In various pathological conditions, however, there is uncontrolled generation of the reactive oxygen or nitrogen species and/or a reduction in the endogenous antioxidant capacity leading to the development of oxidative stress. Membrane-associated nicotinamide adenine dinucleotide phosphate (NADPH) oxidase is also a major source of reactive oxygen species (ROS) in the kidneys, particularly in the presence of angiotensin II. According to a number of experimental studies, it is also a likely source of Ox-induced superoxide production. Angiotensin II is implicated in causing oxidative stress by stimulating membrane bound NAD (P) H oxidase leading to increased generation of superoxide. TGF-β participates in ROS production through the activation of NADPH oxidase. Hyperoxaluria-induced production of renal lipid peroxides. Oxidative stress followed by renal cell injury and inflammation due to lipid peroxidation. Loss of membrane integrity subsequently facilitates the retention of calcium oxalate crystals and growth of stones in renal tubules.

Role of Promoters and Inhibitors in stone formation:
Urine is having several substances that change or modify the crystal formation [15]. These can further be divided into inhibitors, promoters and complexors. Substances which prevent or reduce the crystallization are called inhibitors. Urinary inhibitors attach to the growth sites on crystals, retarding further growth and aggregation. Inhibitors exert their effects in multiple ways, including inhibition of primary and secondary nucleation and crystal growth and aggregation.

Promoters promote the growth of crystals and facilitate the formation of urinary calculi. It may be possible that a substance may promote one stage of crystal formation such as growth and inhibits another stage such as aggregation.

Certain substances which form soluble complexes with lattice ions of specific crystals decrease the free ion activity of that ion and effectively decrease the state of saturation for that ion system. These substances are known as complexors. Citrate is the potent complexor of calcium in urine and reduces ionic calcium concentration.

Urine analysis: Protein may be noted because of the presencees of hematuria. Pus cells and bacteria may be seen. Oxalate bodies are often observed in hyperthyroidism, renal tubular acidosis, and hyperparathyroidism.

pH: Urinary pH can be measured easily using nitrazine paper. Persistently alkaline urine may be indicative of renal tubular acidosis or may be related to urease-producing organisms.

24-hour urine: Volume, Creatinine, Oxalate, Citrate, Uric acid and some ions like Na+, Ca++ and PO₄.

Blood count: The white blood count increased as a result of complicating infection, if renal function is not adequate, anaemia may be found.

Radiological Investigation:
Sonography: The main advantage of ultrasound is non opaque calculi as well as opaque calculi are detectable and exhibit the same sonographic findings. Patients who are recurrent stone formers and have histories of recurrent urinary tract infections benefit from sonography.

KUB x-ray: It involves low doses of electromagnetic energy to produce a picture of the kidney-ureter-bladder area. This x-ray will reveal kidney stones in these areas.

Ultrasound: It is a diagnostic technique in which high frequency sound waves are passed into the kidney to detect obstruction and changes.

CT scan: This technique is more sensitive than radiography or sonography. CT scan is not only detects the oxalate and phosphate calculi but also struvite, cystine, and uric acid calculi, which are not detected by radiography.

ACT scan: Involves injecting a dye into the body that infiltrate the kidneys and accentuates the images. Using a series of cross-sectional x-rays, the images, made by the dye, make it possible to detect kidney stones.

Intravenous Urography: Intravenous urogram is the standard well accepted test for documenting obstruction and urinary function in acute ureteric colic patients. The examination is relatively inexpensive, safe, and easily performed.

MANAGEMENT OF KIDNEY STONES:
I. Medical Management:
Diet recommendations [16, 17]:

High fluid intake:
Patients are advised to take maximum intake of fluid within three hours after taking meals, during periods of physical exercises, bed time and once at midnight. Plain water is good enough but potassium rich citrus fruit
juices such as orange, grape, lime, lemon are preferable. Increased fluid intake actually has been demonstrated to have positive effect on two urinary inhibitors, citrate and Tamm-Horsfall protein. Urinary dilution has been found to increase the inhibitory activity of Tamm-Horsfall protein on the calcium oxalate monohydrate crystal aggregation in the urine of the stone formers.

**Restriction of animal proteins:**

Animal proteins are rich in sulphur containing amino acids such as cystine, methionine, which on oxidation produces sulphate which forms soluble complexes with calcium in the nephron and limits the reabsorption of this cation. High protein intake of animal origin, especially red meat, contributes to hyperuricosuria, hyperoxaluria, hypercitraturia, and hypercalciuria.

**Oxalate restriction:**

Avoidance of nuts, spinaches, dark roughage, chocolates, tea, and vitamin C with the advice to maintain recommended daily intake of calcium and to ensure that calcium consumption accompanies the ingestion of oxalate rich foods to prevent the absorption of oxalate.

