

Evaluation of Anti-Urolithiatic potential of the Siddha formulation Kalladaippu Chooranam in Ethylene glycol induced urolithiasis in rats

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Abstract

Urolithiasis is the third prevalent disorder of the urinary system. It may cause serious medical consequences such as extreme obstruction, hydronephrosis, infection, and hemorrhage in the urinary tract system. The major drawback of clinical management of renal calculi is its reoccurrence rate. Currently available stone removal techniques like extracorporeal shock wave lithotripsy (ESWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PNL), are considered to be costly, making them an option of choice for limited number of patients. Siddha is one of the ancient medical systems in India considered as the mother medicine of ancient Tamils/Dravidians in South India. The word Siddha means established truth or "one who is accomplished" and refers to perfected masters who according to Hindu belief have transcended the ahamkara (ego or I-maker), have subdued their minds to be subservient to their awareness, and have transformed their bodies composed mainly of dense Rajotama gunas into a different kind of bodies dominated by sattva. The main objective of the present research work is to evaluate the anti-urolithiatic potential of the Siddha formulation Kalladaippu Chooranam (KC) against ethylene glycol (EG) induced urolithiasis in Wistar rats. Induction of urolithiasis in experimental animals carried out by administering ethylene glycol (EG) 0.75% in drinking water for a period of 28 days followed by single dose of sodium oxalate injection (35 mg/kg, i.p) on 14th day of induction. It was observed from the study that administration of EG in drinking water resulted in increased level of serum calcium, creatinine, uric acid, oxalate and phosphate level in the experimental animals. Results on urine investigation reveals similar pattern of increase in urine calcium, creatinine, uric acid, oxalate and phosphate. Estimation of urine volume has shown tremendous decrease in urine volume of EG treated rats. Treatment with KC at the dose of 100 and 200 mg/kg shown marked decrease in uric acid, creatinine, oxalate and phosphate level both in serum and urine samples of group II when compared to that of the EG alone treated rats. From the data's obtained from the present study it was evident that the Siddha formulation Kalladaippu Chooranam possesses significant anti-urolithiatic property and may be used for clinical management of renal calculi.

Keywords: Urolithiasis, Renal calculi, Siddha, Kalladaippu Chooranam, Ethylene glycol, Creatinine, Uric acid.

1. Introduction

Urolithiasis, urinary stone formation, is the third most common problem of the urinary tract, sparing no geographical, racial and cultural boundaries and is associated with high rate of recurrence [1,2]. Calcification is a multifactorial phenomenon [3], developing as a result of a cascade of events initiated by supersaturation, including crystal nucleation, growth, aggregation and retention [4]. Various crystal inhibitors like potassium-sodium citrate and magnesium oxide have been shown to decrease the saturation of CaOx and inhibit crystal nucleation, growth and aggregation, while reduced crystallization in urine of stone forming patients [5]. Interference with crystal growth and aggregation therefore seems a possible therapeutic strategy for the prevention of recurrent stone disease.

An imbalance between urinary stone promoting and inhibiting factors is predominantly responsible for the formation of renal stones [6], which is a multistep process involving nucleation, crystal growth, aggregation and finally retention of crystals [7]. The current treatment strategies for urolithiasis include shockwave lithotripsy, ureteroscopy and percutaneous stone extractions. However, these treatments are wrought with various side effects. When coupled with the high recurrence rate of stone formation (over 50% in 10 years [8]), it strongly calls for new treatment options.

Herbs have been used as traditional healthcare system from the centuries. The WHO has listed 20,000 medicinal plants globally in which contribution of India is 15–20% [9]. The WHO reported that 80% of global countries depend on the medicinal plants [10]. A large body of evidence has collected to show potential of medicinal plants used in various traditional systems. In the last few years more than 13 000 plants have been studied for the various diseases and ailments all over the world [11]. Kidney stones are also major disorders prevailing all over the world. About 75% of kidney stones are composed of calcium oxalate crystals [12].

