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Urolithic property of *Varuna (Crataeva nurvala)*: An experimental study

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Abstract

Despite modern techniques, the recurrence rate of Urolithiasis is approximately 50% within 5 years. Thus, there must be some drug that corrects the metabolic errors and prevents the formation of stone. In Ayurveda, a detailed description of urolithiasis is mentioned under the heading of *Ashmari*. A group of Ayurvedic drugs are described for the management of Urolithiasis, like *Pashanbheda* (*Bergenia ligulata*), *Varuna* (*Crataeva nurvala*), *Kullattha* (*Dolichos biflorus*), *Gokshur* (*Tribulus terrestris*), etc. in our ancient texts. The present work was designed to study the effect of *Varuna* (*Crataeva nurvala*) on the experimental model of urolithiasis (albino rats). The study was categorized into two groups: Group I, treated and Group II, control. In all albino rats, stone was surgically implanted into the urinary bladder. Estimation of the urinary and serum electrolyte done periodically and x-rays were exposed at a regular interval. This study suggests the decoction of *Varuna* (*Crataeva nurvala*) is effective in the management of urolithiasis.

Key words: *Gokshur, kullattha, Pashanbheda*, urolithiasis, *Varuna*

Introduction

Urolithiasis is a problematic condition, especially with regards to its treatment, in all the systems of medical sciences. In the system of modern medicine, which is supposed to be the most advanced and highly scientific system, the problem of urolithiasis has no satisfactory answer. Despite modern techniques, the recurrence rate of Urolithiasis is approximately 50% within 5 years.[1] The only rational treatment in this therapy is surgical removal or lithotripsy of the stone. But, this does not stop the formation of a subsequent stone. Thus for, there is no drug or therapy known that would dissolve or fragment the stone in the system by changing the lithogenic potential of a particular person.

In Ayurveda, urinary stone diseases have been described in detail under the heading of *Ashmari*. *Sushrut*, "The Father of Surgery," being a surgeon himself has described in detail its etiopathogenesis, symptomatology, medical and surgical treatment and prognosis separately.

In Ayurveda, a number of drugs have been described that are very effective against urolithiasis, namely *Shatavari*, *Gokshur*, *Varuna*, *Shilajeet*, etc. In the present work, an attempt has been made to determine the effect of *Varuna* (*Crataeva nurvala*) on the metabolic correction or on serum as well as urinary electrolytes in the experimental model, i.e. in albino rats.

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Materials and Methods

Study design

This study was an open, experimental trial and was designed in the following two phases:

1. Pre-experimental study for 1 month
2. Experimental study of 3 months

Experiment no. 1

Objectives: To determine the pre-experimental normal serum electrolyte and urinary electrolyte values and variations.

To obtain the pre-experimental normal values of urinary output, 24 h water intake and pH of 24 h urine sample.

Experiment no. 2

Objectives: Experimental production of vesicle calculus by implanting glass beads in the urinary bladder of albino rats and to observe the effect of the drug on the formation and growth of the vesicle calculus.

To determine the effect of the drug on the serum and urinary electrolytes.

The experimental study in the present work was carried out in 18 albino rats of either sex, with a weighting range between 225 and 250 g. They were divided into two groups, with nine rats in each

group, termed as control and treated. A balanced diet of 10–15 g/day and water for drinking were provided to all albino rats. The whole study was carried out for 90 days.

Drug: The drug *Varuna Kashaya* (decoction) was used in this study.

The dose for the study was selected by converting the human dose to animal dose on the basis of body surface area ratio by referring to the table of Paget and Barnes (1969).[2]

Human dose × conversion factor (0.018) for rat = "x"/200 g

i.e., 0.9 ml/100 g body weight of albino rat.

Method of collection of urine
Urine was collected in the experimental cage.

Method of collection of blood sample
Blood was collected by puncturing the optic artery through the capillary tube.

Method of producing urinary stone
Measured glass beads, approximately uniform in size (1.5–2.0 mm in diameter) and shape, with a weight in the range of 9–10 mg, were implanted into the urinary bladder of each rat. From the third post-operative day, the rats of the control group were started on treatment with a calculated 2.25 ml dose of distilled water in a single dose per day, whereas the rats of the treated group were provided with a calculated 2.25 ml dose of *Varuna Kashaya* in a single dose per day by adopting the method described earlier.

For the estimation of serum electrolyte (calcium, phosphorus), serum creatinine and serum phosphorus in the pre-experimental animals, the amount of blood was collected by puncturing the optic artery through the capillary tube.[3] This was repeated at least three times at an interval of 10 days.

