



PRECLINICAL EVALUATION OF ANTI UROLITHIATIC ACTIVITY OF THE POLYHERBAL FORMULATION 'RENSOL'

Pharmacology

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ABSTRACT

The present study was carried out to evaluate the anti urolithiatic activity of the polyherbal formulation Rensol. Models used in this study were sodium oxalate induced urolithiasis and ethylene glycol induced urolithiasis in wistar rats. Both doses of rensol showed statistically significant anti urolithiatic activity.

KEYWORDS

anti urolithiatic, rensol, rats

INTRODUCTION

When urine (which contains minerals and salts) becomes concentrated, then stones are formed in kidney. These stones can stay in kidney or can travel down, through the urinary tract and in the process gets stuck over there and cause pain. It can also block the flow of urine and aggravate pain, bleeding¹.

One of the most common disorders of the urinary tract is the kidney stone disorder. In India approx 5-7 million people suffer from kidney stone disease².

Some of the allopathic medicines which are used in the treatment of kidney stones are thiazide, sodium cellulose phosphate, allopurinol, potassium citrate, penicillamine, ketorolac etc. But these drugs carries various side effects too such as dizziness, weakness, convulsions, loss of appetite, rashes, fever, joint pain, abdominal discomfort, vomiting, diarrhea, ulcers, shortness of breath, skin rashes, rapid weight gain etc^{3,4}.

Hence naturally available alternatives are needed to find out. Pharmacological therapy for kidney stones using medicinal plants has been increasingly adopted because of the above reasons⁵.

Herbal medications provide a wide range of advantages over allopathic medicines. They are cost effective, and do not require any surgery or hospitalization. They are known to have lesser side effects and are usually well tolerated compared to allopathic medications. Herbal medications are also easily available and accessible to populations⁶.

Polyherbal formulations are extensively used as they are relatively patient friendly, have lesser side effects etc. Polyherbal exploits combining of several medicinal herbs to achieve extra therapeutic effectiveness. Most of the polyherbal products available are widely used but are not scientifically validated yet^{7,8,9,10}.

Rensol (Sagar Pharmaceuticals, Bangalore) is a polyherbal formulation which contain *Emblica officinalis*, *Dolichos biflorus*, *Berginia cilata*, *Crataeva nurvala*, *Piper longum* and *Hordeum vulgare*. No scientific report is available as of now for its combined anti urolithiatic potential. Hence, the present study is aimed to investigate the anti urolithiatic activity of the polyherbal formulation Rensol.

ANIMALS, DRUGS, DOSAGE, CHEMICALS

Wistar male rats were housed in standard environmental conditions at 25±5°C, relative humidity 50±5% in a well-ventilated animal house under 12 hour day and night cycle. CPCSEA guidelines were followed. Institutional animal ethics committee (IAEC) approved the experiment.

The dose of Rensol was calculated from human dose by using dose conversion formula. Accordingly low and high doses were found out to be 100 mg/kg and 200 mg/kg body weight respectively¹¹.

Thiazide was selected as standard and its dose was selected as 150µg/kg¹².

Rest of the chemicals, reagents, biochemical kits used were of/from analytical/laboratory pure grade/standard companies.

METHODOLOGY

Sodium oxalate induced urolithiasis^{13,14,15,16}

Male wistar rats were selected and made into 5 groups of 6 animals each. Group 1 served as normal and received regular rat food and drinking water ad libitum. Group II received sodium oxalate i.p. for 7 days to induce renal calculi. Groups III, IV, V received the same above. Group III and IV received Rensol at low and high doses respectively from day 1-7. Group V received standard drug thiazide from day 1-7. The parameters which were evaluated were, in urine (calcium, phosphate, oxalate, uric acid) and kidney homogenate (calcium, phosphate, oxalate, uric acid).

Ethylene glycol induced urolithiasis^{14,16,17,18,19}

Wistar male rats were divided into 5 groups of 6 animals each. Group 1 served as normal and received regular rat food and drinking water ad libitum. Ethylene glycol (0.75 %) was fed to groups II-V to induce renal calculi for 28 days. Group III and IV received Rensol at low and high doses respectively from day 15 - day 28. Group V received standard drug thiazide from day 15 - day 28. All administrations were done orally and were given once daily. Same parameters as in above were evaluated.

STATISTICAL ANALYSIS

Statistical analysis was done using Graph pad Prism version 4 software (Graph Pad Inc, USA). ANOVA followed by Bonferroni's multiple comparison test (compare all) was applied. Data was presented as MEAN ± SEM. Confidence level was taken as 95%.

RESULTS

Sodium Oxalate Induced Urolithiasis

Treatment with Rensol brought an extremely significant (p<0.001) decrease in the urine parameters (calcium, phosphate, uric acid) levels and moderately significant (p<0.01) decrease in urine oxalate level when compared to its diseased group. See table 1.

Treatment with Rensol brought a moderately significant (p<0.01) decrease in kidney parameters (calcium, phosphate, oxalate, uric acid) levels when compared to its diseased group. See table 2.

Ethylene glycol induced urolithiasis

Treatment with Rensol brought an extremely significant (p<0.001) decrease in urine parameters (calcium, phosphate, oxalate, uric acid) levels when compared to its diseased group. See table 3.