Siddha formulations are considerably safe and efficacy as it renders both therapeutic and prophylactic against several dreadful disorders. Herbs and minerals has become an integral part of the siddha system of medicine. Kalladaippu Chooranam (KC) is one such novel preparation comprises of purified Padigaram, Purified Venkaram, Purified Induppu, Purified Savukkaram, Nayuruvi, Panaingathir and Vaazhai Mattai. All these listed ingredients are known best remedies for urolithiasis as per vedic and recommended siddha text books. The main aim of the present research work is to evaluate the anti-urolithiatic potential of the formulation KC in ethylene glycol induced experimental urolithiasis model.

2. Materials and Methods

Urolithiasis, urinary stone formation, is the third most common problem of the urinary tract, sparing no geographical, racial and cultural boundaries and is associated with high rate of recurrence [1,2]. Calcification is a multifactorial phenomenon [3], developing as a result of a cascade of events initiated by supersaturation, including crystal nucleation, growth, aggregation and retention [4]. Various crystal inhibitors like potassium-sodium citrate and magnesium oxide have been shown to decrease the saturation of CaOx and inhibit crystal nucleation, growth and aggregation, while reduced crystallization in urine of stone forming patients [5]. Interference with crystal growth and aggregation therefore seems a possible therapeutic strategy for the prevention of recurrent stone disease.

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3. Results

3.1. Effect of *Kalladaippu Chooranam* on routine Urine volume in ml on 0th, 14th & 28th day

Result analysis of total urine volume on 0th, 14th and 28th days reveals that the total volume of urine output seems significantly decreased in ethylene glycol treated rats. Treatment with *Kalladaippu Chooranam* at both the dose level has significantly increased the urine volume when compare to that of the disease control group.

Table 1: Effect of *Kalladaippu Chooranam* on routine Urine volume in ml on 0th, 14th & 28th day

Days	Group I	Group II	Group III	Group IV	Group V
0	7.72±1.24	7.54±2.12	7.82±2.21	7.66±2.42	8.52±1.56
14	7.79±3.22	6.89±1.22	8.32±1.86	9.10±1.32	11.20±1.66
28	8.30±4.10	6.28±2.11	8.58±1.24	10.22±1.46	11.90±1.82

Values are expressed as mean ± SEM, Values were calculated by using One Way Anova

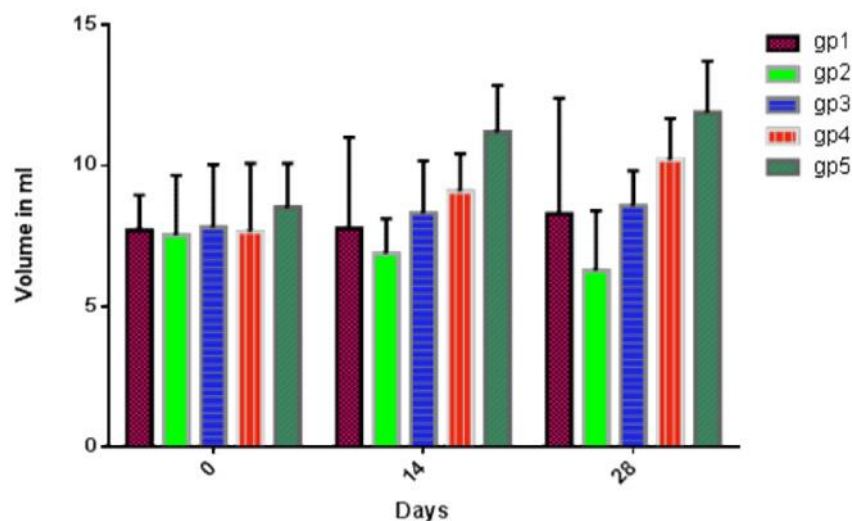


Figure 1: Results of routine Urine volume in ml on 0th, 14th & 28th day

3.2. Effect of *Kalladaippu Chooranam* on urine Biochemistry analysis on 14th day

Result analysis of the urine biochemistry on 14th days reveals that the level of calcium, uric acid, creatinine, oxalate and phosphate level were elevated significantly. Treatment with

Kalladaippu Chooranam at both the dose level has significantly decrease such parameters when compare to that of the group II rats. Whereas the levels of magnesium were significantly increased in treatment groups when compare to that of the disease control group.