The total experiment was carried out up to 90 days after implantation of the glass beads and the estimation of serum and urinary electrolytes was performed periodically at an interval of 15 days.

Observation

Table 1 shows that the mean urinary output was 9.19 ml/24 h. The variation in urinary pH was 8.0–9.0 and the mean observed value of urinary pH was 8.33.

Table 2 and Figure 1 show the mean values of water intake, urine output and urinary pH in the pre-experimental animals and in the control and the treated groups.

Serum and urinary electrolytes
Table 3 shows that the mean value of serum creatinine, calcium, phosphorus and uric acid in the pre-experimental albino rats were 0.55 mg%, 10.79 mg%, 4.50 mg% and 2.55 mg%, respectively.

Table 4 and Figure 2 show that the mean standard value of serum creatinine, calcium, phosphorus and uric acid were 0.30 mg%, 10.70 mg%, 5.20 mg% and 1.44 mg%, respectively.

Urinary electrolytes
Table 5 shows that the mean value of urinary excretions of urinary creatinine, calcium, phosphorus and uric acid in the pre-experimental albino rats were 0.31 mg/24 h, 11.09 mg/24 h, 5.12 mg/24 h and 38.23 mg/24 h, respectively.

Table 6 and Figure 3 show that the mean standard value of urinary creatinine, calcium, phosphorus and uric acid were 0.40 mg/24 h, 11.20 mg/24 h, 5.26 mg/24 h and 37.40 mg/24 h, respectively.

Table 7 shows the mean values of excretion of urinary creatinine, calcium, phosphorus and uric acid with reference to urinary output in the pre-experimental, control and treated groups.

Effect of drug on the implanted glass beads in the control and the treated groups
The progress of stone formation in the urinary bladder was assessed during the period of the experiment by studying the albino rats exposed to X-rays on the 30th, 60th and 90th days in the control and the treated groups.

The above table shows that in the control group, of the nine rats, one rat was found dead probably due to post-operative complications or due to environmental factors. Therefore, assessment was made only on the observation of eight rats. At the end of the experiment, stones were formed in five albino rats by deposition of crystals over the glass beads. Apart from this, all the albino rats were sacrificed at the end of 90 days of the experiment and stones were collected by suprapubic cystolithotomy.

All the stones got dried and the weight of individual stones was taken. In the control group, the mean weight of the glass beads was 9.66 mg and the mean weight of the stone formed was

Table 1: Water intake, urine output and urinary pH in the pre-experimental albino rats

Parameter	10th day	20th day	30th day	Mean of observed values
Mean water intake (ml/24 h)	24.72	27.40	29.80	27.30
Mean urinary output (ml/24 h)	8.03	9.96	9.60	9.19
Mean urinary pH	8.0	8.0	9.0	8.33

Table 2: Comparison of the mean water intake, mean urinary output and mean urinary pH in different groups

Parameters	Mean value		
	Pre-experimental	Control group	Treated group
Water intake (ml/24 h/albino rat)	27.30	29.68	31.94
Urine output (ml/24 h/albino rat)	9.19	7.32	10.03
Urinary pH	8.33	8.25	8.29

Table 3: Estimation of serum creatinine, calcium, phosphorus and uric acid in the pre-experimental albino rats

Parameter	Mean value (mg%)			Mean of observed values (mg%)
	10th day	20th day	30th day	
Serum creatinine	0.55	0.82	0.30	0.55
Serum calcium	10.65	11.02	10.70	10.79
Serum phosphorus	4.50	3.80	5.20	4.5
Serum uric acid	3.20	3.00	1.44	2.55

Table 4: Effect of drug on serum electrolytes in the pre-experimental, control and treated groups

Serum electrolytes	Mean value (mg%)		
	Pre-experimental	Control group	Treated group
Creatinine	0.30	0.31	0.27
Calcium	10.70	10.25	9.66
Phosphorus	5.20	5.96	3.66
Uric acid	1.44	1.49	1.45

Table 5: Estimation of urinary creatinine, calcium, phosphorus and uric acid in the pre-experimental albino rats

Parameter	Mean value (mg/24 h)			Mean of observed values (mg/24 h)
	10th day	20th day	30th day	
Urinary creatinine	0.27	0.25	0.40	0.31
Urinary calcium	10.62	11.46	11.20	11.09
Urinary phosphorus	4.37	5.74	5.26	5.12
Urinary uric acid	38.27	39.02	37.40	38.23

