ISSN 2456-3110
Vol 5 · Issue 5
Sept-Oct 2020

Journal of Ayurveda and Integrated Medical Sciences

www.jaims.in

JAIMS

An International Journal for Researches in Ayurveda and Allied Sciences

Charaka Publications

Indexed

Journal of
Ayurveda and Integrated Medical Sciences
ISSN 2456-3110
ORIGINAL ARTICLE Sept-Oct 2020

An experimental evaluation of the Lithotriptic Activity of Ayurvedic drug *Kāśīśa Bhasma*

Dr. Kusuma TV[1], Dr. Jeevesh KB[2], Dr. Chaitra LV[3]

[1]Post Graduate Scholar, [2]Professor & Head, [3]Associate Professor, Department of Rasashastra and Bhaishajya Kalpana, Ramakrishna Ayurveda Medical College, Hospital and Research Centre, Yelahanka, Bengaluru, INDIA.

ABSTRACT

Kāśīśa (Ferrous Sulphate, $Fe_2SO_4.7H_20$), is among the most commonly used mineral drug in Ayurveda, and has been specifically indicated in *Mutrashmari*. Urolithiasis, (*Mutrashmari* in Ayurveda) is the third most common urinary system disorder globally with high recurrence rate. The present study is to determine the underlying mechanism of *Kāśīśa Bhasma* as lithotriptic drug in animal model. Ethylene glycol (0.75% v/v) induced urolithiasis model was used to study the lithotriptic activity of *Kāśīśa Bhasma* in Wistar albino rats. 30 rats were divided into five groups and were allocated interventions accordingly. Two trial drug groups were given single and double doses of *Kāśīśa Bhasma* (150mg/kg & 300mg/kg respectively), and were compared against the standard control group (Tab. Cystone 750mg/kg), administered for 14 days. Relevant biochemical assay and histopathological analysis was done and analysed. In vivo study revealed, *Kāśīśa Bhasma* administered at 300mg/kg b.w. was associated with better lithotriptic activity. The results showed significant reduction in calcium oxalate deposits in the kidneys, restoring the elevated values of serum Creatinine, BUN, uric acid and urine parameters like calcium, phosphate and oxalate while also maintaining optimal urine pH when compared to negative control. The lithotriptic activity of *Kāśīśa Bhasma* was found to be corresponding to that of standard drug Tab Cystone.

Key words: *Urolithiasis, Ethylene Glycol, Lithotriptic. Kāśīśa, Mustrashmari.*

INTRODUCTION

Ayurveda is a rich indigenous wisdom of India, becoming a part of global medicine today. *Rasa Shastra* is a branch of Ayurveda with its unique heritage of herbo-mineral drugs in treating the diseases. These herbo-mineral drugs have several indications where the same drug acts differently based on the *Dravyas* used in its pharmaceutical method of preparation.

Kāśīśa (Green vitriol), one among the *Uparasa*, is a mineral compound containing Iron, composed of Ferrous Sulphate ($FeSO_4.7\ H_2O$).[1] The Rasashastra texts have elaborated description of *Kāśīśa* and its broad spectrum of therapeutic efficacy in the management of numerous ailments when administered after proper purification and incineration of the drug. Therapeutically *Kāśīśa Bhasma* is indicated in *Netra Rogas* (eye diseases), *Pandu* (Anaemia), *Switra* (leukoderma), *Mutrarogas* (dysuria), *Krimi* (helminthiasis,) *Jwara* (fever), *Pleehagada* (Splenomegaly), *Kastartava* (Amenorrhea).[2] Classical Texts like Sushrutha Samhitha,[3] Bhava Prakasha,[4] Ayurveda Prakasha[2] cited *Kāśīśa* in *Mutrakruchra* and *Ashmari* (Urolithiasis), the unexplored potential of this drug.

Urolithiasis, the third most prevalent disease characterised by the formation of stone in the urinary

Address for correspondence:
Dr. Kusuma TV
Post Graduate Scholar, Department of Rasashastra and Bhaishajya Kalpana, Ramakrishna Ayurveda Medical College, Hospital and Research Centre, Yelahanka, Bengaluru, INDIA.
E-mail: kusuma.tv@gmail.com

Submission Date: 17/09/2020 Accepted Date: 13/10/2020

Access this article online

Quick Response Code

Website: www.jaims.in

DOI: 10.21760/jaims.5.5.28

ISSN: 2456-3110 ORIGINAL ARTICLE Sept-Oct 2020

tract.[5] Abundance of promoters and unavailability of inhibitors leads to the formation of stones in the urinary tract. The geographical, climatic, ethnic, dietary, genetic factors & underlying medical conditions, and modern lifestyles i.e. industrialization and malnutrition play a vital role in occurrence and relapse of urinary stones. Approximately 2 million people are affected every year in India, with the stone belt showing most prevalence - Gujarat, Maharashtra, Punjab, Rajasthan, Delhi, Haryana, parts of North East. An analysis from India shows an increase from 0.9% to 9.0% over 20 years, where 12% of the population is expected to have urinary calculi, out of which 50% may end up with as multiple infections and haemorrhage, chronic kidney disease or end stage renal disease.[6]

The major treatment modalities in the conventional medicine for Urolithiasis are dietary management, Medical expulsive therapies, and advanced surgical interventions which have their own downsides and incompetent in preventing its recurrence. The over use of the synthetic drugs, or surgical interventions results in higher incidence of adverse drug reactions or events, which has motivated humans to return to nature for safe effective and inexpensive remedies.

