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A PRECISE REVIEW ON VARIOUS INDUCTION METHODS OF RENAL FAILURE

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ABSTRACT

Several models for modelling renal failure are compiled in this article. Medical research has always placed a high value on the use of animal models. The nepharolithisis and urolithasis models are also most frequently utilised in mouse and rat experimental procedures. Around 100,000 Americans in the US are diagnosed with ESRD each year, according to epidemiology, and the risk factors are primarily cirrhosis, obesity and smoking. They also exhibit management therapy. Then, abstracts show different induction models using induced extracts of various leaves and plants, including Melia azedarach Linn leaves, methanolic extract of Cucumis melo, Chenopodium album Linn leaves, *G. fruticosus* solvent extracts, Urtica dioica methanol extract, and Hygrophila spinosa. Using various techniques leads to the observation of various types of activities. The administration techniques employed in induction procedures include oral, parenteral, and implanted. The outcomes of these techniques show that many parameters are seen. These strategies are seen and documented together with improvements in renal tissues, urine volume, oxalate levels, serum creatine, blood urea nitrogen levels, and hyperoxaluria uric levels. Some techniques increased activity while others caused it to decrease.

Keywords: Urolithasis, Nepharolithasis, Ethylene glycol, Hyperoxaluria, Kidney, Animal models, Induction

INTRODUCTION:

When the kidneys are unable to carry out their excretory duties, nitrogenous waste products from the blood are retained, which is referred to as renal failure. Kidney functions include the following:

- Managing volume and electrolytes
- The elimination of nitrogenous waste
- Exogenous compounds, like many medications, are eliminated
- The metabolism of low molecular weight proteins, such as insulin
- The synthesis of a variety of hormones, such as erythropoietin **[1]**

Since their initial descriptions by doctors such as Bright **[5]**, Heber den **[6]**, and Abercrombie in the 19th century, chronic kidney disease (CKD) and acute kidney injury (AKI) have been recognized as significant but separate diseases **[7]**. Convention had it that oligarch AKI was frequently fatal if left untreated until recent years **[8]**, but with the development of dialysis full recovery was frequently feasible **[9]**. The progression of CKD to end-stage renal disease was thought to be a distinct, irreversible, and frequently progressing entity.

- **Kidney failure comes in two different forms: acute and chronic:**

Renal Failure Acute (ARF): Glomerular filtration reduces suddenly (over hours to days) and is typically reversible in ARF syndrome. KDIGO criteria from 2012 state that AKI can be identified by any of the following: (1) A rise in creatinine of 0.3 mg/dl within 48 hours, (2) A rise in creatinine of 1.5 times baseline within the previous 7 days, or (3) A decrease in urine output of less than 0.5 mL/kg/hour for six hours **[1]**. ARF has recently been superseded by the term acute kidney injury (AKI), which encompasses the complete clinical range from a slight rise in blood creatinine to overt renal failure **[2]**.

Chronic Kidney Failure (CRF): A persistent impairment of kidney function, also known as chronic renal failure (CRF) or chronic kidney disease (CKD), is indicated by either a computed glomerular filtration rate (GFR) of less than 60 ml per minute / 1.73 m2 or by excessively increased serum creatinine for more than 3 months. It frequently involves a progressive decrease of kidney function, requiring renal replacement treatment (dialysis or transplantation). End-stage renal disease is the term used to describe a patient who requires renal replacement treatment (ESRD) **[1]**.

Figure 1: Acute renal failure

Figure 2: Chronic renal failure

EPIDEMOLOGY:

Up to 37% of patients in intensive care units (ICUs), 2% to 5% of patients who are hospitalised, and 4% to 15% of patients who have undergone cardiovascular surgery have been recorded to have AKI **[10, 11]**.

- AKI affects 209 cases per million persons annually, with 36% of these patients requiring renal replacement therapy.
- It is well established that men are more likely than women to develop CRF. ESRD is affected by this gender inequality.
- In the United States, ESRD manifests in approximately 100,000 people annually **[12]**.
- Racial disparities exist in ESRD rates. Blacks get ESRD three to four times more frequently than whites do, both in incidence and prevalence **[13]**.

PATHOPHYSIOLOGY:

A renal failure when acute insult results in acute renal failure, a series of events can be used to depict pathophysiology. In cases of chronic kidney disease, however, a series of events can be used to describe pathophysiology progressively over time.

