Antilithiatic activity of roots of *Hemidesmus indicus* (L.) R. Br. var. *pubescens* (Wight. & Arn.) Hook. f.

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Abstract: The active principle or compound with similar structures and activity are manufactured chemically to produce the synthetic drugs used in allopathic or modern system of medicine. As a result of modern isolation techniques and pharmacological testing procedures new plant drugs usually find their way into medicine as purified substance rather than in the form of galenical preparation. The experimental model of urolithiasis utilizes toxic mechanism of ethylene glycol poisoning. Following ingestion, ethylene glycol is first hepatically metabolized to glycoaldehyde by alcohol dehydrogenate. Glycoaldehyde is then oxidized to glycolic acid, then glyoxalic acid and finally oxalic acid (Brent, 2001). Chelation of oxalic acid with calcium ions forms insoluble CaOx which leads to nephrotoxicity and renal failure.

Keywords: Antilithiatic, Animal Study, Uric Acid, Urea, Potassium

Introduction

Medicinal plants are value added for the content and chemical composition of their active components. Therefore, the demand on plant-based therapeutics has increased manifold in both developing and developed countries due to the growing recognition that they are natural products, being non narcotics, having no side effects, easily available at affordable prices. In a wider context, there is a growing demand for plant-based medicines, health products, pharmaceuticals, food supplements, cosmetics to mention a few [1].

Plant based drugs may be used directly, i.e., they may be collected, dried and used as therapeutic agents or their chief constituents/active principles separated by various chemical process may be employed as medicines. The active principle or compound with similar structures and activity are manufactured chemically to produce the synthetic drugs used in allopathic or modern system of medicine. As a result of modern isolation techniques and pharmacological testing procedures new plant drugs usually find their way into medicine as purified substance rather than in the form of galenical preparation [7].

Methodology

Screening of Antilithiatic activity of roots of *Hemidesmus indicus* (L.) R. Br. var. ***pubescens*** (Wight. & Arn.) Hook. f. **[8]**

Ethylene glycol-induced urolithiasis- The rats (n=6) were divided into 9 groups. Group I: Normal control (NC) received distilled water only.

Group II: Urolithatic vehicle control (UVC) received the vehicle of the drug/extract. Group III: Received standard drug Cystone 750 mg/kg.

Groups IV–VI: Fed orally with Plant methanolic extract in 100, 200 and 400 mg/kg doses for 28 days.

Groups VII–IX: Fed orally with Plant aqueous extract in 100, 200 and 400 mg/kg doses for 28 days.

The groups II–IX received ethylene glycol (EG) 0.75% in drinking water ad libitum for 28 days to induce urolithiasis and generate Ca Oxalate deposition into kidneys.

The experimental model of urolithiasis utilises the toxic mechanism of ethylene glycol poisoning. Following ingestion, ethylene glycol is first hepatically metabolised to glycolaldehyde byalcohol dehydrogenase. Glycoaldehyde is then oxidised to glycolic acid, and finally, oxalic acid is formed (Brent, 2001). Chelation of oxalic acid with calcium ions forms the insoluble compound CaOx, which can lead to nephrotoxicity and renal failure. Though there are different mechanisms and components involved in stone formation, the experimental model of ethylene glycol- induced urolithiasis correlates and mimics the condition of human clinical lithiasis.

Body weight of animals, Biochemical estimations such as creatinine, urea, uric acid, calcium,

and phosphorus (inorganic phosphate content) will be determined in urine and blood. The data were analysed using one-way ANOVA followed by the Newman-Keuls multiple comparison post hoc test. A statistical difference of $P < 0.05$ was considered significant in all cases.

Observation and Result

Relative body weight: - The antiurolithiatic activity of roots of *Hemidesmus indicus* (L.) R. Br. var. *pubescens* (Wight. & Arn.) Hook. f., an herb traditionally used for urinary disorders, indicates that its methanolic extract (HIPME) and aqueous extract (HIPAE) play a crucial role in managing metabolic changes during stone formation. In rats with ethylene glycol-induced urolithiasis, the chronic administration of the lithogenic agent typically leads to a significant decrease in body weight. This weight loss is attributed to renal toxicity, the accumulation of calcium oxalate crystals in the kidneys, and subsequent metabolic disturbances like hyperoxaluria and azotemia, which impair the animals' overall health and food intake.