In Ayurveda, Urolithiasis is co-related to *Mutrashmari*, one among the Astamahagadhas,[7] affecting one of the *Trimarmas* - *Basti*. Acharyas opined before opting surgical interventions one should try with oral medications which possesses the properties that facilitates the elimination of the urinary stones.

In the present work, an attempt has been made to determine the lithotriptic effect of *Kāśīśa Bhasma* in the experimental model.

Materials and Methods

Ethylene glycol induced lithiasis study design was used to assess the lithotripsic activity in Wistar albino rats. The calculi was induced by adding Ethylene Glycol (EG) to the drinking water to a final concentration of 0.75%.

The acclimatized animals were divided into 5 groups, from Group I to Group V, each with 6 rats and urolithiasis (stone) was induced in all the groups except Group-I as it was reserved as "Normal control". Group II, animals received 0.75% ethylene glycol in drinking water ad libitum for 28 days and served as the Disease control. The G-III group animals received 0.75% ethylene glycol in drinking water ad libitum along with standard drug -tab Cystone 750 mg/kg body weight, from 15th day till 28th day. G-IV animals treated with *Kāśīśa Bhasma* 150 mg/kg + 0.75% ethylene glycol in drinking water ad libitum and G-V group animals received 0.75% ethylene glycol in drinking water ad libitum, treated with *Kāśīśa Bhasma* 300 mg/kg body weight orally from 15th to 28 days.

Group	Treatment	Dose
1.	Normal control	-
2.	Ethylene Glycol	0.75%v/v in drinking water
3.	Ethylene glycol + Cystone	0.75%v/v + 750mg/kg
4.	Ethylene Glycol+ *Kāśīśa Bhasma* single dose	0.75%v/v + 150mg/kg
5.	Ethylene Glycol + *Kāśīśa Bhasma* double dose	0.75%v/v + 300mg/kg

Collection of Raw materials

Raw *Kāśīśa* was procured from a genuine supplier (Amruth Kesari Depot, Bangalore) and authenticated as per their *Grahya Lakshana* (accepted characters - the *Pushpa Kāśīśa* is small crystalline form with bright green color used for medicinal purpose.) specified in the authoritative texts of Rasa-Shastra.[8]

Preparation of *Kāśīśa Bhasma*

Bhasma was prepared in Rasashala, Department of Rasashastra and Bhaishajya Kalpana, RAMC. The *Shodhana* (Purification) of the *Ashoditha Kāśīśa* (500gms) was carried out by subjecting it to *Swedana* in *Dolayantra* with *Shwetha Bhringaraja Swarasa*

ISSN: 2456-3110 ORIGINAL ARTICLE Sept-Oct 2020

(1700ml) for 3 hours.[2] This was later dried to get crystalline form of *Shodhitha Kāśīśa*. This was triturated with *Nimbu Swarasa* and *Chakrikas* were prepared, kept in a *Sharava Samputa* subjected to *Marana* (incineration) using Horizontal electrical muffle furnace[9] at temperature of 645˚C. The incineration process was repeated 5 times till *Kāśīśa Bhasma* was obtained. (*Niramlata - Bhasma Lakshana* of *Kāśīśa* - sour taste of *Kāśīśa* was not appreciated).

Animals

Wistar albino rats were housed in Polypropylene cages at 23˚± 2 C, humidity 55 ± 5% and were kept on a 12h light/dark cycle. They were fed with standard Pelleted rodent feed (VRK nutrition solutions) and water ad libitum and acclimatized for 15 days before the study. Experimental protocol reported in this study was approved by the Institutional Animal Ethical Committee of CPCSEA, Govt. of India (IAEC- Approval No Invivo/082 on 30-8-2019) and carried out according to Organisation for Economic Cooperation Development (OECD) guidelines.

Chemicals and drugs

Ethylene glycol (0.75% v/v) were purchased from S D fine chemicals, Bangalore. Standard drug was purchased from Himalaya Herbal Healthcare, Bangalore. Demineralized water and analytical grade chemicals/solvents were procured from local market.

Drug administration

Cystone tablet and *Kāśīśa Bhasma* were administered orally through stainless steel oral tube. *Kāśīśa Bhasma* was mixed with 0.25% of gum acacia solution for preparing the test doses.

Acute toxicity assay

Acute toxicity study was performed on female Sprague Dawley rats by using fixed dose method as per OECD guideline 420. In this study, a sighting dose of 300 mg/kg was used, and no adverse signs were found. Subsequently additional doses of 1000 and 2000 mg/kg were used. Total of 5 animals were used for each dose and was observed for 14 days. No clinical signs/adverse effects or death occurred in any of the doses tested.

Evaluation of Lithotriptic activity of *Kāśīśa Bhasma* on ethylene glycol induced albino rats

Ethylene glycol induced lithiasis study design was used to assess the lithotripsic activity in Wistar albino rats. The calculi was induced by adding Ethylene Glycol (EG) to the drinking water to a final concentration of 0.75% (day 1 to day 14-induction period).