Three general categories can be used to categorise AKI: **[3]**

1. Prerenal azotemia is the first sign of decreased renal blood flow. Prerenal AKI arises either from an absolute drop in extracellular fluid volume or from a decrease in circulation volume despite a normal total fluid volume, as in the case of severe cirrhosis, heart failure, and sepsis. By forcing afferent arterioles to widen and efferent arterioles to constrict, the s renal autoregulation system typically preserve intra capillary pressure throughout the early phase. When pre-renal diseases are severe, the kidneys' adaptive systems are unable to compensate, causing GFR to decline and BUN and creatinine levels to rise and disguise the condition.

2. Intrinsic, the glomeruli, vasculature, and tubulointerstitium can all be affected by different disorders. respectively. They are known as intrinsic renal parenchymal diseases (renal azotemia).

3. Preventing urine from leaving the body (post renal azotemia)

Mostly certain starting mechanisms are connected to the pathophysiology of CRF. As a result, the remaining functional nephrons begin to compensate by compensatory hyper filtration and hypertrophy. Podocyte activity becomes abnormal, filtration is disrupted, and sclerosis develops as a result of subsequent histopathologic changes that include glomerular architectural distortion, improper podocyte function, and disruption of filtration **[4]**.

MANAGEMENT OF KIDNEY DISEASES:

Therapy directed at specific cause

↓

Acute and chronic renal failure were examined and treated.

↓

Sluggish development

↓

Handling of difficulties

↓

The process of making renal replacement therapy

↓

Treatment for kidney replacement

MAJOR RISK FACTORS INVOLVED IN THE ARF AND CRF:

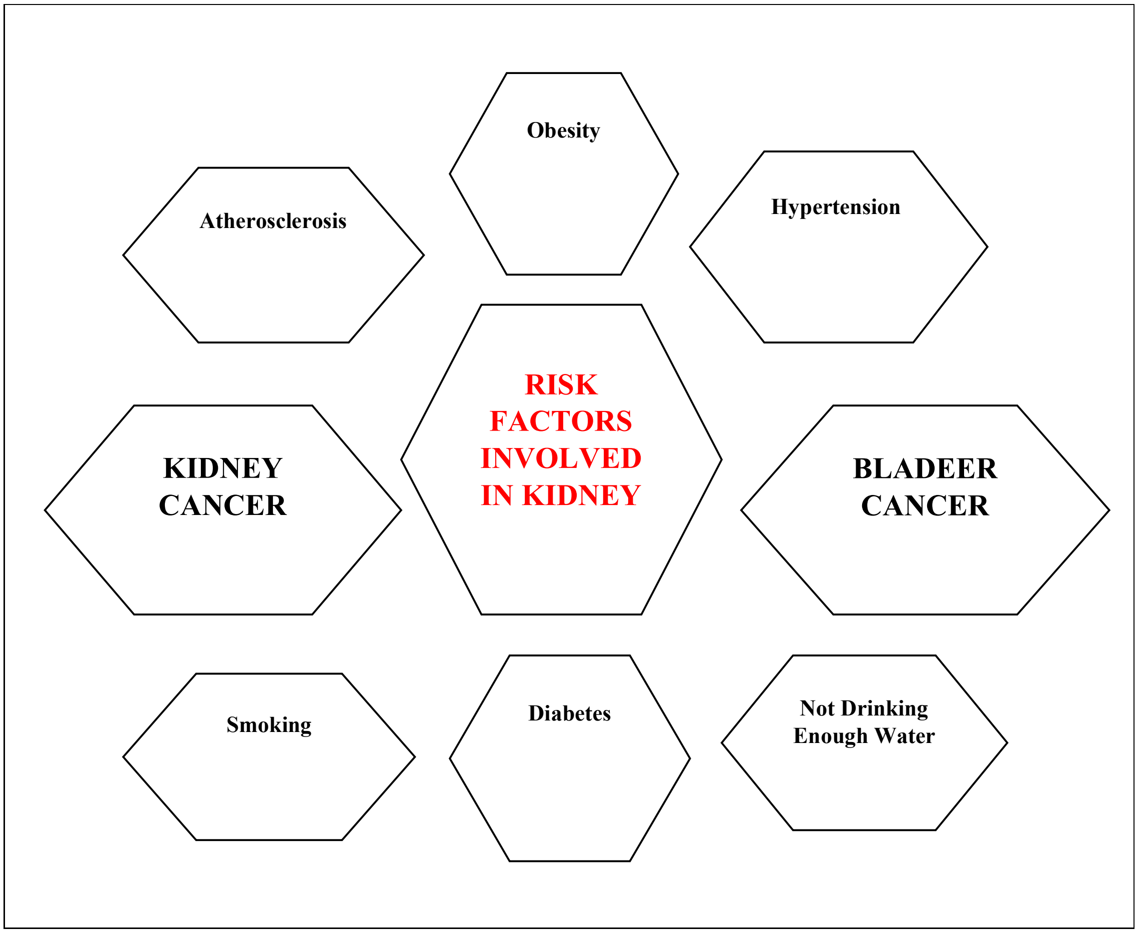

Table 1: Represents Various Induction Methods and Parameters

S. No.	TYPES OF KIDNEY COMPLICATIONS	INDUCTION METHODS	PARAMETERS	REFERENCES
1.	Urolithiatic Activity in rats	oral administration of Melia azedarach Linn leaves	It contains triterpenoids ,steroids,carbohydrates ,glycosides,saponins	[14]
2.	Nephrolithias activity in rats	Methanolic cucumins melo extract in ethylene glycol induced	It includes hyperoxaluria, calcium oxalate deposition, and increased urine excretion	[15]
3.	Urolithiatic Activity in rats	Induced by citrus limon peel aqueous methanol extract	The extract efficiently reduces the accumulation of creatinine and urea in the serum	[16]
4.	urolithiasis activity in male Sprague Dawley rats	On ethylene glycol and ammonium chloride-induced Piper cubeba L. fruit	rise in magnesium and a significant fall in calcium, sodium, chloride	[17]
5.	Urolithiasis activity in rats	Chenopodium album Linn leaves induced	Calcium, phosphorus, urea, uric acid, and creatinine levels in urine and plasma were elevated by EG,	[18]
6.	Nephrolithiasis activity in rats	Acanthaceae's Hygrophila spinosa in induced ethylene glycol	Increased renal excretion of calcium and serum uric acid, as well as decreased renal excretion of urine magnesium	[19]
7.	Urolithiasis activity in rats	Induced by zinc disc implantation, an extract of Biophytum sensitivum	The MBS therapy also avoided the augmentation of serum creatinine, uric acid, and blood urea nitrogen levels	[20]

8.	**Nephrolithiatic activity Wistar male rats**	**extracts from the artificially induced *G. fruticosus***	**EtOAc and BuOH extracts of *G. fruticosus* reduced serum oxalate excretions when compared to lithiatic control**	**[21]**
9.	**Nephrolithiatic activity in male Sprague Dawley rats**	**Hydroalcoholic extract induced by rhizomes of Cyperus rotundus L.**	**HyperEG results in hyperphosphaturia, hypercalciuria, and hyperoxaluria**	**[22]**
10.	**Urolithiatic activity in rats**	**Dioica urtica extract of methanol against artificially induced**	**pH between 5.0 and 6.3. The formation of calcium oxalate calculi a drop in urine pH from 7.0-7.3 to 5.0-5.4.**	**[23]**
11.	**Nephrolithiasis activity in Rats**	**Effects of Fruit Extract from Solanum xanthocarpum on Ethylene-Glycol-Induced**	**In addition to improving renal function, S. xanthocarpum therapy also has antioxidant properties and reduces hyperoxaluria, calcium, and uric acid levels**	**[24]**
12.	**Nephrolithiasis in rats**	**On the Ethylene Glycol-Induced Activation of Copaifera Langsdorffii Desf. Leaf Extract**	**Phosphorus, magnesium, calcium, and uric acid were all examined (Labtest Diagnostics, Brazil).**	**[25]**

METHODS ARE INVOLVED BY THE VARIOS INDUCTION MODELS:

1. **Melia azedarach linn leaves induced by oral administration:**
   It has been investigated how calcium oxalate urolithiasis is affected by oral ingestion of Melia azedarach Linn leaf aqueous and ethanol extracts. During 28 days, male albino rats received an oral dose of ethylene glycol (0.75% v/v) to induce lithiasis. Each extract had a weight of 250 mg/kg and was administered orally on days 0 and 15 for therapeutic and preventative purposes, respectively. Hyperxaluria caused by repeated ethylene glycol injection increased renal oxalate, calcium, and phosphate retention and excretion. Histopathological investigation of a kidney homogenate, urine microscopy, serum analysis, and biochemical analysis were all performed.