**Sodium restriction:**

Increased sodium intake may promote a variety of metabolic changes i.e. increase in the urinary pH, calcium and cystine excretion and decrease in citrate excretion. Therefore, patients are advised to avoid high sodium – containing food with restriction of salt in the diet.

**Restriction of calcium:**

Calcium restriction becomes a very popular recommendation in the past based on the high incidence of hypercalciuria.

**Drug therapy [8, 18]:**

Generally, 85% of the time, it is possible to spontaneously pass a kidney stone with urination. Stones larger than 6 millimetres will require some form of intervention. Assuming there is no high grade of obstruction or associated infection in the urinary tract, and symptoms are relatively mild, various non-surgical measures can be used to encourage the passage of a stone.

**In normal calciuria** - Oral administration of potassium citrate increases urine pH and citrate excretion in the urine.

**In hypercalciuria** - Thaizide diuretics are reserved for patients who have severe hypercalciuria or patients who have mild hypercalciurea and reduce bone mineral density. The hypercalciuric action of thaizide is attributed to enhance calcium reabsorption. In addition, thaizide induced extracellular sodium depletion promotes sodium and calcium reabsorption in the proximal renal tubule further reducing urinary calcium.

**In hypokalaemia** - If magnesium loss is a common because of chronic diuretic use, consider potassium magnesium citrate.

**In hyperuricaemia or hyperuricosuria** – the following were the drugs used.

- **Allopurinol:** It reduces urinary uric acid level and prevent recurrent. Allopurinol is a xanthine oxidase inhibitor that prevents the conversation of hypoxanthine to xanthine, the precursor of uric acid. The drug is also used in patients with gout or hyperuricemia (high serum uric acid levels).
- **Potassium citrate:** It is effective in the treatment of patients who have calcium stones and normal urinary calcium. By providing an alkali load, potassium citrate increase urinary pH and citrate, thereby increasing urinary inhibitory activity, and perhaps reducing urinary calcium.

**In hyperoxaluria** - No specific drugs are available to reduce oxalate excretion in the urine.

- **Pyridoxine,** a cofactor in the alanine-glyoxylate pathway, may reduce production of oxalate by inducing enzyme activity; In an observation study, high intake of vitamin B6 (>40 mg/day) was inversely associated with risk of oxalate stone formation in women.
- **Cholestyramine** reduces intestinal absorption of oxalate, but no trials have shown its efficacy in preventing recurrent stones.

**II. Surgical Treatment [19, 20]:** Surgery should be reserved as an option for cases where other approaches have failed or should not be tried. Surgery may be needed to remove a kidney stone. If it

- Does not pass after a reasonable period of time and causes constant pain.
- is too large to pass on its own or is caught in a difficult place
- blocks the flow of urine
- damages kidney tissue or causes constant bleeding
- Has grown larger.

The following equipments were used to remove the stone by surgery.

1. ESWL(Extracorporeal Shock wave Lithotripsy)
2. PNL (Percutaneous Nephrolithotomy)
3. USR (Ureteroscopic stone removal)
4. Open Surgery

**Extracorporeal Shock wave Lithotripsy:**
Extracorporeal shock wave lithotripsy (ESWL) is the most frequently used procedure for the treatment of kidney stones. In ESWL, shock waves that are created outside the body travel through the skin and body tissues until they hit the denser stones. The stones break down into small particles and are easily passed though the urinary tract in the urine.

Several types of ESWL devices exist. Most devices use either x rays or ultrasound to help the surgeon pinpoint the stone during treatment. For most types of ESWL procedures, anaesthesia is needed. Complications may occur with ESWL, some patients have blood in their urine for few days after treatment. Bruising and minor discomfort in the back or abdomen from the shock waves can occur. Patients are advised to avoid taking aspirin and other medicines that affect blood clotting for several weeks before treatment.

Sometimes, the shattered stone particles cause minor blockage as they pass through the urinary tract and cause discomfort. In some cases, a tube was inserted i.e. stent through the bladder in to the ureter to help the fragments pass. Sometimes the stone is not completely shattered with one treatment, and additional treatments may be needed

**Percutaneous Nephrolithotomy (PNL):**

This treatment is often used when the stone is quite large or in a location that does not allow effective use of ESWL. In this procedure, a tiny incision is made in the back and creates a tunnel directly into the kidney, using an instrument called a nephroscope. For large stones, some type of energy probe-ultrasonic or electro hydraulic may be needed to break the stone into the small pieces. One advantage of percutaneous nephrolithotomy is that the surgeon can remove some of the stone fragments directly instead of relying solely on their natural passage from the kidney.