The acclimatized animals were divided into 5 groups, from Group I to Group V, each with 6 rats and urolithiasis (stone) was induced in all the groups except Group-I as it was reserved as “Normal control”. Group II, animals received 0.75% ethylene glycol in drinking water ad libitum for 28 days and served as the Disease control. The Group-III animals received 0.75% ethylene glycol in drinking water ad libitum along with standard drug Tab. Cystone 750 mg/kg body weight, from 15th day till 28th day (treatment period). Group-IV animals treated with *Kāśīśa Bhasma* 150 mg/kg + 0.75% ethylene glycol in drinking water ad libitum and Group-V group animals received 0.75% ethylene glycol in drinking water ad libitum, treated with *Kāśīśa Bhasma* 300 mg/kg body weight orally from 15th to 28th day.

Urine and serum analysis was done at the end of the study. The blood sample (1ml) was collected on 28th day from each animal through retro-orbital plexus under anaesthetic conditions. Urine samples were collected through metabolic cage on 28th day. Biochemical investigations of calcium, oxalate, magnesium, phosphate, and pH from urine samples and BUN, Creatinine, uric acid from retro orbital artery blood samples was performed. Histopathological study was performed by isolating both kidneys for detecting the calculi in kidneys .

Histopathology of harvested kidney section and staining method

Histopathological study of the harvested kidney section was carried out to detect the outcome of *Kāśīśa Bhasma* on the calculi in kidneys and also to

ISSN: 2456-3110 **ORIGINAL ARTICLE** Sept-Oct 2020

know its effect on the internal structures of the kidney which shall give information about efficacy of the drug as well as its toxicity. This was carried out as per standard protocols. Staining of the kidney section was carried out as per the standard techniques of histology.

Statistical analysis

The urinary and blood parameters data were recorded, calculated and expressed as Mean ± SEM. The results were analysed using one-way ANOVA followed by Dunnett's multiple comparison test. P values <0.05 were considered as statistically significant.

RESULTS

Kāśīśa Bhasma in double dose has shown significant decrease in urine calcium, urine oxalate, urine phosphate and urine pH when compared with negative control.

In serum biochemistry the *Kāśīśa Bhasma* has shown significant decrease in Blood Urea Nitrogen (BUN), Serum Creatinine and Serum uric acid when compared with negative control.

Histopathological study

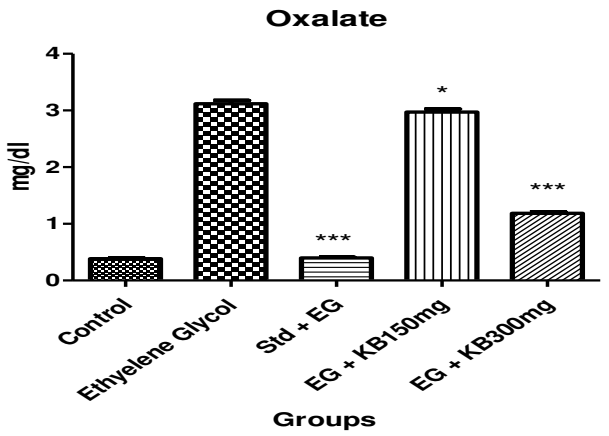
Kidneys of all animals harvested after 28 days were subjected to histopathological studies.

Histopathology of Kidney, confirms the absence of stones and associated relevant abnormalities in normal control animals (Group I). A significant (P< 0.001) Calcium Oxalate crystal deposition was observed in calculi-induced group II. The associated abnormalities such as marked inflammation of renal tissue along with proximal tubules dilation and deposition of the intratubular and interstitial crystal inside the tubules was a found as a characteristic sign of calculi development. Both, Cystone treated and *Kāśīśa Bhasma* double dose treated showed very few areas of inflammatory cells and rare deposition of the intratubular and interstitial crystals.

Urine biochemistry

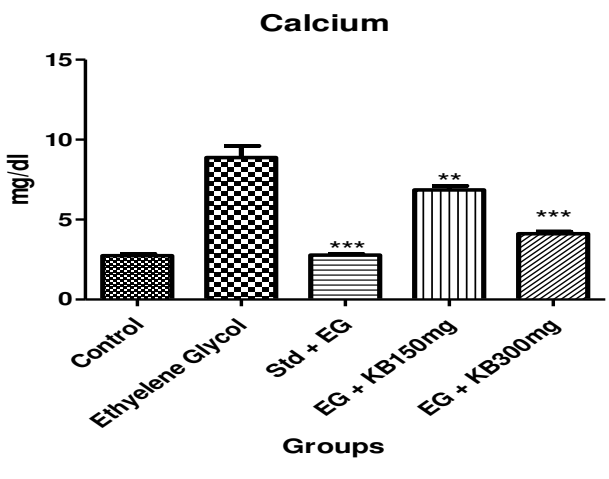
From the urine analysis it was found that the levels of calcium, oxalate and phosphate were high in the disease induced animals,with mean ± SEM 9.609±0.719, 3.122±0.092 and 10.024±0.174, where as the levels of these ions were found to be significantly less ($p < 0.05$) in the urine samples of the animals treated with the Double dose of *Kāśīśa Bhasma*.(Table 1)

Graph 1: Urine Oxalates



Oxalates values in Ethylene Glycol treated animals was found to be elevated with mean ± SEM of 3.03 ±0.092. Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in Oxalate values levels with mean ± SEM and significance of 1.18± 0.029 and p<0.005 & 3.02 ± 0.063 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed substantial decrease of oxalates with mean ± SEM of 0.40 ± 0.013 and p<0.005.(Graph1)