- The results demonstrate that ethylene glycol-induced calcium oxalate urolithiasis in male albino rats can be effectively treated with aqueous and ethanol extracts of Melia azedarach Linn leaves.

2. **Cucumis melo in methanolic extract of ethylene glycol-induced:**
   There were each group contains 6 animals. The regular and testing medication treatments lasted 28 days. If needed, all groups were provided with standard rat food. All animals excluding group I purchased an EG solution in pay water at a concentration of 0.75 during study period. Group -I also obtained clean, drinkable water in accordance with its needs. Up to the 28th day, Cystone was administered

intravenously once day to Group-III at a dose of 750 mg per kg body weight. Group IV, on the other hand, was given Cucumis melo (200 mg per kg b.w.) orally once every day throughout the course of the experiment.

- The results showed that rats given EG ingested the methanolic extract of Cucumis melo seed, and that this resulted in the development of urinary calculi, which was thereafter reduced and terminated. These actions may lead to the conclusion that Cucumis melo possesses antiurolithiatic qualities.

3. **Induced by citrus limon peel aqueous methanol extract:**

There were 6 animals in each group. The regular and test medication treatments lasted 28 days. If needed, all groups were provided with standard rat food. all animals excluding group I purchased an EG solution in pay water at a concentration of 0.75 during studying period. Group I also obtained clean, drinkable water in accordance with its needs. Group-III got cystone (750 mg per kg body weight) intravenously once each day up until the 28th day. Group IV was given Cucumis melo (200 mg per kg body weight) orally once daily during the trial period.

- Using the Cucumis melo seed methanolic extract reduced and prevented the development of urinary calculi in rats with EG, according to the data shown. These actions may lead to the conclusion that Cucumis melo possesses antiurolithiatic qualities.

4. On ethylene glycol and ammonium chloride-induced *Piper cubeba L.* fruit:

Rats were used to create six groups of six each. Group I received regular rat food and limitless water. Groups II to VI received drinking water with ethylene glycol (EG) 0.75% (V/V) and ammonium chloride (AC) 1% (W/V) for 7 days in order to induce urolithiasis. Beginning on day eight, group I received 1 mL of 5% gum acacia. Group IV received Cystone, whereas Groups V and VI received *Piper cubeba L.* hydro-alcoholic extract. Animals were slaughtered following an additional 14 days of therapy. Shortly after receiving EG and AC treatment for seven days, the animals in Group II were put to death. Before being sacrificed on day 22, Group III went without treatment for 14 days.

- Showed that kidney tissue in the treated groups had improved histologically and had a large rise in magnesium and a significant decrease in calcium, sodium, chloride, and phosphorus.

5. Induced *Chenopodium album* Linn leaves:

HPLC was used to standardise the leaf extract. Researchers were able to induce urolithiasis in rats by administering 0.75% v/v ethylene glycol (EG) in distilled water, combined with Cystone (750 mg/kg) or vehicle, methanol, or aqueous extracts of Chenopodium album leaves, every day for 28 days. Determining the concentrations of the minerals calcium, phosphorus, urea, uric acid, and creatinine in both urine and plasma allowed researchers to evaluate urolithiasis. Also estimated for urine were its volume, pH, and oxalate content. Oxalate deposits made of calcium were seen histologically, and the renal oxalate concentration was calculated.

- In conclusion, Chenopodium album leaves demonstrated an antilithiatic effect, validating their usage as an ethnomedicinal treatment for kidney stones and urinary problems.

6. Ethanol-induced *Hygrophila spinosa* (acanthaceae):

Hygrophila spinosa (HSME) methanolic extract was administered orally in doses of 250 and 500 mg/kg body weight to male Wistar albino rats. Ethanol glycol was used to cause nephrolithiasis (EG). Among the variables looked at were water intake, urine volume, pH, urinary and renal oxalate and calcium, urinary magnesium, and serum uric acid.

- Hygrophila spinosa's traditional claim is supported by the findings, which show that the aerial parts of the plant have antiurolithiatic activity.