Table 6: Effect of drug on urinary electrolytes in the pre-experimental, control and treated groups

Urinary electrolytes	Mean value (mg/24 h)		
	Pre-experimental	Control group	Treated group
Creatinine	0.40	0.47	0.27
Calcium	11.20	10.80	13.12
Phosphorus	5.26	6.84	8.10
Uric acid	37.40	37.86	38.06

Table 7: Effect of drug on urinary electrolytes in the pre-experimental, control and treated groups with reference to urinary output (mg/ml)

Urinary electrolytes	Mean value (mg/ml)		
	Pre-experimental	Control group	Treated group
Creatinine	0.04	0.06	0.02
Calcium	1.21	1.47	1.30
Phosphorus	0.57	0.93	0.80
Uric acid	4.07	5.17	3.79

89.75 mg. The mean net weight gain of the formed stone was 80.12 mg. The minimum net weight of the stone was found to be 8.0 mg whereas the maximum was 539 mg. The size of the urinary bladder was also found to be enlarged according to the size of the stone.

In the *Varuna* decoction-treated group, of nine rats, one rat was found dead and the assessments were made only on the observation of eight rats. Of eight rats, only in two rats stones were formed while in the remaining six albino rats, stone was not formed. In this group, the mean weight of the implanted glass beads was 9.55 mg and the mean weight of the formed stones was 12.00 mg. Thus, the net gain of weight of the formed stones was 2.5 mg.

Hence, on the basis of the above observations, it can be said

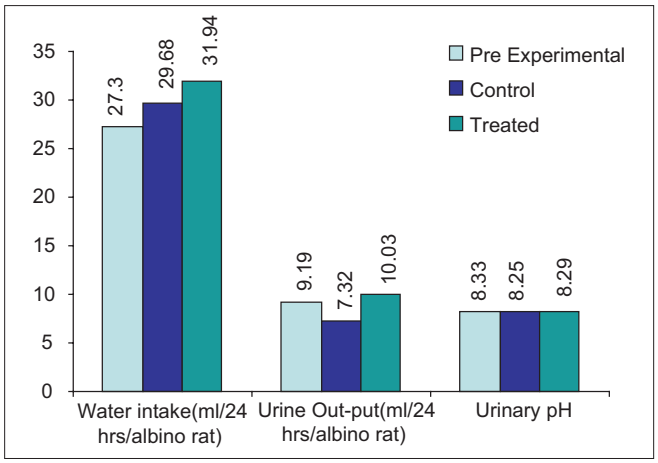

Figure 1: Graphical presentations of comparison of the mean water intake, mean urinary out--put and mean urinary pH in different groups

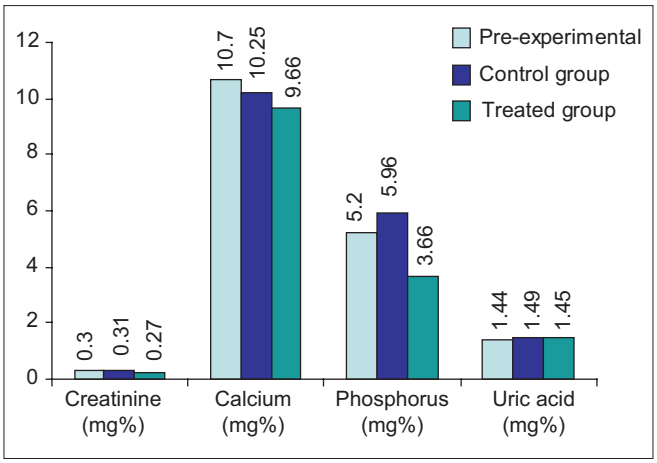

Figure 2: Graphical presentation showing the effect of drug on serum electrolytes in the pre--experimental, control and treated groups

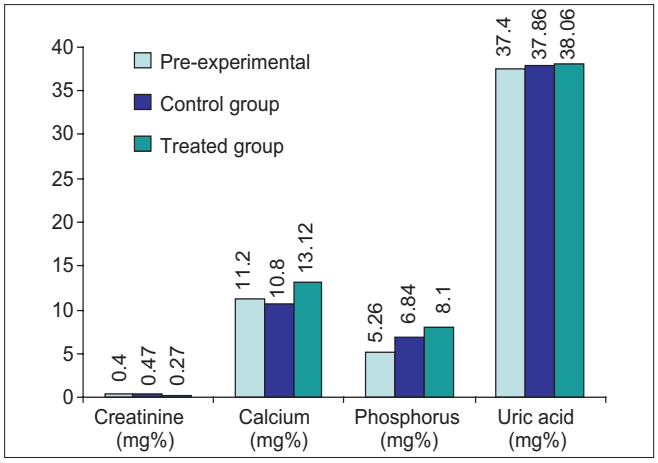

Figure 3: Graphical presentation showing the effect of drug on urinary electrolytes in the pre--experimental, control and treated groups