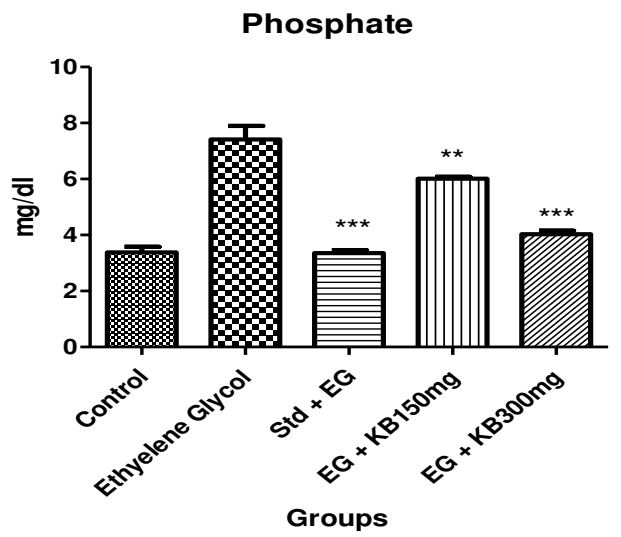
Graph 2: Urine Calcium



ISSN: 2456-3110 ORIGINAL ARTICLE Sept-Oct 2020

Calcium values in Ethylene Glycol treated animals was found to be elevated with mean ± SEM of 8.89 ±0.0719.Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in calcium values levels with mean ± SEM and significance of 4.12± 0.128 and p<0.005 & 6.86 ± 0.241 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed substantial decrease of oxalates with mean ± SEM of 3.48 ± 0.215 and p<0.005. (Graph2)

Graph 3: Urine phosphate

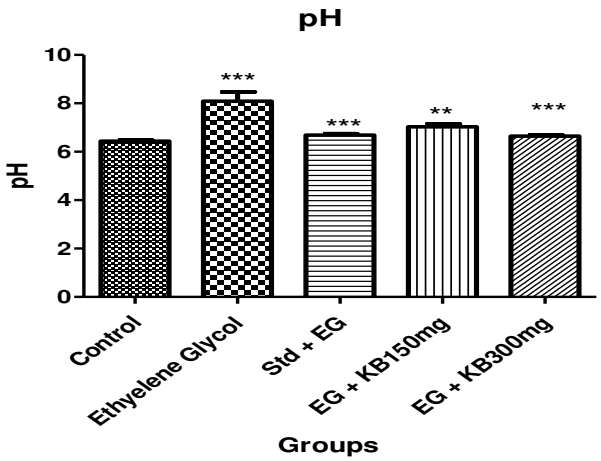


Phosphate values in Ethylene Glycol treated animals was found to be elevated with mean ± SEM of 9.85 ±0.174.Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in Phosphate values levels with mean ± SEM and significance of 4.03 ± 0.127 and p<0.005 & 6.02 ± 0.067 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed substantial decrease of Phosphate with mean ± SEM of 3.47± 0.217 and p<0.005.(Graph 3)

However, in Cystone tablets & *Kāśīśa Bhasma* double dose treatments, there was an increased degree of reduction in the levels of urine calcium, oxalate and phosphate. (*P*< 0.05)

The pH of urine intreated animals with *Kāśīśa Bhasma* was found to be maintained at normal urine pH (6.64 ± 0.049) unlike the diseased group (8.03 ±0.184). (Graph 4)

Graph 4: Urine pH



**p<0.05 ***p<0.005 versus group-II

Urine pH values in Ethylene Glycol treated animals was found to be elevated with Mean ± SEM of 8.03 ±0.184. Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in pH values levels with mean ± SEM and significance of 6.64 ± 0.049 and p<0.005 & 7.03 ± 0.109 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed substantial decrease of pH with mean ± SEM of 6.68 ± 0.061 and p<0.005.

Serum analysis

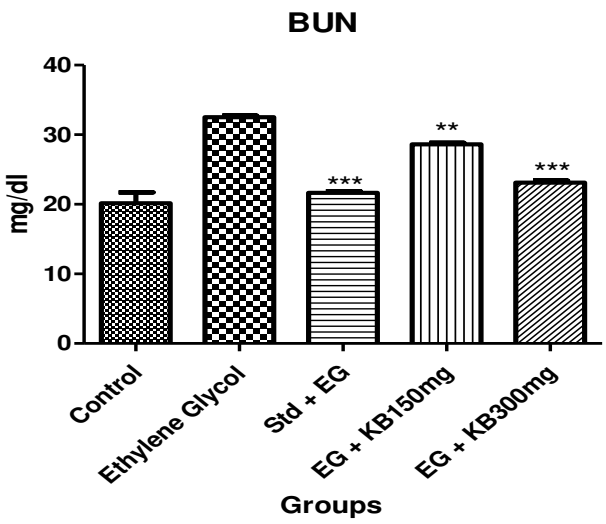
On 28thday, Serum analysis was carried out to know the levelsof creatinine, uric acid and BUN. It was found that creatinine, uric acid and BUN values were more in case of disease induced animals than the normal rats and were significantly reduced (p < 0.05) in treated animals. (Table1)