**Ureteroscopic stone removal (USR):**

Although some stones in the ureters can be treated with ESWL, ureteroscopy may be needed for mid- and lower-ureter stones. No incision is made in this procedure. Instead, the surgeon passes a small fiberoptic instrument called an ureteroscope through the urethra and bladder into the ureter. A small tube or stent may be left in the ureter for a few days to help urine flow. Before fiber optics made ureteroscopy possible, physicians used a similar “blind basket” extraction method. But this technique is rarely used now because of the higher risks of damage to the ureters.

**Open Surgery:**

Open surgery involves incisions through the patient's flank and into the kidney. The kidneys are cooled down using ice and x-rays are used during the procedure to locate specific areas and the stone. The arteries in the kidney are identified and isolated away from the surgical region. The surgeon locates the collecting system and retrieves the stone. If the surgeon finds any blockage, this is corrected. The surgery is very invasive and is now restricted to the patients with very large or complex stones that cannot be removed using less invasive measures and for very obese patients.

The procedure is not appropriate for the following patients:

- Those with bleeding or clotting disorders.
- Those with untreated widespread infection.
- Those with severe and chronic kidney insufficiency.

**The following are the animal models for urolithiasis**

- Diet-induced
- Chemical induced
- Foreign body insertion method
- *In vitro* models

**REVIEW OF LITERATURE**

**Withenia somnifera**

Rimple R Patel et al., (2014) studied anti urolithiatic activity of *Withenia somnifera* in ethylene glycol induced urolithiasis in rats. After completion of treatment after 24 hrs urine was collected and blood was collected by retro orbital puncture and kidney histopathology was done. The methanolic extract of withenia somnifera showed increased in urinary volume and PH. All the treated groups showed decrease in calcium, oxalate, phosphate, creatinine, urea, uric acid level in EG induced urolithiasis [21].

**Melia azedarach linn**

Senthil rajan dharma lingam et al., (2014) investigate the anti urolithiatic activity of the aqueous and alcoholic extracts of *Melia azedarach linn* leaves in calcium oxalate urolithiasis in male albino rats. Treatment with aqueous or ethanol extract (250mg/kg, p.o) significantly reduced the elevated levels of calcium, oxalate and phosphate excretion in urine. The both extracts demonstrate that melia azedarach linn leaves have potent anti urolithiatic activity [22].

**Orthosiphon stamineus**

Ramesh K et al., (2014) in the present investigation the ethanolic extracts of *Orthosiphon stamineus* leaves have been used. The ethylene glycol used to inducing the urolithiasis in albino rats. The final results shows the ethanolic extracts of plants have good nephroprotective activity when compared with the standard drug. It was proved by analyzing the biomarkers and enzymes level [23].
**Portulaca oleracea**

D.V. Kishore et al., (2013) conclude that the ethanolic extract of *Portulaca oleracea* is effective against ethylene glycol and ammonium chloride induced urolithiasis in albino rats [24].

**Glochidion velutinum**

Thatikonda vijaya et al., (2013) investigate the methanolic extract of dried leaves of *Glochidion velutinum* as a preventive agent in experimentally induced urolithiasis model in rats. The efficacy of 250 and 500 mg/kg GV extract was studied in 0.75% ethylene glycol and 1% ammonium chloride induced urolithiasis for 21 days in rats. The histopathological analysis and other parameters were measured. The results indicating that the dried leaves of GV have antiurolithiatic activity [25].

**Musa paradisiaca**

Tirumala k et al., (2013) investigated the aqueous extract of stem core of *Musa paradisiaca* on ethylene glycol and ammonium chloride induced urolithiasis in rats. Phytochemical estimation was done for the presence of phytocconstituents. Dose selection was made on the basis of acute oral toxicity study (200 mg/kg 1,400 mg/kg body weight) as per OECD guidelines. Oral administration of extract of musa paradisiaca for 28 days resulted in significant reduction in urine level, results suggests that the aqueous extracts of stem core of musa paradisiaca restored the metabolic changes in ethylene glycol and ammonium [26].

**Tecoma stans**

Kameshwaran S et al., (2013) investigate the Antiurolithiatic activity of aqueous and methanolic extracts of *Tecoma stans* (AETS & METS) was carried out on ethylene (0.75% v/v) induced urolithiasis in rats. The presented data indicate that administration of AETS METS to rats with experimentally-induced urolithiasis reduced and also prevented the formation of urinary stone forming constituents in urine and renal tissue brought about by *T. stans* could contribute to its antiurolithiatic property [27].