7. *Biophytum sensitivum* extract in opposition to zinc disc implantation-induced:

Six groups of six rats each were randomly selected among the rats who had fully recovered. Group I underwent surgery without a zinc disc being implanted as a control group. Also, for the following seven days, they were given 5% gum acacia solution (5 ml/kg, p.o.). Following the implantation of a zinc disc, Group II received 5% gum acacia solution (5 ml/kg, p.o.) for the following seven days. After receiving cystone (500 mg/kg) for the next seven days, Group III underwent zinc disc implantation. Groups IV, V, and VI's zinc disc-implanted and MBS-treated groups got 100, 200, and 400 mg/kg of MBS over the course of the following seven days, respectively. Cystone and MBS were administered orally once each day (5 ml/kg) for seven days while suspended in a 5% gum acacia solution.

- The results of the investigation demonstrated that administration of the complete *B. sensitivum* plant's methanolic extract significantly reduced disc weight and other related biochemical markers. Although the precise method of action is unknown, it is thought to be mediated by a number of phytochemicals working in concert. The plant's diuretic, antioxidant, and anti-inflammatory properties all mediate the potential mechanism underlying this action. To determine the precise mechanism of action, more phytochemical research is needed.

8. *G. fruticosus* solvent extracts in experimentally induced:

Male Wistar rats developed urolithiasis when administered ethylene glycol in drinking water for 28 days. The curative effects were evaluated following oral administration of the extracts at a dose of 200 mg/kg for 15 to 28 days. Urine samples were collected one day previous to the animals being slaughtered. As of day 28, anaesthesia was used to collect samples of the kidney, liver, and blood. The urine crystals were examined under a light microscope.

- The study found that administration of the complete B. sensitivum plant's methanolic extract significantly reduced disc weight and other related biochemical parameters, indicating anti-urolithiatic efficacy. Although the precise mechanism of action has not been determined, it is suggested that it is mediated by a number of phytochemicals working in concert. The diuretic, antioxidant, and anti-inflammatory properties of the plant work together to mediate the potential mechanism underlying this action. Establishing the precise mechanism of action requires more research into phytochemicals.

9. Rhizome-induced *Cyperus rotundus* l. hydroalcoholic extract:

The animals were divided into six groups of six. Group I received regular rat food and unrestricted water. Groups II to VI were given a 7-day treatment of drinking water with ethylene glycol (0.75%, V/V) and ammonium chloride (1%, W/V) to cause urolithiasis. Group II was slaughtered after 7 days of lithogenic agent administration, but group IV began receiving Cystone (750 mg/kg) on the eighth day, and groups V and VI received a hydroalcoholic extract of Cyperus rotundus (100 mg/kg and 170 mg/kg, respectively) for an additional 14 days.Group III was kept untreated after seven days of lithogenic agent injection for a total of 14 days before being sacrificed on day 22. Analyses of kidney homogenate, urine, biochemical parameters, and histology were completed. Analysis of crystalluria using light microscopy**.**

- The results showed a considerable reduction in the amount of crystals, an improvement in renal cell dysregulation, and a significant antilithiatic effect on the solute balance.

10. Methanolic extract of *Urtica dioica* in the presence of experimentally induced:

Extract preparation and plant materials. U. dioica leaves were gathered in Jiuzhaigou, China, between May and June 2013. A verified the plant matter. taxonomist. The leaves of U. dioica were washed with water, dried in the shade, and homogenised. Using a Soxhlet extraction device, heated extraction was carried out for three hours using methanol (95%) as the solvent The extract was then kept at 4 °C for later use after being concentrated under decreased pressure in a rotating evaporator at 40 °C.

- The results of this study suggest that Urtica dioica has significant antiurolithiatic action and may be useful as a natural remedy for a number of urological diseases.

11. Effects of solanum xanthocarpum fruit extract on ethylene-glycol-induced:

Effects of fruit extract from Solanum xanthocarpum on ethylene glycol-induced urolithiasis in male Wistar rats. Male Wistar rats developed nephrolithiasis when ethylene glycol (0.75%) was introduced to drinking water for 28 days. Each of the six groups of animals had six individuals in it. Vehicle control is performed using three doses of *S. xanthocarpum* methanol extract (100, 200, and 400 mg/kg), as well as model control. Use was made of the Cystone reference dose (750 mg/kg, po). Hypercalcaluria, impaired renal function, oxidative imbalance in the kidney, increased excretion of calcium, phosphate, and uric acid in the urine, and decreased excretion of citrate and magnesium were all present in the calculi-induced group. Therapy with S. xanthocarpum enhances renal function while lowering calcium, uric acid, and hyperoxaluria levels and acting as an antioxidant.