Treatment with Rensol brought a moderately significant (p<0.01) and extremely significant (p<0.001) decrease in kidney (calcium level and

phosphate, oxalate, uric acid levels) respectively when compared to its diseased group. See table 4.

DISCUSSION

The anti urolithiatic effect of Rensol was studied in rats by inducing urolithiasis using various toxic substances like ethylene glycol and sodium oxalate¹³⁻¹⁹.

Sodium oxalate causes tubular obstruction. Its administration results in hyperoxaluria. This is an important risk factor, in the mechanism of formation of renal stones. Ethylene glycol causes tubular injury and interstitial inflammation. It causes stone formation due to hyperoxaluria. This causes an increase in renal retention and excessive excretion of oxalate in urine. This results in increased urinary phosphate excretion and oxalate stress. This creates a good environment for stone formation by forming calcium phosphate crystals. This causes calcium oxalate deposition. Inducing agents (sodium oxalate, ethylene glycol) induce lipid peroxidation, decrease the antioxidant potential and in turn damage the renal tissue^{12,15,16}.

In all the experimental models of the present study, the polyherbal formulation Rensol showed anti urolithiatic activity. This might be because of the presence of mainly phenols, phytosterols, alkaloids, terpenoids, flavonol glucosides, polyphenols, flavonoids, tannins and glycosides. Rensol is showing anti urolithiatic activity.

CONCLUSION

From the findings of the present study, it can be concluded that Rensol has significant anti urolithiatic activity.

TABLES

Values are expressed as MEAN±SEM. n=6. *p<0.05, **p<0.01, ***p<0.001 when compared to normal group. #p<0.05, ##p<0.01, ###p<0.001 when compared with diseased group.

Table 1. Effect of Rensol on urine parameters in sodium oxalate induced urolithiasis

Treatment	Calcium (mg/g)	Phosphate (mg/g)	Oxalate (mg/g)	Uric acid (mg/g)
Normal	5.67±0.29	3.19±0.31	1.85±0.14	0.28 ± 0.09
Diseased	13.89±0.74 ***	8.97±0.56 ***	2.97±0.28 ***	4.62±0.28 ***
Low dose rensol	9.28±0.47 ###	4.11±0.48 ###	2.01±0.26 ###	2.25±0.22 ###
High dose rensol	8.37±0.42 ###	3.96±0.44 ###	1.99±0.23 ###	1.71±0.18 ###
Standard	7.14±0.38 ###	3.81±0.40 ###	1.91±0.21 ###	1.13±0.14 ###

Table 2. Effect of Rensol on kidney parameters in sodium oxalate induced urolithiasis

Treatment	Calcium (mg/g)	Phosphate (mg/g)	Oxalate (mg/g)	Uric acid (mg/g)
Normal	4.27±0.32	3.43±0.39	2.54±0.31	1.82±0.10
Diseased	6.84±0.68 **	6.71±0.68 ***	5.83±0.54 ***	4.96±0.29 ***
Low dose rensol	5.80±0.59 ###	5.01±0.59 ###	4.07±0.48 ###	3.23±0.22 ###
High dose rensol	5.10±0.48 ###	4.22±0.51 ###	3.76±0.41 ###	2.84±0.19 ###
Standard	4.90±0.44 ###	3.92±0.46 ###	3.18±0.36 ###	2.36±0.15 ###

Values are expressed as MEAN±SEM. n=6. *p<0.05, **p<0.01, ***p<0.001 when compared to normal group. #p<0.05, ##p<0.01, ###p<0.001 when compared with diseased group.

Table 3. Effect of Rensol on urine parameters in ethylene glycol induced urolithiasis

Treatment	Calcium (mg/g)	Phosphate (mg/g)	Oxalate (mg/g)	Uric acid (mg/g)
Normal	5.8±0.29	3.25±0.26	2.0±0.10	0.4±0.09
Diseased	14.1±0.69 ***	9.12±0.68 ***	3.40±0.31 ***	4.8±0.28 ***
Low dose rensol	9.4±0.54 ###	4.90±0.54 ###	2.3±0.26 ###	2.35±0.21 ###
High dose rensol	8.6±0.48 ###	4.10±0.42 ###	2.2±0.19 ###	1.9±0.16 ###
Standard	7.3±0.39 ###	3.9±0.35 ###	2.1±0.75 ###	1.2±0.13 ###

Table 4. Effect of Rensol on kidney parameters in ethylene glycol induced urolithiasis

Treatment	Calcium (mg/g)	Phosphate (mg/g)	Oxalate (mg/g)	Uric acid (mg/g)
Normal	3.80±0.24	3.24±0.14	2.73±0.12	2.10±0.12
Diseased	7.10±0.62 ***	6.92±0.24 ***	5.98±0.26 ***	5.2±0.26 ***
Low dose rensol	4.98±0.55 ###	4.98±0.20 ###	4.21±0.22 ###	3.45±0.22 ###
High dose rensol	4.55±0.50 ###	4.52±0.18 ###	3.98±0.19 ###	2.97±0.18 ###
Standard	4.20±0.42 ###	4.12±0.17 ###	3.32±0.15 ###	2.46±0.15 ###

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