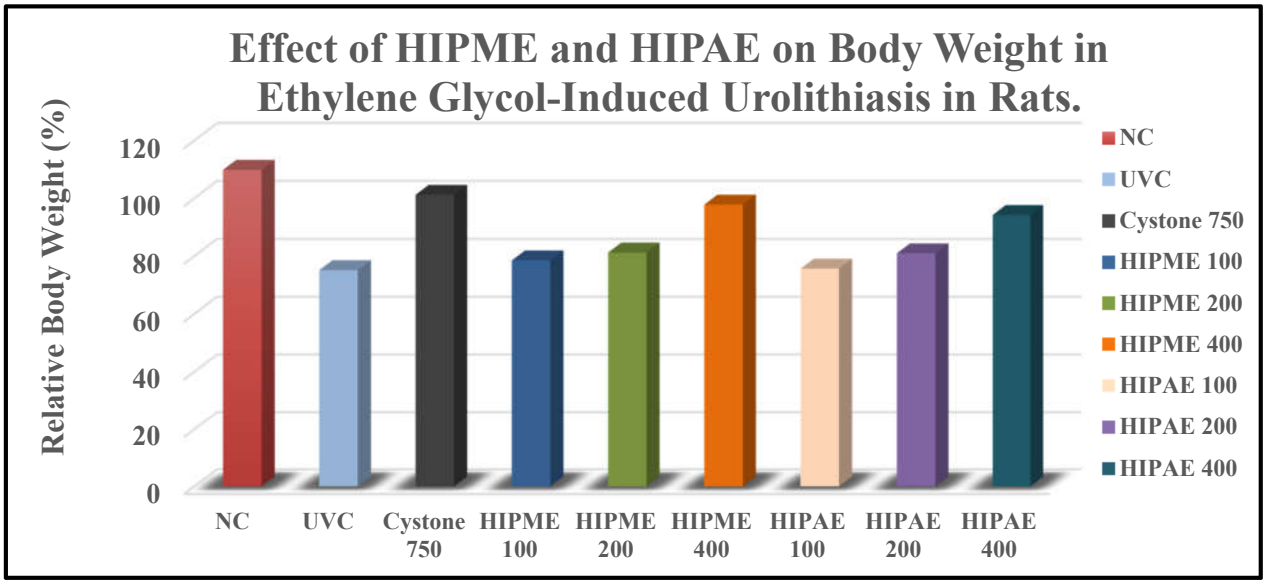
However, treatment with HIPME and HIPAE significantly mitigates this effect. Rats receiving these extracts demonstrate a restoration or stabilisation of body weight compared to the disease-control group. This improvement in weight gain is a reflection of the extracts' nephroprotective properties by inhibiting crystal nucleation and promoting the dissolution of stones, and they reduce renal tissue damage and restore normal metabolic function. While both extracts show efficacy, the HIPAE (alcohol extract) often exhibits a more potent effect in maintaining body weight, likely due to a higher concentration of bioactive phytoconstituents such as flavonoids and alkaloids that counteract the oxidative stress induced by ethylene glycol. (Table 1, Figure 1)

Table 1: Relative body weight

Effect of HIPME and HIPAE on Body Weight in Ethylene Glycol-Induced Urolithiasis in Rats.

Treatment	Dose(mg/kg)	Relative body weight (%)
NC	**…...**	**109.90 ± 0.04**
UVC	**…...**	**75.20 ± 0.06**
Cystone	**750**	**101.25 ± 0.08**
HIPME	**100**	**78.55 ± 0.91**
	200	**81.25 ± 0.76**
	400	**97.87 ± 0.60**
HIPAE	**100**	**75.71 ± 0.61**
	200	**80.99 ± 0.74**
	400	**94.25 ± 0.88**

Figure 1: Effect of HIPME and HIPAE on Body Weight in Ethylene Glycol-Induced Urolithiasis in Rats.