In serum analysis, BUN values in Ethylene Glycol treated animals was found to be elevated with mean ± SEM of 32.70 ±0.258. Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in BUN values levels with mean ± SEM and significance of 23.13± 0.278 and p<0.005 & 28.12 ± 0.346 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed

ISSN: 2456-3110 ORIGINAL ARTICLE Sept-Oct 2020

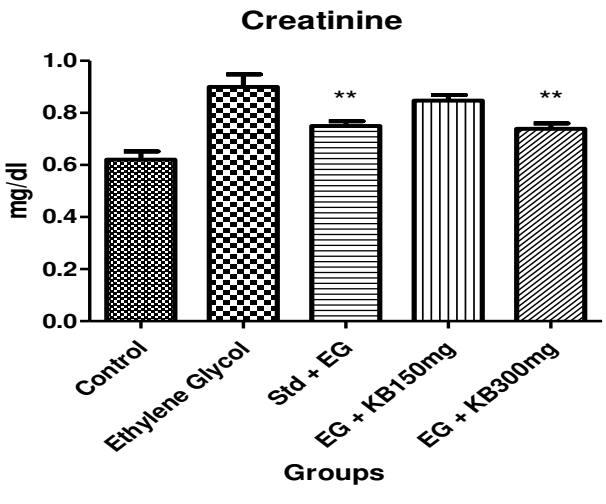
substantial decrease of BUN with mean ± SEM of 21.65 ± 0.246 and p<0.005. (Graph 5)

Graph 5: Serum BUN



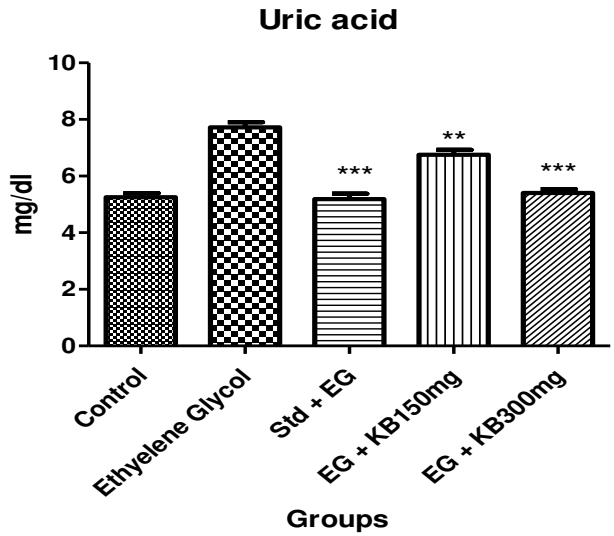
Creatinine values in Ethylene Glycol treated animals was found to be elevated with mean ± SEM of 0.90 ± 0.048. Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in Creatinine values levels with mean ± SEM and significance of 0.74 ± 0.021 and p<0.005 & 0.85 ± 0.022 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed substantial decrease of Creatinine with mean ± SEM of 0.75± 0.018 and p<0.005. (Graph 6)

Graph 6: Serum Creatinine



Uric acid values in Ethylene Glycol treated animals was found to be elevated with mean ± SEM of 7.72± 0.183. Rats treated with *Kāśīśa Bhasma* 300mg/kg and 150mg/Kg showed significant reduction in Uric acid values levels with mean ± SEM and significance of 5.40± 0.134 and p<0.005 & 6.75 ± 0.177 and p<0.05, in minimum and maximum dose rats respectively. Cystone treated rats also showed substantial decrease of Uric acid with mean ± SEM of 5.18± 0.194 and p<0.005. (Graph 7)

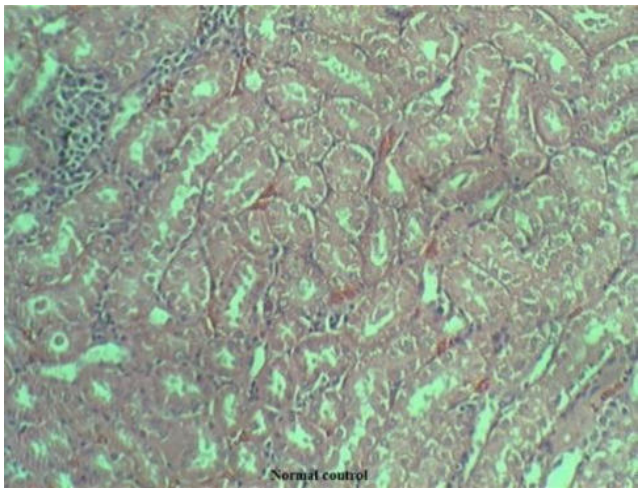
Graph 7: Serum Uric acid



**p<0.05 ***p<0.005 versus group-II

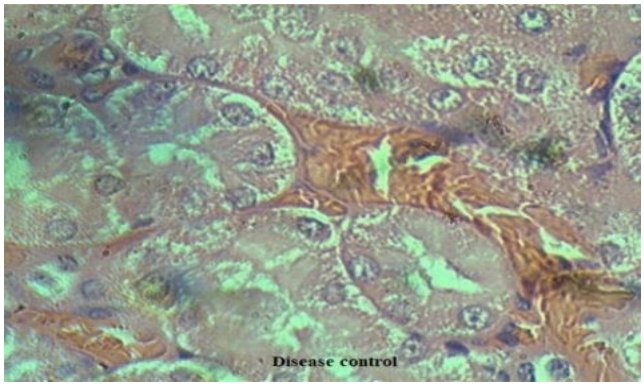
Histopathological images of Kidney tissues