**Solanum virginianum**

Krishna mohan chinnala et al.,(2013) investigate the ethanolic extract of *Solanum virginianum* (20 mg/kg, 400 mg/kg) was administered orally from 1st day for preventive regimen and from 15th day for curative regimen on ethylene glycol induced urolithiasis in rats. Treatment with ethanolic extract of solanum virginiam significantly reduced the elevated levels of ions in urine as well as BUN, serum creatinine and serum uric acid level [28].

**Bryophyllum pinnatum**

Apexa Bhanuprasad Shukla et al., (2014) investigate the anti urolithiatic effect of aqueous extract of leaves of *Bryophyllum pinnatum* on ethylene glycol induced renal calculi [29].

**Ajowan**

Swamy ranga reddy K et al., (2012) investigate the anti urolithiatic activity of *Ajowan seeds* on ethylene glycol induced urolithiasis in rats. Several parameters like urea, uric acid, creatinine, calcium, potassium in serum analysis and ultra sound scanning are used to assess the activity. The results indicated that the dose 300 mg/kg body weight [30].

**Ceropegia bulbosa**

Mohd Azaz Khan et al., (2012) investigate the hydro alcoholic extract of leaves of *Ceropegia bulbosa* was used in animal models of urolithiasis [31].

**Swertia chirata**

Parmar R.K. et al., (2012) investigate the methanolic extract of *Swertia chirata* drug in experimentally induced urolithiasis model in rats. Histopathological analysis also reveals deposition of calcium oxalate crystals and disruption of tubular cells and juxtагlomerular cells. That deposition and disruption were also reduced in rats treated with swertia chirata [32].

**Hordeum vulgare**

Jignesh G. Shah et al., (2011) studied the antiurolithic potential, the ethanolic extract of seeds of *Hordeum vulgare* was tested in an animal model of urolithiasis. Glycolic acid induced hyperoxaluria in urolithiatic rats. And, there were significant elevated urine output, kidney weight loss and some renal injury markers in glycolic acid induced rats. In vivo antioxidant parameters including lipid peroxidation (MDA), superoxide dismutase (SOD) and catalase (CAT) were also determined [33].

**Vediyuppu cheyaneer**

Velpandian V et al., (2012) investigate the *vediyuppu cheyaneer* has been widely used in the Siddha system of medicine for various diseases. For the in vivo antiurolithic activity on ethylene glycol induced hyperoxalurea rat, the liquid form of vediyuppu cheyaneer showed a significant inhibitory effect at 500 mg/kg [34].

**Citrus medica Linn**

Chavada kalpeshsinh S et al.,(2012) investigate the anti urolithiatic activity of FFFCM (flavonoids rich fraction of *Citrus medica Linn*) at all dose level significantly prevented the EG induced changes in
calcium, inorganic phosphate, uric acid, oxalate, urea, citrate, mg level, creatinine clearance and oxidative stress. Cystone (750 mg/kg, p.o) was used as standard drug after completion of treatment period of 28 days, 24 hr urine sample and blood were collected. All can be attributed to its diuretic action, decrease in promoters and increase in inhibitors level and antioxidant potential [35].

**Musa stem**

Prosobh GR et al., (2012) investigated the evaluation of *Musa stem juice* will prevent the development of stones in kidneys against the ethylene glycol induced urolithiasis in rats. The treatment of urolithiasis induced rats by musa tablet also restored all the elevated biochemical parameters (creatinine, BUN, and uric acid) restored the urine PH of normal and increased the urine volume significantly [36].

**Leea macrophylla Roxb**

Abu Nasim Nizami et al., (2012) investigate the antilithiatic effect of the whole *Leea macrophylla Roxb* ethanol extract in ethylene glycol induced urolithiasis model of rats. The results of this study demonstrated very promising anti-urolithiatic effect L.macrophylla extract with preventive and therapeutic treatments [37].

**Celosia argentea**

Joshi pranav et al., (2012) investigate the effect of *Celosia argentea* in chemically induced urolithiasis in rats. The ethanolic extract of celosia argentea seeds was scientifically evaluated to study anti urolithiatic activity at low dose (500 mg/kg; p.o). At the end of the treatment changes in various physical parameters, promoters, inhibitors, renal function markers in urine and serum sample and Anti oxidant parameters and histopathology of kidneys were observed [38].

**Lawsonia inermis L.**

K.J. kore et al., (2011) investigate the hydro alcoholic extract of *Lawsonia inermis L* leaves (HELI) showed significant antiurolithiatic activity against calcium oxalate-type stones. The results obtained in this study provide evidence for the efficacy of HELI as antiurolithiatic agent [39].

