Original Article

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Improvement in the Outcome of Urolithiasis Patients using Traditional Indian Medicine: A Systematic Review and Meta-analysis

Complementary/Alternative Medicine Section

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ABSTRACT

Introduction: Urolithiasis (UL) is a prevalent disorder that significantly burdens the global healthcare system. Except for acute surgical conditions, most kidney stones don't show any symptoms during presentation. Patients with asymptomatic renal calculi frequently seek alternative treatments. Several Ayurvedic preparations mentioned in Ayurvedic compendia have shown encouraging results in patients after long-term use. However, the results of several Randomised Controlled Trials (RCTs) on the effectiveness of Ayurvedic preparations in UL vary.

Aim: To conduct a systematic review and meta-analysis to assess the effectiveness of Ayurvedic preparations in patients with UL.

Materials and Methods: The electronic databases Web of Science, PubMed, Cochrane Library, Embase, and ARP were searched upto August 2023 to recognise applicable studies. The modified Jadad Scale was used to assess the quality of the studies. The Cochrane Risk of Bias (RoB) tool was used to determine the RoB for randomised trials.

Results: The search retrieved 1459 studies, but only 19 studies were found eligible for inclusion in the study. Statistical analysis revealed a substantial decrease in the number and size of calculi in 178 cases in the intervention group compared to only 101 events in the control group (OR: 3.03, 95% CI; 2.00, 4.61). It also showed a significant reduction in the size of stones, a significant improvement in haematuria with p=0.18, a highly significant improvement in dysuria with p=0.04, and highly significant relief in pain with p<0.0001.

Conclusion: This review concludes that Ayurvedic drugs have optimistic results in the treatment of UL. More substantial clinical trials with a larger sample size must be conducted to generate stronger evidence for using Ayurvedic Medicines (AyM) as a treatment choice for UL.

Keywords: Ashmari, Ayurveda medicine, Herbal drug, Kidney stones, Urolithiasis

INTRODUCTION

Urolithiasis (UL), commonly known as renal calculi, is a common and challenging urological disorder that affects millions across the globe. UL occurs when crystals form in the urine and build-up to form solid masses or stones. Defined as the formation of solid crystalline structures within the urinary tract, UL poses substantial challenges to patient well-being and healthcare systems [1].

Urinary Lithiasis (UL) is caused by an electrolyte imbalance in the circulating blood volume, which promotes the precipitation of specific ions such as calcium, phosphate, oxalates, and urate, leading to stone formation. Another crucial factor thought to play a significant role in stone creation is stasis. Infection creates a nidus for the salts to precipitate, initiating a vicious cycle of stasis and infection that leads to calculus production [2]. In Ayurveda, *Mutrashamari* can be correlated with UL. The mechanism indicated in Ayurvedic classics, Sushruta Samhita, states that *srotovaigunya* (channel blockage) from vitiated *kapha* (earth and water, which manage assimilation in the body) located in *basti* (urinary bladder) in association with vitiated vata (space and air, which govern movement) and pitta (fire and water, which regulate metabolism) are accountable for producing calculus. Initially, dosha vitiation occurs in the urinary tract, which may be catalysed by the presence of a developing lesion and is eventually attributed to the pathophysiology of *Mutrashamari* (UL) [3].

With a prevalence that has surged over the past few decades, kidney stones have become a significant health concern, resulting in considerable pain, reduced quality of life, and escalating medical costs. India is home to approximately seven million cases of UL with a prevalence rate of 15% [4]. The country's diverse population, dietary habits, and lifestyle factors contribute to variations in the prevalence of kidney stones across different regions. Historically, certain regions in India, such as the "stone belt" in the northwest, have reported higher rates of UL due to factors like high ambient temperatures, low fluid intake, and dietary practices that can increase the risk of stone formation [5].

As conventional treatment options have their limitations, there is an imperative to explore alternative approaches that can effectively alleviate this burden. This systematic review aimed to evaluate the therapeutic potential of traditional Indian medicine, Ayurveda, in managing UL. By synthesising the existing proofs, present review aims to provide in-depth knowledge of the role Ayurvedic medicine might play in preventing and treating urinary calculi, offering insights that could shape clinical practice and guide future research endeavours. Currently, no specific medication of choice exists to treat UL effectively. Surgical interventions like Percutaneous Nephrolithotomy (PCNL) or Extracorporeal Shock Wave Lithotripsy (ESWL) are generally the preferred choices. Hydrotherapy or flushing is another treatment option, but it has drawbacks like risk of stone migration, calculus relocation, incomplete removal, potential trauma, and patient suitability.