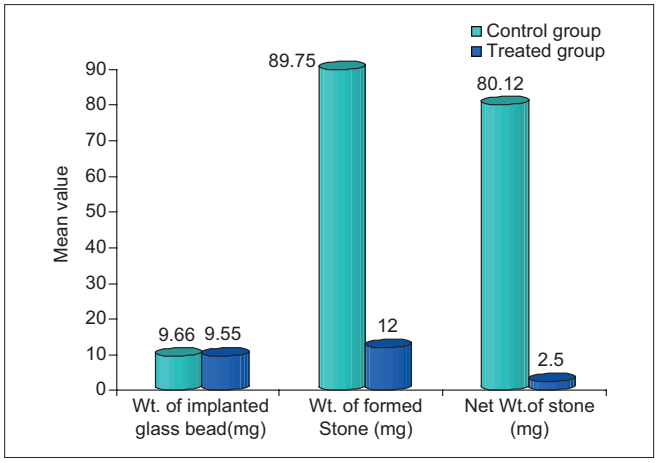

Figure 4: Graphical presentation showing the effect of drug on implanted glass beads in the control and treated groups

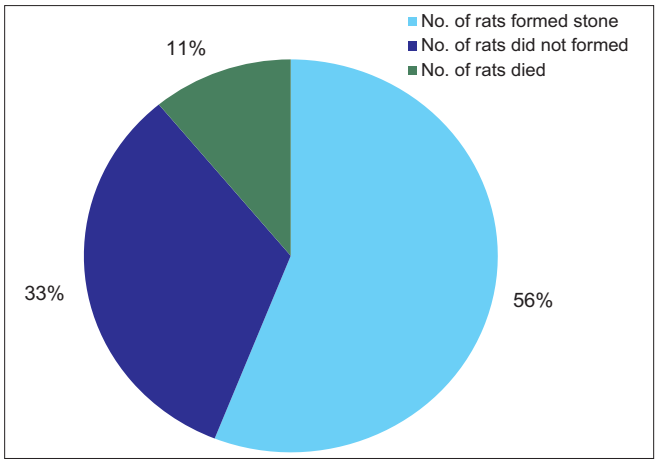

Figure 5: Graphical presentation showing percentage of stone formation in the control group

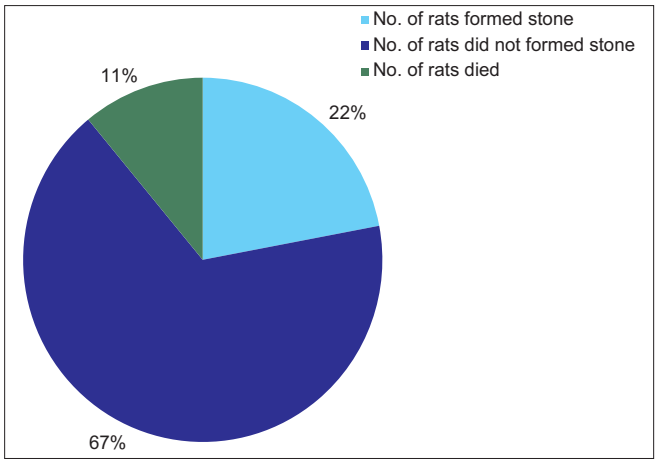

Figure 6: Graphical presentation showing percentage of stone formation in the treated group

that the incidence of formation of stone was low in the treated group in comparison with the control group [Table 8, Figure 4]. Table 9 and Figure 5 show that in 56% of the albino rats, stone was formed in the control group. In the treated group, only 22%

Table 8: Effect of drug on implanted glass beads in the control and treated groups

Control			Treated		
Weight of implanted glass bead (mg) (A)	Weight of formed stone* (mg) (B)	Net weight of stone** (mg) (B – A)	Weight of implanted glass bead (mg) (A)	Weight of formed stone* (mg) (B)	Net weight of stone** (mg) (B – A)
09	09	00	10	Died after 75 days	
10	18	08	10	28	18
10	75	65	09	09	00
10	10	00	10	10	00
10	10	00	10	12	02
09	548	539	09	09	00
10	30	20	09	09	00
09	18	09	09	09	00
10	Died after 60 days		10	10	00
9.66	89.75	80.12	9.55	12.00	2.5

*Glass bead + stone; **Without glass bead

Table 9: Percentage of stone formation in the control and treated groups

Groups	Number of rats in which beads were implanted	Number of rats that formed stone	Number of rats that did not form stone	Percentage of stone formation
Control	9	5	3	56
Treated	9	2	6	22

of the rats showed stone formation [Figure 6].