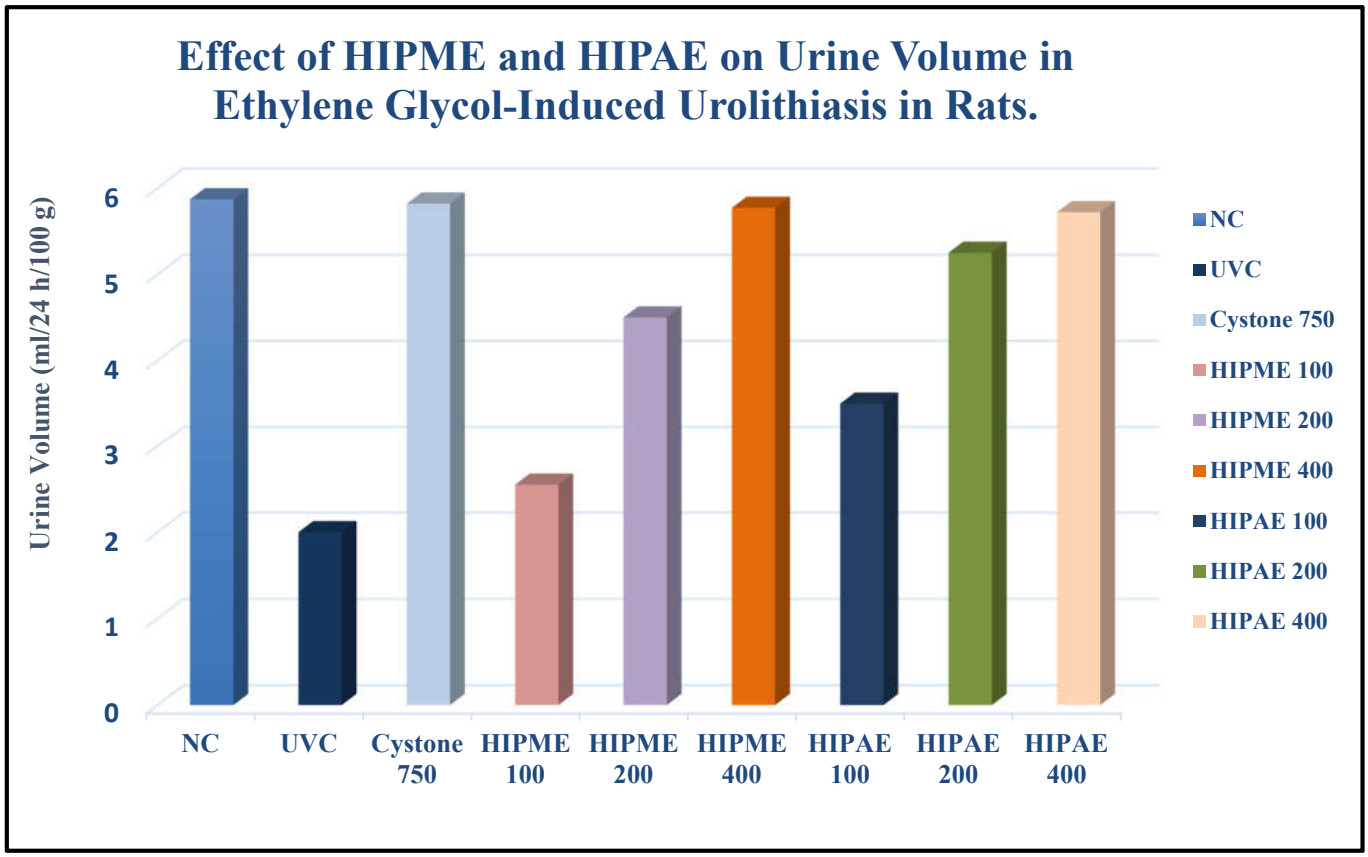
Urine Volume (ml/24 h/100 g): - The result shows that, the administration of ethylene glycol in the Urolithic Vehicle Control (UVC) group caused a drastic reduction in urine volume (2 ml/24 h/100 g) compared to the Normal Control (NC) group (5.87 ml/24h/100g), indicating renal obstruction and dysfunction due to stone formation. However, treatment with both the methanolic extract (HIPME) and the aqueous extract (HIPAE) of *Hemidesmus indicus* (L.) R. Br. var. *pubescens* (Wight. & Arn.) Hook. f., showed a significant, dose-dependent increase in urine volume, suggesting a potent diuretic and antiurolithiatic effect. At the highest dosage of 400 mg/kg, both extracts successfully restored urine output to near-normal levels, with HIPME reaching 5.77 ml/24 h/100 g and HIPAE reaching 5.72ml/24 h/100 g ml, performing comparably to the standard drug Cystone (5.82ml/24 h/ ml). Notably, at lower doses (100 and 200 mg/kg), the HIPAE extract demonstrated a more rapid recovery of urine volume than HIPME, indicating that the alcoholic extract may contain a higher concentration of the bioactive compounds responsible for flushing out micro-crystals and preventing urinary tract blockage.