- Coax crystal deposition in the calculi-induced group was significant, whereas the kidney Coax crystal deposition in the treated group was minimal. The findings suggest that Coax crystal inhibition may be a possible mechanism underlying S. xanthocarpum's antiurolithiatic action. This study justified its medical usage in urolithiasis since it is a diuretic, antioxidant, and maintains a balance between stone promoter and inhibitor elements.

12. Extract from the leaves of *Copaifera langsdorffii* desf. on the ethylene glycol-induced:

Using an ethylene glycol (EG) animal model of nephrolithiasis and an in vitro crystallization experiment, the ability of the Copaifera langsdori leaves extract to prevent stone formation was examined. Rats receiving EG treatment received a variety of dosages of the *C. langsdori* leaves extract. Quantization of urine biochemical parameters was done. On kidneys fixed in formalin, a Coax deposits count and osteopontin expression study were done. The in vitro test was carried out using turbidimetry. By using HPLC-UV-DAD to perform phytochemical investigations on the extract, numerous substances were identified. Stone formation could be prevented by *C. langsdori* leaf extract.

- The extract diluted the crystals produced during the in vitro test. Stone-preventing phenolic chemicals are abundant in the extract, according to phytochemical tests. Based on our findings, we hypothesise that *C. langsdori* leaf extract may be useful in preventing kidney stone formation.

DISCUSION:

A balanced diet, lifestyle modifications, and safer medical care are all required to manage kidney stone disease and its recurrence. Finding a single drug that can address each risk factor for Coax stone generation has proven to be the main challenge. Hence, urolithiasis can be managed with the aid of medications that target important risk factors such supersaturation, crystal deposition, and membrane breakdown. and other traditional medicines are used to treat kidney stone illness. Several authors have used the EG model to examine nephrolithiasis in rats with success **[26, 27, 28]**. Several hepatic enzymes convert EG to oxalic acid, precipitating and growing the epithelium of the renal tubules contains insoluble Coax crystals **[29]**. Animals EG exhibit increased water consumption and urination as well as a number of illnesses, including hypercalciuria, hyperoxaluria, hypocitraturia, hypomagnesiuria, and hyperuricosuria **[33]**. Due to these conditions, the pH of the urine is altered and calcium, oxalate, citrate, magnesium, potassium, and uric acid are excreted. A crucial element in crystallization is the oversaturation of urine with Coax **[30]**. Oxalate salts that are soluble when formed with magnesium but insoluble when manufactured with calcium are produced when urine oxalic acid complexes with many cationic salts. This results in the crystalline precipitation of renal calculi of the Coax type **[31]**. Male rats were chosen for the current study because their urinary systems mirror those of men, and because earlier research had found that the amount of stone deposition in female rats was substantially lower **[32]**. One of the common causes of kidney stones is thought to be urinary supersaturation with regard to the substances that can form stones. An accurate predictor of the likelihood of stone formation is the examination of urine for substances that cause stones to form. According to earlier research. The increased urinary calcium is what favors the nucleation, precipitation, and subsequent crystal formation of calcium oxalate from urine **[33]**. Stone formation is significantly slowed down by urinary magnesium (Mg) **[34]**. Both stone-forming rats and people have been found to have low magnesium levels **[35]**.

CONCLUSION:

According to the study's findings, employing various extracts can effectively stop the progression of the condition and prevent the production of kidney stones. Effectively reducing serum buildup of creatinine and urea as well as excessive excretion of calcium, oxalate, phosphate, and citrate in the urine. The data reported above provide evidence for the nephroprotective and antiurolithiatic effects of crude extracts in the treatment of urolithiasis and nepharolithasis. Also, in order to learn more about the many extracts being used to lessen or sustain the activity of renal disorders.