Control

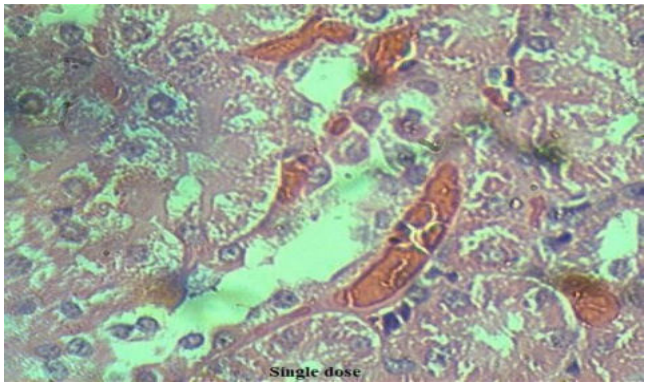


ISSN: 2456-3110 **ORIGINAL ARTICLE** Sept-Oct 2020

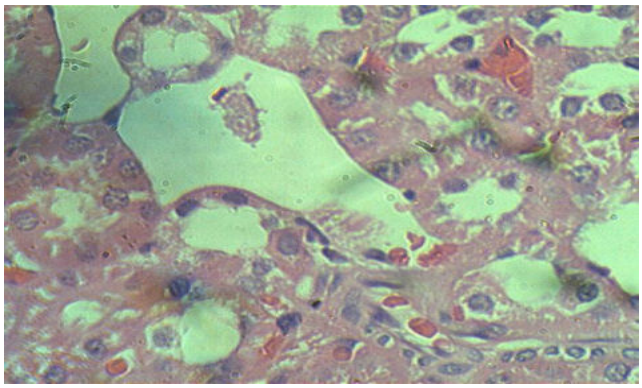
Disease control



Single dose



Cystone



Double dose

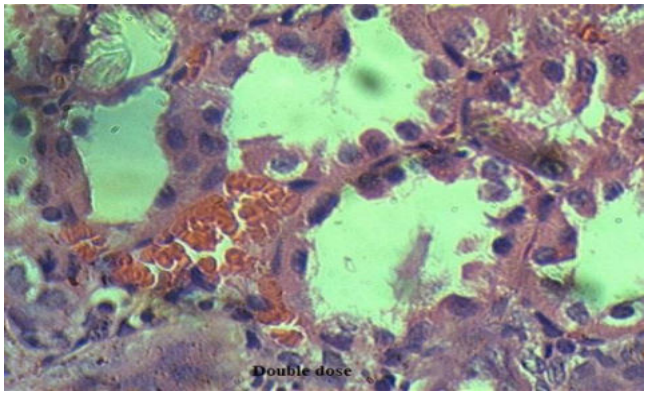


Table 1: Estimation of Serum and Urine Analysis of normal and Lithotriptic activity in Rats

Group	Groups	BUN (mg/dl)		Creatinine (mg/dl)		Uric acid (mg/dl)		Oxalate (mg/dl)		Calcium (mg/dl)		Phosphate (mg/dl)		pH	
		Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
1.	Control	20.16	1.549	0.62	0.032	5.25	0.145	0.39	0.016	2.745	0.115	3.58	0.054	6.43	0.042
2.	Ethylene Glycol	32.50	0.258	0.90	0.048	7.72	0.183	3.03	0.092	8.89	0.719	9.85	0.174	8.03	0.184
3.	STD (Cystone) + Ethylene Glycol	21.65***	0.246	0.75**	0.018	5.18***	0.194	0.40***	0.013	3.48***	0.215	3.47***	0.217	6.68***	0.061
4.	Ethylene Glycol + *Kāśīśa Bhasma* single dose (150mg/kg)	28.12**	0.346	0.85	0.022	6.75**	0.177	3.02*	0.063	6.86**	0.241	6.02**	0.067	7.03**	0.109
5.	Ethylene Glycol + *Kāśīśa Bhasma* double	23.13***	0.278	0.74**	0.021	5.40***	0.134	1.18***	0.029	4.12***	0.128	4.03***	0.127	6.64***	0.049

ISSN: 2456-3110 ORIGINAL ARTICLE Sept-Oct 2020

	dose (300mg/kg)														

Values given are mean ± S.E.M. (*n* = 6).**p<0.05 ***p<0.005 versus group-II

DISCUSSION

Urolithiasis is seemingly disturbing mankind since ages and is said to be a cause for renal failure if left untreated. Surgery is considered the best option when the other system of medications fail. There is a need to explore an effective drug from the ancient treasure of herbo mineral formulations. *Kāśīśa Bhasma* is a herbo mineral drug which has been indicated to treat *Mutrashmari* which ought to be analysed. The study is to evaluate the lithotriptic activity of *Kāśīśa Bhasma* in invivo model on calculi induced wister albino rats by Ethylene glycol (0.75% v/v) for 28 days.

The drug with multiple mechanism which breaks the pathogenesis of Urolithiasis and also inhibits stone formation had to be selected. (Table 2)

Ayurveda emphasis on *Doshahara Chikitsa* as line of treatment. *Kapha* and *Vata Prakopakara Aahara* and *Vihara* results in formation of *Ashmari*. *Ashmari* is a *Tridoshaja Vyadhi* with predominance of *Kapha* associated with *Vata Dosha. Apana Vayu* responsible for act of micturition is affected in its major *Stana* i.e. *Kati* and *Basti* giving rise to urolithiasis.