(Table 2, Figure 2)

Table 2: Urine Volume (ml/24 h/100 g)
Effect of HIPME and HIPAE on Urine Volume in Ethylene Glycol-Induced Urolithiasis in Rats.

Treatment	Dose(mg/kg)	Urine Volume (ml/24 h/100 g)
NC	.....	5.87 ± .122
UVC	.....	2 ± 0.097
Cystone	750	5.82 ± 0.094
HIPME	100	2.55 ± 0.066
	200	4.5 ± 0.124
	400	5.77 ± 0.077
HIPAE	100	3.5 ± 0.097
	200	5.25 ± 0.084
	400	5.72 ± 0.073

Figure 2: Effect of HIPME and HIPAE on Urine Volume in Ethylene Glycol-Induced Urolithiasis in Rats.

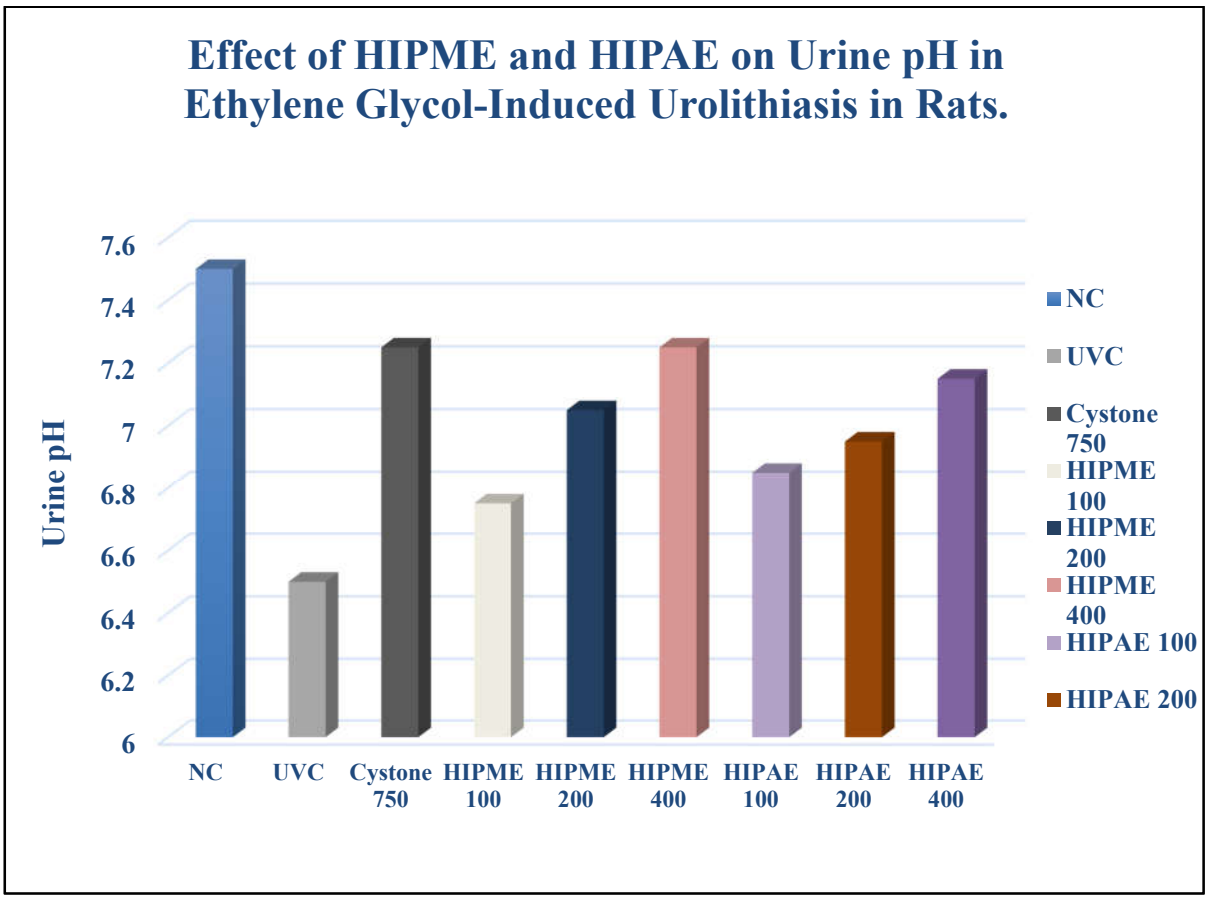


Urine pH:- In this activity, the administration of ethylene glycol in the Urolithic Vehicle Control (UVC) group led to a significant acidification of urine, with pH levels dropping from a normal 7.50 ± 0.10 to 6.50 ± 0.07. This decrease in pH is a critical factor in urolithiasis, as an acidic environment promotes the precipitation of calcium oxalate crystals and reduces the solubility of uric acid. Treatment with HIPME and HIPAE effectively reversed this trend, showing a dose-dependent increase in urine pH toward neutral/alkaline levels. At the maximum dose of 400 mg/kg, HIPME achieved a pH of 7.25 ± 0.05, which was identical to the standard drug Cystone (7.25 ± 0.08), while HIPAE reached 7.15 ± 0.08. By restoring the urine pH, these extracts create a less favourable environment for crystal aggregation and growth. Notably, even at the lowest dose of 100 mg/kg, the alcohol extract (HIPAE) showed a slightly better performance in raising pH (6.85) compared to the petroleum ether extract (HIPME, 6.75), suggesting that its bioactive constituents may be more effective at stabilising the urinary acid-base balance.
(Table 3, Figure 3)