REFERENCES:

[1] Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol. 2005 Nov;16(11):3365-70. [PubMed] [Reference list]

[2] Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X., Beijing Acute Kidney Injury Trial (BAKIT) workgroup. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. Crit Care. 2014 Jul 08;18(4):R144. [PMC free article] [PubMed] [Reference list]

[3] Lindner A, Sherrard DJ. Acute renal failure. N Engl J Med. 1996 Oct 24;335(17):1320-1; author reply 1321-2. [PubMed] [Reference list]

[4] lmirall J. Sodium Excretion, Cardiovascular Disease, and Chronic Kidney Disease. JAMA. 2016 Sep 13;316(10):1112. [PubMed] [Reference list]

[5] Berry, D., Mackenzie, C. Richard Bright 1789-1858: physician in an age of revolution and reform. Royal Society of Medicine Services; 1992.

[6] Heberden, W. Commentaries on the History and Cure of Diseases. London: Payne; 1802.

[7] Abercrombie J. Observations on *Ischuria renalis*. Edinburgh Med J. 1821; 10:210–22. 1821.

[8] Bywaters EG, Beall D. Crush Injuries with Impairment of Renal Function. British medical journal. 1941 Mar 22; 1(4185):427–32. [PubMed: 20783577]

[9] Liano F, Felipe C, Tenorio MT, Rivera M, Abraira V, Saez-de-Urturi JM, *et al*. Long-term outcome of acute tubular necrosis: a contribution to its natural history. Kidney Int. 2007 Apr; 71(7):679–86. [PubMed: 17264879]

[10] Bagshaw SM, George C, Bellomo R., ANZICS Database Management Committe. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. Nephrol Dial Transplant. 2008 May;23(5):1569-7415.

[11] Kaufman J, Dhakal M, Patel B, Hamburger R. Community-acquired acute renal failure. Am J Kidney Dis. 1991 Feb;17(2):191-8. [PubMed]

[12] Correa A, Patel A, Chauhan K, Shah H, Saha A, Dave M, Poojary P, Mishra A, Annapureddy N, Dalal S, Konstantinidis I, Nimma R, Agarwal SK, Chan L, Nadkarni G, Pinney S. National Trends and Outcomes in Dialysis-Requiring Acute Kidney Injury in Heart Failure: 2002-2013. J Card Fail. 2018 Jul;24(7):442-45017.

[13] Garg AX, Kiberd BA, Clark WF, Haynes RB, Clase CM. Albuminuria and renal insufficiency prevalence guides population screening: results from the NHANES III. Kidney Int. 2002 Jun;61(6):2165-75

[14] Dharmalingam SR, Madhappan R, Chidambaram K, Ramamurthy S, Gopal K, Swetha P, Kumar KS. Anti-urolithiatic activity of *Melia azedarach* Linn leaf extract in ethylene glycol-induced urolithiasis in male albino rats. Tropical Journal of Pharmaceutical Research. 2014;13(3):391-7.

[15] Afzal M, Alharbi KS, Alzarea SI, Quazi AM, Zafar A, Patel DM, Patel AB, Trivedi R, Kazmi I, Al-Abaasi FA. Methanolic extract of Cucumis melo attenuates ethylene glycol-induced nephrolithiasis in Wistar rats. Urolithiasis. 2021 Aug;49:301-8.

[16] Sridharan B, Michael ST, Arya R, Mohana Roopan S, Ganesh RN, Viswanathan P. Beneficial effect of Citrus limon peel aqueous methanol extract on experimentally induced urolithic rats. Pharmaceutical biology. 2016 May 3;54(5):759-69.

[17] Bano H, Jahan N, Makbul SA, Kumar BN, Husain S, Sayed A. Effect of *Piper cubeba L.* fruit on ethylene glycol and ammonium chloride induced urolithiasis in male Sprague Dawley rats. Integrative Medicine Research. 2018 Dec 1;7(4):358-65.

[18] Wanjari MM, Sikarwar I, Dey YN, Sharma A, Gaidhani S, Jadhav A. Chenopodium album Linn Leaves Prevent Ethylene Glycol-induced Urolithiasis in Rats. Journal of Ravishankar University. 2016 Jul 1;29(1).

[19] Ingale KG, Thakurdesai PA, Vyawahare NS. Effect of *Hygrophila spinosa* in ethylene

glycol induced nephrolithiasis in rats. Indian journal of pharmacology. 2012 Sep; 44(5): 639.