**Cynodon dactylon**

Abolfazl Khajavi Rad et al., (2011) investigate the preventive effects of hydro alcoholic extract of *Cynodon dactylon* roots on calcium oxalate calculi in rats. C. dactylon was able to decrease the body weight of kidneys. Urine oxalate level decreased in nephrolithiatic rats treated with the extract [40].

**Lantana camera linn**

Mayee R. et al., (2011) investigate the ethanolic extract of *Lantana camera linn* leaves were evaluated for antiurolithiatic activity against 0.75% v/v ethylene glycol and 2% w/v ammonium chloride induced calcium oxalate urolithiasis and for anti oxidation activity against hyperoxaluria induced oxidative stress in rats. The extract administration also decreased the extent of lipid peroxidation and hence enhanced the levels of antioxidant enzymes in kidneys of urolithic rats [41].

**Bergenia ciliata**

Sarmistha saha et al., (2011) investigate the hydro alcoholic extract of *Bergenia ciliata* standard drug cystone were administered simultaneously at a dose of 150 and 300 mg/kg body weight and absolute organ weight of ethylene glycol (0.75% v/v) for 28 days [42].

**Crataeva magna lour.**

Suman Kumar mekap et al., (2011) investigate the *Crataeva magna lour.bark* for its anti urolithiatic activity in two conventional models (in vivo) of urolithiasis in rats. The two methods chosen were lactose (30%) +ethylene glycol (1%) & ammonium chloride (2%) + ethylene glycol (0.75%) induced urolithiasis res. The results shown by the ethanol extract (400 mg/kg bw) group was compared to standard polyherbal drug (cystone: 5 ml/kg) treated group and thus exhibited potent antiurolithiatic activity [43].

**Hygrospila spinosa**

Satish R et al., (2010) investigate the aqueous extract of *Hygrospila spinosa* (200 mg/kg) was administered orally from 1st day for preventive regimen and 15th day for curative against the ethylene glycol induced urolithiasis in rats. The hygrospila spinosa significantly reduced the elevated levels of these ions and proteins in urine. The histological findings also showed after treatment with extract [44].

**Coleus aromaticus**

Venkatesh G et al., (2010) investigated the Anti urolithiatic of *Coleus aromaticus* in ethylene glycol induced urolithiasis rats. Treatment with hydro alcoholic extract of coleus aromaticus leaves (CALHAЕ) significantly reduced the cholesterol levels ay 300 & 600 mg/kg and triglyceride levels at 600 mg/kg in urolithic rats. Histopathological reports confirmed that chronic administration of CALHAЕ (300 & 600 mg/kg) diminished the no. of calcium oxalate crystals in kidneys [45].
| S.No | Plant Name                  | Family          | Part Used | References                               |
|------|----------------------------|-----------------|-----------|------------------------------------------|
| 1    | Adiantum Capillus Veneris   | Carryophyllaceae| Whole plant| Ajij Ahmed et al., 2013 [46]             |
| 2    | Ceropegia bulbos L.         | Asclepidae      | Tubers    | Khan et al., 2012 [47]                   |
| 3    | Hypericum perforatum       | Hypericaceae    | Leaves    | Mohsen K et al., 2012 [48]               |
| 4    | Kigelia pinnata            | Bignoniaceae    | Fruits    | Ravindra K et al., 2012 [49]             |
| 5    | Lawsonia inermis L.        | Lythraceae      | Leaves    | Kore KJ et al., 2011 [50]                |
| 6    | Macrotyloma uniflorum      | Fabaceae        | Seeds     | Anantha Krishna Chaitanya D et al., 2010 [51] |
| 7    | Plantago Major             | Capparaceae     | Whole Plant| Sharifa AA et al., 2012 [52]             |
| 8    | Punica Granatum            | Lythraceae      | Fruits    | Rathod NR et al., 2012 [53]              |
| 9    | Solanum xanthocarpum       | Solanaceae      | Fruits    | Paras K et al., 2012 [54]                |
| 10   | Terminalia Chebula         | Combretaceae    | Fruits    | Anil T et al., 2012 [55]                 |
| 11   | Crataeva magna             | Capparaceae     | Bark      | Suman KM et al., 2011 [56]               |
| 12   | Tridex procumbens L.       | Asteraceae      | Leaves    | Sailaja B et al., 2011 [57]              |
| 13   | Helianthus annuus          | Astersaceae     | Leaves    | Khan NI et al., 2010 [58]                |
| 14   | Paronychia argentea        | Caryophyllaceae | Aerial Parts| Bouanani S et al., 2010 [59]            |
| 15   | Moringa oleifera           | Moringaceae     | Root, wood| Ravindra V et al., 2006 [60]             |
| 16   | Tribulus terrestris (L.)   | Zygophyllaceae  | Leaves    | Anand R et al., 1994 [61]                |
Kidney is the most valuable organ in the body. It eliminates the most of the waste products. I.e., urea, uric acid & ammonia from the body. There are number of disorders in urinary system includes Urolithiasis. Urolithiasis (nephrolithiasis) or kidney stone is formation of urinary calculi at any level of urinary tract. It is estimated that 12% of world population experience renal stone disease with a recurrence rate of 70%-80% in male and 47%-60% in female. It is the 3rd most common affliction of the urinary health care systems are going to become more & more expensive, therefore we have to introduce herbal medicine system in our health care. Herbal drugs & medicinal plants play a vital role in kidney stone diseases. Undesirable effect of the modern medicine has already been overcome by herbal drugs which have delivered the attention of the people towards the herbal medicines. To increase the acceptability & awareness among the people. There is an urgent need to develop trust & faith towards the safters indogenous system by establishing its validity in treatment for stone diseases.