Table 3: Effect of HIPME and HIPAE on Urine pH in Ethylene Glycol-Induced Urolithiasis in Rats.

Treatment	Dose(mg/kg)	Urine pH
NC	…...	7.50 ± 0.10
UVC	…...	6.50 ± 0.07
Cystone	750	7.25 ± 0.08
HIPME	100	6.75 ± 0.08
	200	7.05 ± 0.08
	400	7.25 ± 0.05
HIPAE	100	6.85 ± 0.08
	200	6.95 ± 0.08
	400	7.15 ± 0.08

Figure 3: Effect of HIPME and HIPAE on Urine pH in Ethylene Glycol-Induced Urolithiasis in Rats.



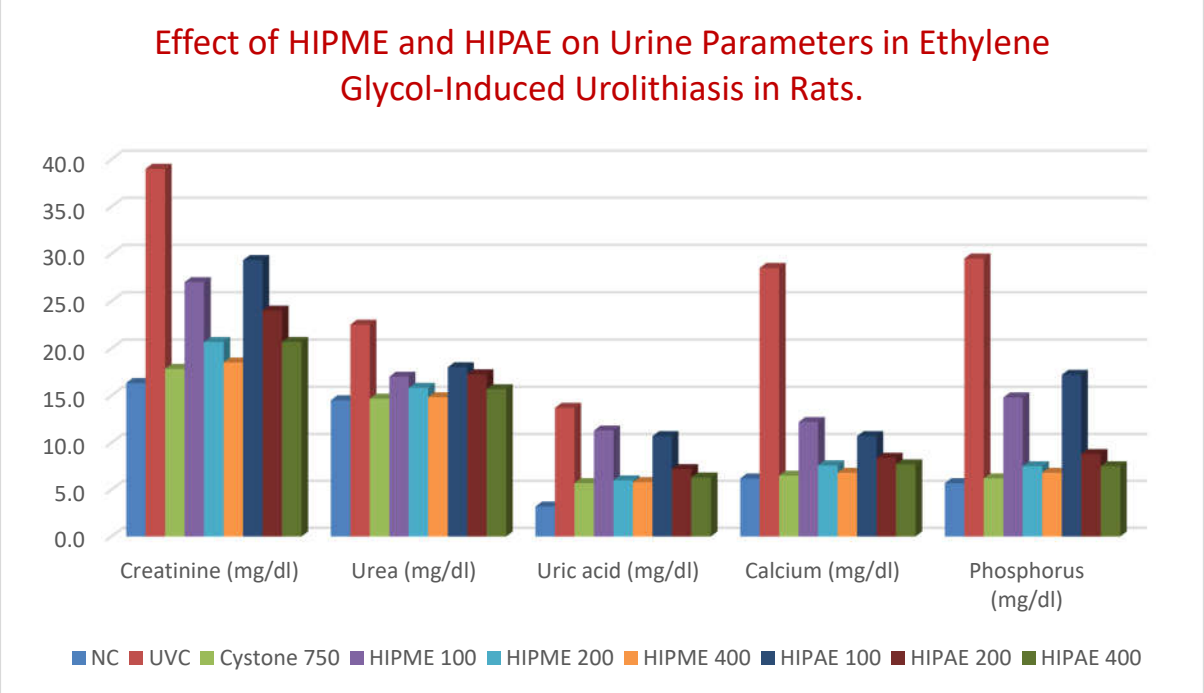
Urine Parameters: - In the study of ethylene glycol-induced urolithiasis, the Urolithic Vehicle Control (UVC) group exhibited a sharp rise in the urinary excretion of various lithogenic markers, indicating severe renal stress and crystal deposition. Specifically, levels of Creatinine (39.00 ± 0.49 mg/dl), Urea (22.50 ± 0.32 mg/dl), and Uric acid (13.70 ± 0.23 mg/dl) were significantly elevated compared to the Normal Control (NC), while electrolyte markers like Calcium (28.50 ± 0.28 mg/dl) and Phosphorus (29.50 ± 0.30 mg/dl) surged, creating a high-risk environment for stone formation. However, treatment with both HIPME and HIPAE led to a dose-dependent reduction in these parameters, effectively lowering the concentration of stone-forming constituents. At the 400 mg/kg dose, HIPME demonstrated superior efficacy, bringing Creatinine (18.50 ± 0.22) and Calcium (6.80 ± 0.07) levels very close to the standard Cystone and the Normal Control values. While HIPAE also significantly reduced these markers, HIPME at high doses appeared slightly more potent in regulating the excretion of phosphorus and creatinine. This reduction in urinary lithogenic substances suggests that the extracts help maintain renal integrity and prevent the supersaturation of urine, which is essential for inhibiting