[20] Pawar AT, Vyawahare NS. Anti-urolithiatic activity of standardized extract of *Biophytum sensitivum* against zinc disc implantation induced urolithiasis in rats. Journal of advanced pharmaceutical technology & research. 2015 Oct;6(4):176.

[21] Alelign T, Tessema TS, Debella A, Petros B. Evaluations of the curative efficacy of *G. fruticosus* solvent extracts in experimentally induced nephrolithiatic Wistar male rats. BMC Complementary Medicine and Therapies. 2021 Dec;21(1):1-4.

[22] Jahan N, Bano H, Makbul SA, Kumar BN, Mushir A. Effect of hydroalcoholic extract of *Cyperus rotundus* L. Rhizome against ethylene glycol and ammonium chloride-induced urolithiasis in male sprague-dawley rats. Urological Science. 2019 May 1;30(3):99.

[23] Zhang H, Li N, Li K, Li P. Protective effect of Urtica dioica methanol extract against experimentally induced urinary calculi in rats. Molecular medicine reports. 2014 Dec 1;10(6):3157-62.

[24] Patel PK, Patel MA, Saralai MG, Gandhi TR. Antiurolithiatic effects of *Solanum xanthocarpum* fruit extract on ethylene-glycol-induced nephrolithiasis in rats. Journal of Young Pharmacists. 2012 Jul 1;4(3):164-70.

[25] Oliveira RB, Coelho EB, Rodrigues MR, Costa-Machado AR, Sousa JP, Berretta AA, Bastos JK. Effect of the *Copaifera langsdorffii* Desf. leaf extract on the ethylene glycol-induced nephrolithiasis in rats. Evidence-Based Complementary and Alternative Medicine. 2013 Jan 1;2013.

[26] Y. Itoh, T. Yasui, A. Okada, K. Tozawa, Y. Hayashi, and K. Kohri, "Preventive effects of green tea on renal stone formation and the role of oxidative stress in nephrolithiasis," The Journal of Urology, vol. 173, no. 1, pp. 271–275, 2005.

[27] M. Asselman, A. Verhulst, M. E. de Broe, and C. F. Verkoelen, "Calcium oxalate crystal adherence to hyaluronan-, osteopontin-, and CD44-expressing injured/ regenerating tubular epithelial cells in rat kidneys," Journal of the American Society of Nephrology, vol. 14, no. 12, pp. 3155–3166, 2003.

[28] S. R. Khan, "Animal models of kidney stone formation: an analysis," World Journal of Urology, vol. 15, no. 4, pp. 236–243, 1997.

[29] R. A. Corley, M. E. Meek, and E. W. Carney, "Mode of action: oxalate crystal-induced renal tubule degeneration and glycolic acid-induced dysmorphogenesis—renal and developmental effects of ethylene glycol," Critical Reviews in Toxicology, vol. 35, no. 8-9, pp. 691–702, 2005.

[30] Rushton HG, Spector M, Rodgers AL, Magura CE. Crystal deposition in the renal tubules of hyperoxaluric and hypomagnesemic rats. Scan Electron Microsc 1980;(3):387-94, 398.

[31] Akanae W, Tsujihata M, Yoshioka I, Nonomura N, Okuyama A. *Orthosiphon grandiflorum* has a protective effect in a calcium oxalate stone forming rat model. Urol Res 2010;38:89-96

[32] Selvam R, Kalaiselvi P, Govindaraj A, Murugan V, Sathishkumar AS. Effect of *A. lanata* leaf extract and *Vediuppu chunnam* on the urinary risk factors of calcium oxalate urolithiasis during experimental hyperoxaluria. Pharmacol Res. 2001; 43:89–93.

[33] J Lemann, EM Worcester, RW. Gray Hypercalciuria and stones Am J Kidney Dis, 17 (1991), pp. 386-391

[34] K Divakar, AT Pawar, SB Chandrasekhar, SB Dighe, G. Divakar Protective effect of the hydro-alcoholic extract of Rubia cordifolia roots against ethylene glycol induced urolithiasis in rats Food Chem Toxicol, 48 (2010), pp. 1013-1018

[35] P Soundarajan, R Mahesh, T Ramesh, VH. Begum. Effect of *Aerva lanata* on calcium oxalate urolithiasis in rats Indian J Exp Biol, 44 (2006), pp. 981-986