Table 2: Effect of *Kalladaippu Chooranam* on urine Biochemistry analysis on 14th day

Group	Mg+ (mg/dl)	Ca+ (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)	Oxalate (mg/dl)	Phosphate (mg/dl)
Group I	4.35±.64	5.69±0.46	8.19±1.45	0.82±0.12	16.54±2.22	36.10±1.12
Group II	1.10±4.62	26.12±1.42	16.44±1.72	1.61±0.22	30.24±2.54	76.2±2.84
Group III	2.65±1.04	18.76±1.32	9.86±2.04	0.89±3.24	23.21±1.42	47.20±2.12
Group IV	2.62±1.24	16.85±1.24	9.96±1.10	0.86±0.09	24.40±1.68	34.20±1.12
Group V	3.32±1.46	15.42±1.20	8.89±3.04	0.79±1.42	19.18±1.10	34.89±1.08

Values are expressed as mean ± SEM, Values were calculated by using One Way Anova

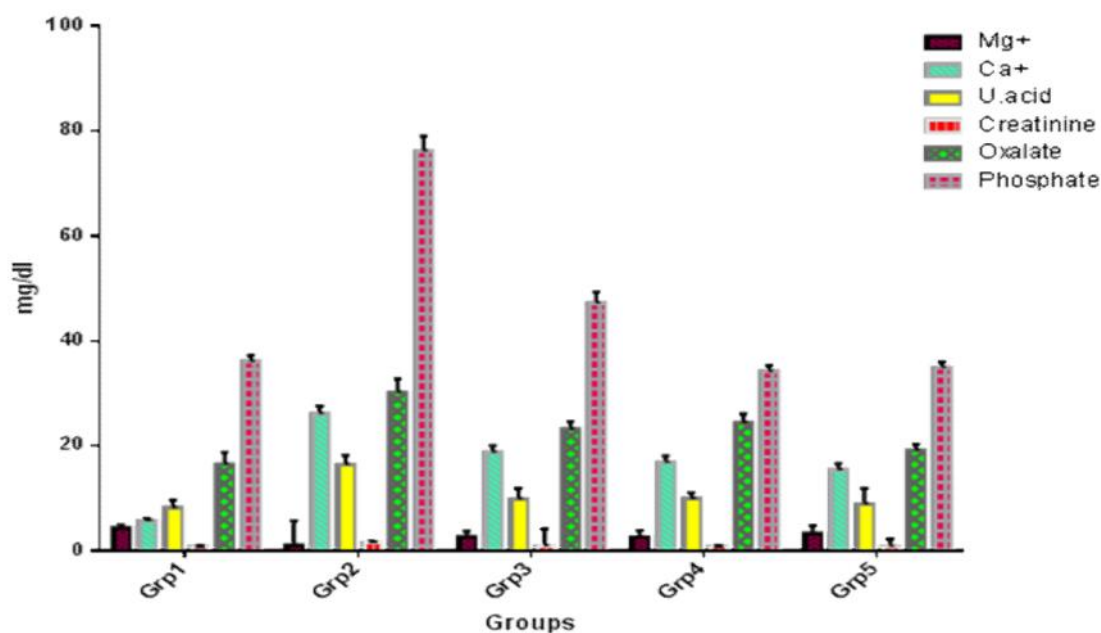


Figure 2: Results of urine biochemistry analysis on 14th day

3.3. Effect of *Kalladaippu Chooranam* on urine Biochemistry analysis on 28th day

On 28th day of treatment the result analysis of the urine biochemistry reveals that the level of calcium, uric acid, creatinine, oxalate and phosphate level were elevated significantly.

Treatment with *Kalladaippu Chooranam* at both the dose level has significantly decrease such parameters when compare to that of the group II rats. Whereas the level of magnesium were significantly increased in treatment groups when compare to that of the disease control group.