Discussion

In the control group, there is a slight increase in the serum and urinary creatinine, which might be due to obstructive uropathy or other pathology developed in the urinary system of the rat. But, in the treated group, the serum and urinary creatinine were decreased. Therefore, it can be assumed that the drug is helpful in reducing or normalizing the serum and urinary creatinine and restoring the normal metabolism of the urinary system.

In the present study, the drug (*Crataeva nurvala*) causes hypercalciuria and hyperphosphoruria, which are the most important factors for urolithiasis.[4] The present study also shows an increase in the urinary output. The total volume of urine increased in 24 h in the treated group in comparison with the control group. This factor dilutes the concentration of the urinary electrolytes. As a result of this, calcium and phosphorus flush out from the urine and there is a lesser chance of precipitation and decrease formation as well as growth of urinary stone. Apart from this, there are certain anti-aggregation factors present in the urine that are responsible for the prevention of crystallization of urinary lithiasis.

The observation reveals very little change in the serum and urinary uric acid, which was almost stationary, indicating that the drug was not very effective on the serum and urinary uric acid.

In the treated group, the size of the implanted glass beads did not increase even after 90 days, except in two albino rats where there was a mild increase in the size of the beads due to deposition on implanted glass beads, showing that the drug *Varuna* (*Crataeva nurvala*) prevents the deposition on implanted glass beads due to its anti-crystallization property and may be due to dieresis.

The formation of stones was found to be higher in the control group, i.e. 55.55%, whereas in the treated group it was found to be only 22.22%, which may be due to the effect of the drug that does not allow the deposition on the bead. The weight of the formed stone in the control group varies from 8 mg to 539 mg. It indicates the individual tendency of stone formation in albino rats.

One rat died in the control and the treated group each either due to post-operative complications or due to environmental factors.

Conclusion

Stone formation is a complex process, which depends on multiple factors, and the presence of nidus in the urinary bladder is not the only main single factor for the formation of stone. Experimentally, the drug *Varuna* prevents stone formation due to the anti-lithogenic activity and the anti-crystallization property. The drug decreases the urinary pH toward acidic. The diuretic action of this drug attributes the metabolic correction of the serum and urinary electrolyte levels in experimentally induced urolithiasis in albino rats.

Therefore, it can be concluded that the *Varuna* (*Crataeva nurvala*) is helpful in reducing the recurrence of urolithiasis.

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हिन्दी सारांश

वरुण का अश्मरीघ्न प्रभाव – एक प्रयोगात्मक अध्ययन

संजय अग्रवाल शिवजी गुप्ता ए. के. सक्सैना नीलम गुप्ता श्वेता अग्रवाल

आधुनिक चिकित्सा तकनीक होने के पश्चात भी पाँच पर्व के भीतर यूरोलिथिएसिस रोग के पुनः होने की संभावना ६०% है इसलिए आवश्यकता है ऐसी औषधि की जो शरीर में चयापचय क्रियाओं को सन्तुलित करे और इसे बनने से रोक सके। आयुर्वेद में इस रोग का वर्णन अश्मरी के अन्तर्गत किया गया है। पाषाणभेद, वरुण, कुलत्थ, गोक्षुर आदि औषधियों का वर्णन अश्मरी चिकित्सा हेतु प्राचीन संहिताओं मे किया गया है। यह कार्य अश्मरी के प्रयोगात्मक मॉडल्स पर वरुण के अश्मरीध्न प्रभाव के अध्ययन हेतु किया गया है जो दो भागो में विभाजित है, जिनमे सभी एल्विनो रैट्स के ब्लैडर में स्टोन प्रत्यारोपित किए गये तथा एक निश्चित अन्तराल पर रक्तगत व मूत्रगत इलैक्ट्रोलाइट्स तथा एक्स रे परीक्षण किया गया जिसके परिणाम दर्शाते हैं कि वरुण क्वाथ अश्मरी चिकित्सा में उपयोगी है।