In *Mutraashmari*, *Kshara* (medicated alkali preparation) and use of *Ushna Tiksna Dravyapana* is advisable.[10] *Kāśīśa Bhasma* is a herbo mineral preparation where *Bhringaraja Swarasa*[11] and *Nimbu Swarasa*[12] are the ingredients of its preparation having the *Ushna Teekshna Gunas.*

Kāśīśa has the properties like *Amla, Kashaya* and *Tikta Rasa*, with *Ushna Veerya, Katu Vipaka*. The *Karmukata* or action of *Kāśīśa Is Kapha Vatahara, Balya, Yakruth Pleeha Vikarahara, Ashmarighna* and *Mutra Kricharahara.*

The actions of *Bhasma* can be interpreted as follows.

The *Kapha Vatahara* properties of *Kāśīśa*, *Bhringaraja* and *Nimbu* drugs help pacifying the aggravated *Doshas* of *Ashamari* i.e., *Kapha* and *Vata*. By virtue of its *Laghu* and *Ruksha Guna, Amla, Katu* and *Tikta Rasa, Ushna Veerya, Kāśīśa Bhasma* may also exhibit "*Lekhana*" property and dissolve the stones in urine.

Kāśīśa, *Bhringraja* and *Nimbu* are drugs known for *Yakruth Vikaras* (Liver disorders). They help in rectifying the *Agni*, enhancing the Protein metabolism in the liver, as proteins in the urine also play significant role in crystallization of stones in urine and they may regulate the crystalloid colloid balance of urine composition. (Table 2)

Kāśīśa is one among the *Ushakaadi Gana Dravyas*[4] i.e., it destroys *Kapha*, it cures *Ashmari Sharkara* (stone gravels / urinary calculi) and *Mootrakruchra* (dysuria). That is, it might act as diuretic and *Ashmarighna* so that the stone might be dissolved, thus reducing the size of the *Ashmari* and expelled out from the body.

The *Gunas* of *Bhasma* here decodes *Samprapti* (etiopathogenesis) of *Mutrashmari*, i.e, the *Kapha-Vataja Sangha* in *Mutravaha Srotas* resulting in expulsion of calculi and also may inhibit further stone formation. Thus in total this drug has the capacity to disintegrate the pathogenesis of the disease *Mutrashmari*.

Metals such as magnesium, zinc, aluminum, iron and copper may act as inhibitors of calcium oxalate growth at very low concentrations. We may infer from this that the iron, copper and zinc in the form of *Kāśīśa Bhasma* might have acted as inhibitor of the calcium oxalates stones.[18] The *Bhasmas* are given in minimal doses or *Alpa Matra*, this serves the purpose of supporting low concentration of the trace elements in urine to inhibit stone formation.

The results of Urine analysis showed increased Urinary oxalates in ethylene glycol induced urolithiasis rats whereas there was decreased excretion of oxalates in *Kāśīśa Bhasma* double dose treated rats which may be due to inhibition of formation of oxalates by the administered drug. The calcium and

ISSN: 2456-3110 **ORIGINAL ARTICLE** Sept-Oct 2020

Phosphate levels were also decreased in the *Kāśīśa* administered rats, while maintaining the pH levels to its normal levels. (Table 1)

The decreased urine flow in the urolithiasis rats, leads to increased nitrogenous waste in the blood. The Serum analysis of creatinine, BUN and Uric acid were also elevated in the ethylene glycol treated rats which was reduced in the *Kāśīśa Bhasma* treated rats, which can be interpreted as minimal urine blockage in the kidneys due to inhibition of stone forming crystals and less damage to kidney tissue. The Histopathological report of Kidney revealed there were rare calculi crystals in the referred drug treated kidneys when compared with the ethylene glycol treated rats.

Table 2: Multiple mechanisms of desirable Drug actions to inhibit stone formation and efficacy of *Kāśīśa Bhasma.*

SN	Factors for inhibiting stone formation[13]	*Kāśīśa Bhasma* - Drug action on *Ashmari*
1.	Drug should help in spontaneous passage of calculi by increasing urine volume, pH and anti-calcifying activity.	*Kāśīśa Bhasma* shows the pH of urine is maintained at normal level and also disintegrates the stones.
2.	Drug should balance the inhibitor and promoter of crystallization in urine and affects the crystal nucleation, aggregation and growth (Crystal inhibition activity)·	*Nimbu Swarasa* in *Kāśīśa Bhasma* contains citrate which prevents the calcium ions from combining with oxalate to form crystals.[14] The high potassium content of lemon is very effective in removal of deposits in kidneys, urinary bladder and its disinfectant properties help cure infections in the urinary system. It clears blockage of urine due to deposition of calcium in the urinary tract.[15]
3.	Drug should relieve the binding mucin of calculi. (Lithotriptic activity)·	*Kāśīśa Bhasma* and *Bhringaraja* have the property of improving function of liver where protein metabolism takes place and thus can probably regulates the crystalloid colloid imbalance in urine and improve renal function, thus prevents recurrence of calculi. Drug attributes the metabolic correction of the serum and urinary electrolyte levels.
4.	Drug should regulate the crystalloid colloid imbalance and improve renal function, thus prevents recurrence of calculi·	
5.	Drug should improve renal tissue anti-oxidant status and cell membrane integrity and prevent recurrence (Anti-oxidant activity)·	*Bringaraja* and *Nimbu* have anti mirobial, anti-inflammatory, Analgesic and antioxidant properties.[16],[17]

CONCLUSION

Urinary stone is a multifactorial disorder and needs to be treated with a Drug which acts at multiple levels to combat it. Acute toxicity study revealed - *Kāśīśa Bhasma* was non toxic. *Kāśīśa Bhasma*, herbo-mineral drug with its broad spectrum of therapeutic benefits has shown significant contribution of lithotriptic activity to combat *Mutrashmari* in the dose of 300mg/kg in ethylene glycol induced urolithiasis model.