Herbal-based medicines with potential anti-urolithic action have also been used for a long time with unsatisfactory outcomes. Oral Ayurvedic therapy can be an effective treatment option for the removal of small-sized UL, considering the disease's national and global burden, patient compliance, clinical profile, diagnosis, and the quest for potent UL medication. Evaluation of the data supporting the effectiveness of Ayurvedic Medicine may result in significantly more effective choices in UL therapy. Hence, this

systematic review and meta-analysis study has been undertaken. The review is planned according to the PRISMA checklist.

MATERIALS AND METHODS

Search Strategy

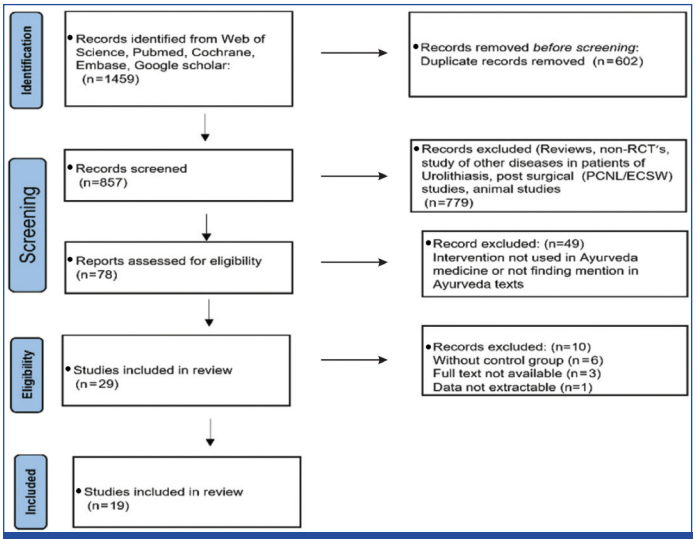
From 2001 to August 2023, electronic databases were meticulously investigated using Web of Science (MyRA Android app), PubMed, Embase, Cochrane Library, and ARP (AYUSH Research Portal, Government of India). The amount of information available was limited to finding applicable RCTs investigating the effect of herbal or Ayurvedic intervention on patients with UL using the Boolean operators 'AND' and 'OR'. [Table/Fig-1] explains the strategy used for literature retrieval.

Urolithiasis (UL)	**"Urolithiasis" (mesh), "kidney stone," "Vrikkashamari," "Ashmari," "Mutrashmari"**
Ayurveda	"Herbal medicine","Phytotherapy", "Ayurveda medicine," "Complementary medicine", "Drugs, Ayurveda herbal" (Mesh), "Medicine, traditional" (Mesh), "Plant preparations" (Mesh), "Medicinal plant", "Plant medicinal product", "Herb", "Herbal compound"

[Table/Fig-1]: Strategy employed for literature retrieval.

Eligibility criteria and screening: The titles and abstracts of each study were assessed to verify that they met the inclusion criteria. The Rayyan online tool was utilised to review the titles and abstracts [6]. RCTs conducted with herbal or Ayurveda intervention on patients with UL from the year 2001 up to August 2023, evaluating the effect of Ayurvedic Medicine on size, pain, or expulsion of kidney stones and published in the English language were included in the study. The search strategy adopted for including the studies was performed in two steps. The first step involved the authentication of the title and abstract and the exclusion of in-vivo studies, non-randomised trials, protocol papers, review articles, meta-analyses, studies related to diet, nutraceuticals, and post-surgical management. In the second step, a full-text assessment was performed to eliminate all non-Ayurvedic Medicine-related trials.

[Table/Fig-2] depicts the PRISMA flowchart of selection, inclusion and exclusion process.



[Table/Fig-2]: The PRISMA flow diagram depicting the methodology used to select included studies. Only 19 of the 1459 identified studies were included in the review.

Data extraction and analysis: Two individuals (BR and PC) evaluated the titles and abstracts using the inclusion criteria stated beforehand. Additionally, investigations of potential significance were retrieved for further evaluation. A data extraction table was created using Microsoft (MS) excel and included the following information: (i) author names; (ii) publication year; (iii) intervention; (iv) sample size; (v) duration of intervention; and (vi) outcome indicators. The Zotero 6.0 software was used to catalog and manage references, while Microsoft 365 was used for extracting and recording the data.

The RoB 2 tool was used to assess the Risk of Bias (RoB) [7]. The RoB 2 tool has been developed by Cochrane collaborators for analysing RoB in reporting the results of RCTs. This tool is results-based and is structured into five domains. Each domain has a set of questions to determine the bias as a judgment (high, low, or unclear) for individual elements from the five domains. The modified Jadad scale [8,9] was used to assess the reporting quality of the studies included in the review. Randomised Controlled Trials (RCTs) with a higher score (>4) were regarded as high-quality studies, while those with a lower score (<4) were deemed low quality.