REFERENCE:

1. Suresh R, Das asis. Essentials of Human Physiology, 4th edition, Books And Allied (P) Ltd., 2013:1:223-230.
2. Van De Graff Human Anatomy, Sixth Edition, Brian Black. Medical Anatomy and Physiology. Unit 11: Urinary System. 2001: pp:1-5.
3. Brian Black. Medical Anatomy and Physiology. Unit 11: Urinary System, 2011.
4. Mute VS, Lithiasis: A Review. Pharmainfo.net, [cited in 2014] Available from: http://www.pharmainfo.net/reviews/lithiasis-review.
5. Trinchieri A. Epidemiology of urolithiasis. Arch Ital Urol Androl 1996; 68(4):203-249.
6. Parmar MS. Kidney stones. BMJ 2004;328(7453):1420-1424.
7. Balaji KC, Menon M. Mechanism of Stone formation. Urol Clin North Am 1997;24(1):11-11.
8. Rumal LA, Pearle MS, Pak CY. Medical therapy, calcium oxalate urolithiasis. Urol Clin North Am 1997; 24(1):117-133.
9. Pietrow PK, Karellas ME. Medical management of common urinary calculi. Am Fam Physician 2006;74(1):86-94.
10. Tiselius HG, Alken P, Buck C, Gallucci M, Knoll T, Sarica K, Turk C. Guidelines on urolithiasis. European Association of Urology 2008: pp.128.
11. Cavendish M. "Kidney disorders". Diseases and Disorders 2 (1st Ed.). Tarrrytown, New York: Marshall Cavendish Corporation. 2008: pp.490–493.
12. Wolf Jr. JS. Pathophysiology: formation of stones. Nephrolithiasis. New York: WebMD. Retrieved 2011.
13. Kok DJ. Intratubular crystallization events. World J Urol 1997;15:219-228.
14. Menon M, Parulkar BG, Drach GW. Urinary Lithiases: etiology, diagnosis, and Medical Management. In: Walsh PC, et al. [eds], Campbell’s Urology [7th edn.]. WB Saunders: Philadelphia, 1998:2661-2705.
15. Pillay SN, Asplin JR, Coe FL. Evidence that calgranulin is produced by kidney cells and is an inhibitor of calcium oxalate crystallization. Am J Physiol. 1998;275(2 Pt 2):F255-261.
16. Gupta NP, Kesarwani P. Current approaches in the medical management of urolithiasis: A review articles. Indian Journal of Urology 2002;19(1): 20-28.
17. Assimos DG, Holmes RP. Role of Diet in the therapy of Urolithiasis. Urol Clin North Am 2000;27(2):225-268.
18. Park S, Pearle MS. Pathophysiology and management of Calcium stones. Urol Clin North Am 2007;34(3):323-334.
19. Hanson K. Minimally invasive and surgical management of urinary stones. Urologic Nursing 2005;25(6):458-465.
20. Miller NL, Lingeman JE. Management of kidney stones. BMJ 2007;334(7591):468-472.
21. Patel RR, Mandal SD. Activity of withania somnifera in ethylene glycol induced urolithiasis in rats. International journal of pharmaceutical archive 2014;3(3):346-355.
22. Lingam SRD, Madhappan R, Chidambaram K, Ramamurthy S, Gopal K, Swetha P and Kumar S. The aqueous and alcoholic extracts of melia azedarach Linn leaves in calcium oxalate urolithiasis in rats. Tropical journal of pharmaceutical research march 2014;13(3):391-397.
23. Ramesh K, Manohar S and Kumar SR. Ethanol extract of Orthosiphon stamineus leaves on ethylene glycol induced urolithiasis in rats. International Journal of PharmTech Research 2014;6(1):403-408.
24. Kishore DV, Moosavi F, Varma RK. Ethanol extract of Portulaca oleracea Linn on ethylene glycol and ammonium chloride induced urolithiasis. International journal of pharmacy and pharmaceutical sciences 2013;5(2):134-140.
25. Thatikonda V, Nallani VRR, Narendra BA, Kumar MS, Sharmila PN, BRedd BS, Nadendla R. The methanic extract of dried
leaves of *glochidion velutinum* using ethylene glycol induced urolithiasis in rats. International journal of biological and pharmaceutical research 2013;4(12):878-844.