the growth of calcium oxalate stones. (Table 4, Figure 4)

Table 4: Effect of HIPME and HIPAE on Urine Parameters in Ethylene Glycol-Induced Urolithiasis in Rats.

Treatment	Dose(mg/kg)	Urine Parameters				
		Creatinine (mg/dl)	Urea (mg/dl)	Uric acid (mg/dl)	Calcium (mg/dl)	Phosphorus (mg/dl)
NC	.....	16.30 ± 0.25	14.50 ± 0.21	3.20 ± 0.09	6.20 ± 0.06	5.70 ± 0.09
UVC	.....	39.00 ± 0.49	22.50 ± 0.32	13.70 ± 0.23	28.50 ± 0.28	29.50 ± 0.30
Cystone	750	17.83 ± 0.26	14.67 ± 0.21	5.70 ± 0.10	6.50 ± 0.06	6.20 ± 0.06
HIPME	100	27.00 ± 0.31	17.00 ± 0.24	11.30 ± 0.17	12.20 ± 0.12	14.80 ± 0.23
	200	20.67 ± 0.37	15.83 ± 0.24	6.00 ± 0.09	7.60 ± 0.07	7.50 ± 0.09
	400	18.50 ± 0.22	14.83 ± 0.18	5.80 ± 0.09	6.80 ± 0.07	6.80 ± 0.09
HIPAE	100	29.33 ± 0.26	18.00 ± 0.24	10.70 ± 0.15	10.70 ± 0.10	17.20 ± 0.22
	200	24.00 ± 0.25	17.25 ± 0.23	7.20 ± 0.13	8.40 ± 0.08	8.80 ± 0.12
	400	20.67 ± 0.37	15.67 ± 0.25	6.30 ± 0.10	7.70 ± 0.07	7.50 ± 0.06

Figure 4: Effect of HIPME and HIPAE on Urine Parameters in Ethylene Glycol-Induced Urolithiasis in Rats.



Conclusion- *Hemidesmus indicus* (L.) R. Br. var. *pubescens* (Wight. & Arn.) Hook. f. exhibits antilithiatic activities similar to those of *Hemidesmus indicus* (L.) R. Br. var. *indicus,* which is the accepted botanical source of the drug Sariva in Ayurveda, *Hemidesmus indicus* (L.) R. Br. var. *pubescens* (Wight. & Arn.) Hook. f. may be used as a good substitute for *Hemidesmus indicus* (L.) R. Br. var. *indicus* as far as antilithiatic activity is concerned.

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