Table 3: Effect of *Kalladaippu Chooranam* on urine Biochemistry analysis on 28th day

Group	Mg+ (mg/dl)	Ca+ (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)	Oxalate (mg/dl)	Phosphate (mg/dl)
Group I	4.20±0.56	7.6±0.24	4.1±1.54	0.87±0.32	18.64±1.12	30.10±1.56
Group II	1.88±1.32	28.14±1.22	19.42±1.52	1.61±0.42	56.24±1.64	84.2±1.62
Group III	2.02±1.20	19.16±1.22	8.36±1.14	1.13±2.12	27.42±1.20	48.22±1.10
Group IV	3.65±1.10	11.64±1.14	7.86±0.64	1.02±0.24	22.32±1.42	44.20±2.10
Group V	3.12±1.41	09.12±1.08	7.19±3.04	0.80±1.36	18.26±1.21	32.60±1.04

Values are expressed as mean ± SEM, Values were calculated by using One Way Anova

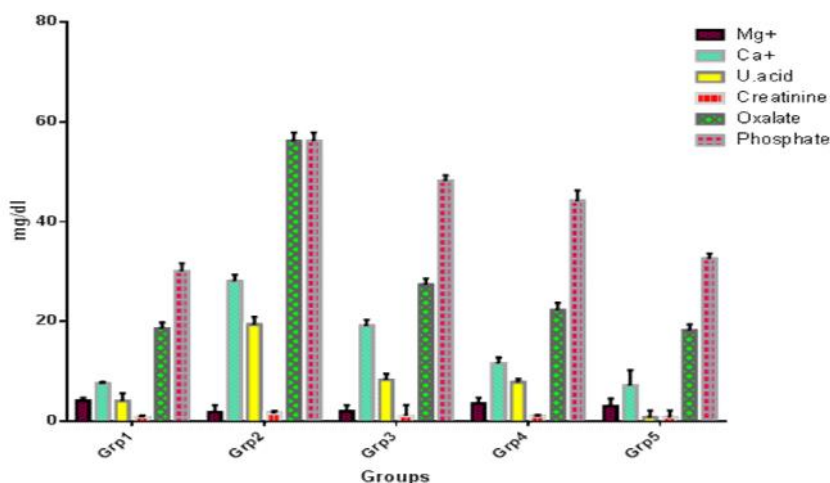


Figure 3: Results of urine biochemistry analysis on 28th day

3.4.Effect of *Kalladaippu Chooranam* on serum profile on 28th day

It was evident from the results of the serum analysis that the calcium, uric acid, creatinine,

oxalate and phosphate level were elevated significantly. Treatment with *Kalladaippu Chooranam* at both the dose level has significantly decrease such parameters when compare to that of the group II rats.

Table 4: Effect of *Kalladaippu Chooranam* on serum profile on 28th day

Group	Mg+ (mg/dl)	Ca+ (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)	Oxalate (mg/dl)	Phosphate (mg/dl)
Group I	4.96±1.14	10.62±1.18	3.24±1.15	0.48±0.21	6.54±1.62	13.10±1.28
Group II	2.01±1.22	19.12±2.44	9.24±1.12	1.31±0.20	13.64±1.44	31.2±1.48
Group III	3.98±1.04	13.76±1.02	4.86±1.24	0.79±1.14	09.21±1.32	27.20±1.20
Group IV	3.86±0.24	12.85±1.40	3.86±1.24	0.56±0.12	09.40±1.72	20.10±1.10
Group V	4.52±1.48	09.12±0.20	3.09±1.02	0.49±1.04	7.08±1.08	14.89±1.28

Values are expressed as mean ± SEM, Values were calculated by using One Way Anova