26. Thirumala K, Janarthan M, Firasat AM. The aqueous extract of stem core of *musa paradisiaca* against ethylene glycol and ammonium chloride induced urolithiasis. International journal of research in pharmacy and biotechnology 2013;1(6):866-868.

27. Kameshwaran S, Thenmozhi S, Vasuki K, Dhanalakshmi M, and Dhanapal C. Antiurolithiatic Activity of aqueous and methanolic extracts of *Tecoma stans* Flowers in rats. International journal of pharmaceutical and biological sciences 2013;4(3):446-450.

28. Chinnala KM, Shanigarm S, Elsani MM. Antiurolithiatic activity of the plant extracts of *solanum virginianum* on ethylene glycol induced urolithiasis in rats. International journal of pharmacy and biological science 2013;3(4):328-334.

29. Shukla AB, Mandavia DR, Barvaliya MJ, Baxi SN, Tripathi CR. Evaluation of anti-urolithiatic effect of aqueous extract of *Bryophyllum pinnatum* (Lam.) leaves using ethylene glycol induced renal calculi. Avicenna J phytomed 2041;4(3):151-159.

30. Reddy KS, Hanumanna P, Prasad SVN, Surendra M, Reddy KS, Thaniya J. Antiurolithiatic Activity of *Carum Copticum*. Journal of scientific research in pharmacy 2012;1(2):58-61.

31. Khan MA and Pradan D. Anti urolithiatic activity of *Ceropegia bulbosa* extract in rats. Der pharmacia sinica 2012;3(1):148-152.

32. Parmar RK, Kachchi NR, Tirgar PR, Desai TR, Bhalodiya PN. The antiurolithiatic activity of *Swertia chirata* stems. International research journal of pharmacy 2012;3(8):198-202.

33. Shah JG, Patel BG, Patel SB, Patel R. *Hordeum Vulgare* Linn seeds on glycolic acid induced urolithiasis in rats. Pharmacognosy communications 2012;2(2):34-39.

34. Velpandian SS, Rajaperidiva V, Bhaumathi J, Anbu and Aswini A. Effect of *Vediyappu Cheyaneer* in ethylene glycol induced Hyperoxaluria model in rats. International journal of Life Science and Pharma research 2012;2(4):63-67.

35. Chavada KS, Fadadu KN, Patel KV, Patel KG, Gandhi TR. Effect of *Citrus medica* Linn on ethylene glycol induced urolithiasis in rats. Journal of drug delivery and Therapeutics 2012;2(4):109-116.

36. Prasobh GR and Ravikumar. The Musa tablet on ethylene glycol induced urolithiasis in rats. International Journal of Research in Pharmaceutical and Biomedical sciences 2012;3(3):1251-1255.

37. Nizami AN, Rahman MA, Ahmed NU, Islam MS. The ethanolic extract of Whole *Leeca Macrophylla* on ethylene glycol induced urolithiasis. Asian Pacific Journal of Tropical Medicine 2012;533-538.

38. Joshi PC, Patil SA and Sambrekar SN. The antiurolithiatic activity of ethanolic extract of *Celosia Argentea* (seeds) in rats. Universal Journal Of Pharmacy 2012;1(1):52-60.

39. Kore KJ, Shete RV, Jadhav PJ, Kabra MP. Antiurolithiatic effects of Hydroalcoholic Extract of *Lawsonia Inermis* L leaves. International Journal of Universal Pharmacy and Life Sciences 2011;1(2):81-95.

40. Rad AK, Hajzadeh MAR, Rajaei Z, Sadeghian MH, Hashemi N, Keshavarzi Z. The Cynodon dactylon against ethylene glycol induced nephrolithiasis in rats. Avicenna Journal of Phytomedicine 2011;1(1):14-23.

41. Mayee R, Thosar A. The Lantana camera L for Anti urolithiatic and Anti oxidant activities in rats. International Journal of Phytomedicine and Clinical Research 2011;3(1):10-14.

42. Saha S and Verma RJ. *Bergenia Ciliata* extracts prevents ethylene glycol Induced histopathological changes in kidney. Acta Poloniae Pharmaceutica-Drug Research 2011;68(5):711-715.