For the meta-analysis, RevMan 5.4 software was used for conducting a meta-analysis of included studies. It is general practice to report the pre- and post-data in terms of mean and Standard Deviation (SD). In this scenario, the SD of the mean changes from pre-treatment or baseline are commonly missing outcome data. As previously reported, conducting a meta-analysis with lacking SDs is not possible [10]. The missing SDs were calculated using the following formula [11,12]:

$$SD_{change}=\sqrt{(SD_{baseline}^{2}+SD_{final}^{2}-(2\times r\times SD_{baseline}\times SD_{final}))}$$

Here, SD_{change} represents the SD of the mean changes from baseline, $SD_{baseline}$ denotes the SD of the pretest, SD_{final} corresponds to the SD of the post-test, and r symbolizes the correlations between the baseline and final measurements. This correlation value is not generally presented in the studies and is usually assigned a value of 0.7, as suggested in previous studies [10,12,13].

Regarding outcome indicators, the intervention's effect (primary outcome) on kidney stone size was measured using Ultrasonography (USG), and pain relief was assessed using the Visual Analogue Scale (VAS). The secondary outcomes included changes in dysuria and haematuria.

STATISTICAL ANALYSIS

Secondary outcomes were reported using the Standard Mean Difference (SMD). Binary data were assessed using the Risk Ratio (RR) and 95% Confidence Interval (CI). The overall combined effect of interventions was assessed with the help of the Cochrane Review Manager software, RevMan 5.4.1. The combined analysis used a 95% CI for effect size. The I^2 test was used to measure heterogeneity. If there was no heterogeneity (I^2 <50% and p>0.1), a fixed-effect model was used to synthesise the data. Otherwise, for heterogeneity (50% <I2<75%), a random-effect model was used. The results were presented using forest plots.

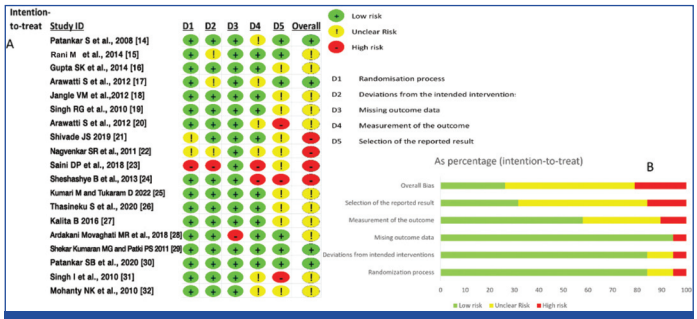
RESULTS

A total of 1459 studies were identified in the preliminary search from the selected electronic databases and related sources. Of these, 602 duplicates were removed, and 857 potentially relevant articles were retained for further evaluation during the screening process. Further screening of titles and abstracts were screened further, and another 779 studies were excluded for multiple reasons (such as animal studies, non-RCTs, reviews, studies related to post-surgical interventions). Subsequently, 78 articles were selected for full-text assessment, and then 49 studies on herbal drugs/interventions not found in Ayurveda texts were further excluded. Ultimately, 29 studies were found eligible for final selection. Of these, ten studies were excluded for being single-arm studies or data not extractable. Eventually, 19 studies, all in English, met the inclusion criteria and were included in the systematic review [14-32].

A total of 19 studies from randomised clinical trials involving 1003 patients were included in the systematic review, with 517 assigned to the intervention group. The charactertsic of the included studies can be found in [Table/Fig-3] [14-32]. The Risk of Bias (RoB) assessment is shown in [Table/Fig-4a,b]. Two authors independently assessed all the studies (BR and PC). All studies outlined their primary outcomes; fortunately, none of the research studies revealed any prior methodology for calculating sample sizes. Sixteen authors