ISSN: 2456-3110 **ORIGINAL ARTICLE** Sept-Oct 2020

REFERENCES

1. The Ayurveda Pharmacopeia of India Part 1, Vol 7, First edition 2008 page 19-21
2. Acharya Sri Madhava, Ayurveda Prakasha by Sri Gulrajsharma Mishra, Chaukambha Bharathi Acadami, Varanasi, Reprinted 2016, 2/ 273-275 page 325-326
3. Kaviraja Kunjalal Bhishagratna, Sushrutha Samhita, Sutra Stana Vol 1, 4th edition, 2012, Chaukambha Sanskrit Series chapter 38, page 333.
4. K.C Chunekar, Bhavamishra, Bhava Prakasha, Vol 1, edition 2006, Chaukamabha Orentalia, Varanasi, Pg 416
5. Retrieved from http://www.merriam-webster.com /dictionary/Urolithiasis (accessed on 4-3-2018)
6. Atul Sohgaura and Papiya Bigoniya, 2017. A review on epidemiology and etiology of renal stone. Am. J. Drug Discov. Dev., 7: 54-62.
7. Dalhanacharya commentary of Srigayadasacarya Sushruta. Sushruta Samhita, by Vaidya Jadavji Trikamji Acharya, Chaukambha Surabharathi Prakashana, Varanasi reprint 2008, sutra stana, chapter 33/4-5 page144
8. Sri Sadananda Sharma, Rasa Tarangini, Upadhatvaadi Vignaneeya Taranga Chapter - 21, Chaukambha Surabharathi Prakashan, Varanasi, - Dr Ravindar Angadi
9. Arun Rasheed, Prasanna Raju, Jamal Basha D, Anvesh M, Azeem, Process and Pharmacological Potentials of *Kāśīśa Bhasma*, a Herbo-Mineral Formulation with Calcinated Ferrous Sulphate, Department of Pharmaceutical Chemistry, Al-Shifa College of Pharmacy, Malappuram, Pharmaceutics Division, Sri Padmavathi School of Pharmacy, Tirupati, Department of Phytochemistry, Sree Vidyanikethan College of Pharmacy, Tirupati.
10. Sharma PV, editor. Trimarmiya chikitsa adhyaya. Verse 54, 59. In: Charaka Samhita of Agnivesha, Chikitsa sthana. 8th ed. Varanasi, India: Chaukhamba Orientalia; 2007. p. 874-5.
11. Chunekar KC, Pandey G, Guduchyadi Varga, Bhavprakash Nighantu, Chaukhamba Vishvabharati Publication, 2002 Varanasi, Shlokaa no. 240-242.
12. K R Srikantamurthy, Bhavamishra, Bhavaprakasha Vol I, Purva Khanda. Amraphala varga , Krishna das academy, Pg 329
13. Rahul Deo Yadav, Shashi Alok, S. K. Jain , Amita Verma , A. Mahor, J. P. Bharti and M. Jaiswal Herbal plants used in the treatment of Urolithiasis: A Review, 2011, IJPSR 5218, http://ijpsr.com/bft-article/herbal-plants-used-in-the-treatment-of-urolithiasis-a-review
14. Dr. Piyush K Gandhi, Dr. Yogini Kulkarni, Citrus aurantifolia Linn, Citrus medica Linn, Citrus jambiri Linn) Journal of Pharmacognosy and Phytochemistry 2018; 7(2): 1192-1196
15. Lemon Juice Prevents Kidney Stones in the Urinary Tract by | 2007, Kidney Health, Stones Chrystal Moulton, and Tatjana Djakovic., https://www.naturalhealthresearch.org/32315-2/
16. Sanjivani Shekokar et.al., A Phytopharmacological Review of Prospective of Bhrungaraj (Eclipta alba Hassk.) IJAM,ISSN: 0976-5921
17. Mithun NM and Sowmya Shashidhara and R Vivek Kumar, Eclipta alba (L.) A Review on its Phytochemical and Pharmacological Profile,2011
18. Słojewski M. Major and trace elements in lithogenesis. *Cent European J Urol*. 2011;64(2):58–61. doi:10.5173/ceju.2011.02.art1

How to cite this article: Dr. Kusuma TV, Dr. Jeevesh KB, Dr. Chaitra LV. An experimental evaluation of the Lithotriptic Activity of Ayurvedic drug Kāśīśa Bhasma. J Ayurveda Integr Med Sci 2020;5:196-205. http://dx.doi.org/10.21760/jaims.5.5.28

Source of Support: Nil, **Conflict of Interest:** None declared.

****