43. Mekap SK, Mishra S, Sahoo S and Panda PK. Antiurolithiatic activity of *Crataeva Magna* Lour bark. Indian Journal Of Natural Products and Resources 2011;2(1):28-33.

44. Sathish R, Natarajan K and Nikhad MM. The *Hygrophila Spinosa* T.Anders on ethylene glycol induced urolithiasis in rats. Asian Journal Of Pharmaceutical and Clinica Research, 2010;3(4):61-63.

45. Venkatesh G, Baburao K, Rajesh BM, Dhanalakshmi S, Indira PDG. The Coleus aromaticus activity. International Journal Of Phytomedicine 2010;2:284-291.

46. Ahmed A, Wadud A, Jahan N, Bilal A, Hajera S. Efficacy of Adiantum capillus veneris Linn in chemically induced urolithiasis in rats. J Ethnopharmacol 2013;146(1):411-416.

47. Khan SR, Glenton PA. Deposition of calcium phosphate and calcium oxalate crystals in the kidneys. J Urol 1995;153(3):811-817.

48. Khalili M, Jalali MR, Azandaryani MM. Effect of hydroalcoholic extract of *Hypericum Perforatum* L. Leaves on ethylene glycol-
induced kidney calculi in rats. Endourology and Stone Disease 2012;9(2):472-479.
49. Kumar R, Kumar T, Kamboj V, Chander H. Pharmacological evaluation of ethanolic extract of Kigelia pinnata fruit against ethylene glycol induced urolithiasis in rats. Asian journal of plant science and research 2012;2(1):63-72.
50. Kore KJ, Shete RV, Jadhav PJ, Kabra MP. Antiurolithiatic effects of hydroalcoholic extract of Lawsonia inermis L. leaves. International journal of universal pharmacy and life sciences 2011; 1(2):81-95.
51. Anantha KCD, Kumar SM, Reddy M, Mukherjee NSV, Sumanth MH, Ramesh A. AntiUrolithiatic activity Of Macrotyloma uniflorum seed extract on ethylene glycol induced urolithiasis in albino rats. JITPS 2010;1(5):216-226.
52. Sharifa AA, Jsmaludin, Kiong LS, Chia LA, Saina OK. Anti-Urolithiatic terpenoid compounds from Plantago major Linn. Sains Malaysiana 2012; 41(1):33-39.
53. Rathod NR, Biswas D, Chitme HR, Ratna S, Muchand IS, Chandra R. Anti-urolithiatic effects of Punica granatum in male rats. J Ethnopharmacol 2012;140(2):234-238.
54. Patel PK, Manish, Patel MA, Vyas BA, Shah DR, Gandhi TR. Antiurolithiatic activity of saponin rich fraction from the fruits of Solanum xanthocarpum Schrad. &Wendl. (Solanaceae) against ethylene glycol induced urolithiasis in rats. J Ethnopharmacol 2012;144:160-170.
55. Pawar AT, Gayatri D, Gaikwad , Kavita S, Metkari, Kiran A et al, Effect of Terminalia chebula fruit extract on ethylene glycol induced urolithiasis in rats. Biomedicine & Aging pathology 2012;2:99-103.
56. Mekap SK, Mishra S, Sahoo S and Kumar PP. Antiurolithiatic activity of Crataeva magna Lour. bark. Indian Journal of Natural Products and Resources 2011; 2(1):28-33.
57. Sailaja B, Bharathi K and Prasad KVSRG. Protective Effect of Tridax procumbens L. on calcium oxalate urolithiasis and oxidative stress. International Journal of Advances in Pharmaceutical Sciences 2011;2(1):9-14.
58. Khan NI, Shinge JS, Naikwade NS. Antilithiatic effect of Helianthus Annuus Linn. Leaf extract in ethylene glycol and ammonium chloride induced nephrolithiasis. International Journal of Pharmacy and Pharmaceutical Sciences 2010;2(4):180-184.
59. Bouanani S, Henchiri C, Migianu-Griffoni E, Aouf N, Lecouvey M. Pharmacological and toxicological effects of Paronchia argentea in experimental calcium oxalate nephrolithiasis in rats. J Ethanopharmacol 2010;129(1):38-45.
60. Karadi R, Gadge NB, Alagawadi KR, Savadi RV. Effect of Moringa oleifera Lam. root-wood on ethylene glycol induced urolithiasis in rats. J Ethnopharmacol 2006;105(1-2):306-311.
61. Anand R, Patniak K, Srivastava S, Kulshreshtha DK, Dhawan BN. Evaluation of Anti urolithiatic activity of Tribulus terrestris. Pharmaceutical Biology 1994;32(3):217-224.

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