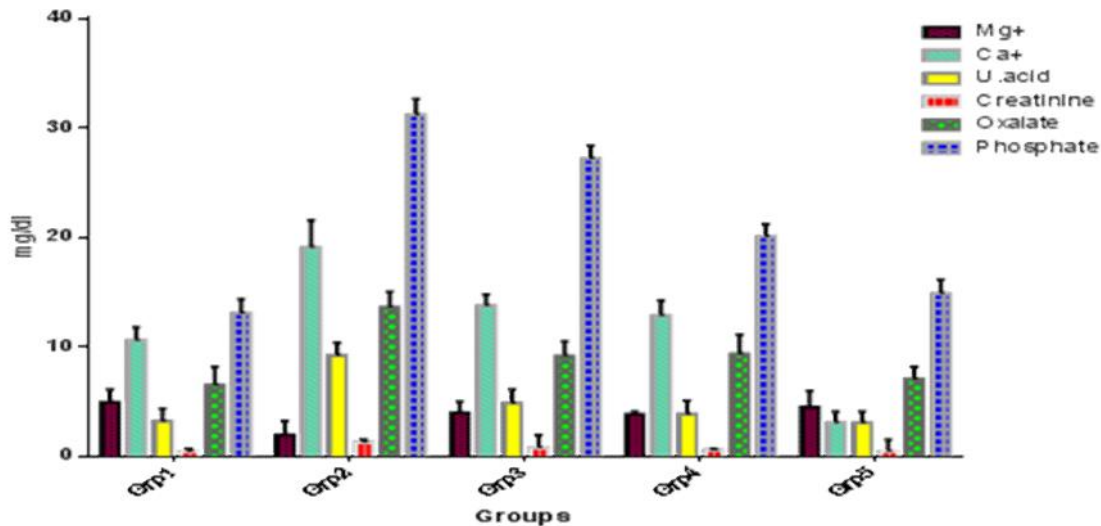


Figure 4: Results of serum analysis on 14th day

4. Discussion

Urinary stones have afflicted humankind since antiquity and can persist with serious medical consequences throughout a patient's lifetime. Kidney stone formation or urolithiasis is a complex process that results from a succession of several physico-chemical events including supersaturation, nucleation, growth, aggregation, and retention within the renal tubule [16]. The incidence of kidney stones has increased worldwide in the last five decades in association with the economic development. Epidemiological data collected during several decades shows that the majority of stones in the urinary system arise from a common component of urine, viz. calcium oxalate (CaOx), representing up to 80% of analyzed stones [17]. Currently, open renal surgery for nephrolithiasis is unusual and rarely performed since the introduction of extracorporeal shockwave lithotripsy (ESWL), which has become the standard procedure for eliminating kidney stones.

The most consistent feature of urolithiasis is the formation and retention of stone (s) in various parts of urinary tract, the kidney, ureter, and bladder wherein the size and type of calculi vary significantly. As per the statistical data reported 12% of world population is affected with urolithiasis. The prevalence is more in the

working class between the age group of 25–50. It occurs more in men as compared to women, may be because of enhancing testosterone and inhibitory property of estrogen in the pathogenesis of uroliths [18].

Result analysis of total urine volume on 0th, 14th and 28th days reveals that the total volume of urine output seems significantly decreased in ethylene glycol treated rats. Treatment with *Kalladaippu Chooranam* at both the dose level has significantly increased the urine volume when compare to that of the disease control group. On 28th day of treatment the result analysis of the urine biochemistry reveals that the level of calcium, uric acid, creatinine, oxalate and phosphate level were elevated significantly. Treatment with *Kalladaippu Chooranam* at both the dose level has significantly decrease such parameters when compare to that of the group II rats. Whereas the level of magnesium were significantly increased in treatment groups when compare to that of the disease control group. It was evident from the results of the serum analysis that the calcium, uric acid, creatinine, oxalate and phosphate level were elevated significantly. Treatment with *Kalladaippu Chooranam* at both the dose level has significantly decrease such parameters when compare to that of the group II rats.

5. Conclusion

Siddha system of medicine empowers the art of healing which was proven from the data's obtained from the present study. There was a significant increase in the levels of calcium, uric acid, creatinine, oxalate and phosphate level in ethylene glycol alone treated rats. Treatment with *Kalladaippu Chooranam* at both the dose level has significantly decrease such parameters when compare to that of the group II rats. It was concluded from the results that siddha formulation *Kalladaippu Chooranam* possess significant ameliorative action against ethylene glycol induced urolithiasis in the treated rats. Hence it may be proven that the formulation KC could be considered a first line drug of choice for clinical management of urolithiasis.

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