Authors	Intervention	Control	Additional confounders	Total no. of patients	No. of patients in intervention group	No. in control group	No. of dropouts	Duration (weeks)
Patankar S et al., 2008 [14]	Herbmed (Varuna and Banana stem)	Placebo	Diclofenac 50 mg	77	47	14	16	12
Rani M et al., 2014 [15]	Varuna Guda	Placebo	None	36	17	15	4	8
Gupta SK et al., 2014 [16]	Varuna and Boerrhavia decoction	Tamsulosin	Pantaprazole 40 mg	110	55	55	-	6
Arawatti S et al., 2012 [17]	Gokshuradi Kashaya	Hydrotherapy	None	30	15	15	-	6
Jangle VM et al.,2012 [18]	Kulatthadi Yog	Control (Cystone)	None	60	30	30	-	8
Singh RG et al., 2010 [19]	*Kulattha*	Potassium citrate	None	47	24	23	-	24
Arawatti S et al., 2012 [20]	*Varuna* decoction	Hydrotherapy	Plenty of water and avoid incompatible diet	30	15	15	-	6
Shivade JS 2019 [21]	*Shigru Kwatha*	Hydrotherapy	None	40	20	20	-	6
Nagvenkar SR et al., 2011 [22]	ShwadastradiGhan Vati (*Gokshura*+varuna)	Control (cystone)	None	30	15	15	2	4
Saini DP et al., 2018 [23]	Varunadi Kwatha and Yavakshar	Trivikram ras	None	30	30		-	6
Sheshashye B et al., 2013 [24]	Yavaksharadi Yog	Placebo	None	60	30	30	-	4
Kumari M andTukaram D 2022 [25]	Palash Kshar and Ashmarihar Kwatha	Placebo	3-4 L of water and avoid incompatible diet	39	20	19	-	8
Thasineku S et al., 2020 [26]	*Gokshura*di Guggul	Gokshuradi Guggul and Varunadi Kwatha	3-4 L of water and avoid incompatible diet	38	19	19	-	6
Kalita B 2016 [27]	*Shigru* Root Kwatha	Placebo	3-4 L of water and avoid incompatible diet	60	30	30	-	12
Ardakani Movaghati MR et al., 2018 [28]	Nigella sativa seed	Placebo	Plenty of water and avoid incompatible diet	60	30	30	7	10
Shekar Kumaran MG and Patki PS 2011 [29]	Cystone	Placebo	3-4 L of water and avoid incompatible diet	60	30	30	-	12
Patankar SB et al., 2020 [30]	Subap plus (Craetevanurvala + Musa paradisiaca + A. aspera +H. vulgare)	Placebo	3-4 L of water and avoid incompatible diet	84	34	31	19	24
Singh I et al., 2010 [31]	Potassium citrate	Calcury Tablet	None	60	30	30	-	12
Mohanty NK et al., 2010 [32]	Cystone	Placebo	None	52	26	26	-	24

[Table/Fig-3]: Characteristics of studies included in the review [14-32].
Varuna (*Craetevanurvala*); Kulattha (*Dolichos biflorus*); Gokshura/Shwadashtra (*Tribulus terrestris*); Banana (*Musa paradisiaca*); Shigru (*Moringa oleifera*); Kshar (Alkali dosage form); Palash (*Butea monosperma*); Punarnava (*Boerrhaviadiffusa*); Cystone and Calcury are proprietary medicines used widely in management of urolithiasis traditionally



[Table/Fig-4]: (a) Risk of Bias (RoB) of included studies; (b) Graph showing Risk of Bias (RoB).

mentioned their studies to be randomised; however, a well-defined randomisation and concealment process was stated in only five studies. Only nine studies reported the number of dropouts or patient withdrawals. A total of 48 patients were considered dropouts across these nine studies, while all other RCTs did not report any dropouts. Three studies were 24 weeks and eight weeks long each; four were 12 weeks, and six were six weeks in duration. Two studies lasted four weeks, and only one study included in the review was conducted over 10 weeks. The published studies were evaluated for quality using a modified Jadad score. Three studies with a score equal to or less than four were classified as low-quality.

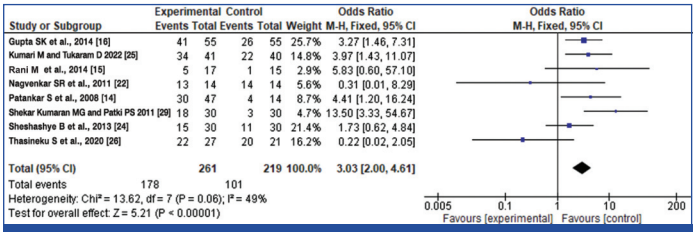
Intervention and control comparison: The interventions evaluated in the included studies are documented in [Table/Fig-5]. Among the total studies included in the review, four RCTs compared two different interventions [19,23,26,31], while nine RCTs were compared against placebo treatment [14,15,24,25,27-30,32]. Six interventions were assessed against a control. Two RCTs used Cystone as a control [18,22], three performed hydrotherapies in the control group [17,20,21], while one was against tamsulosin [16].

Ayurveda advocates the use of drugs having diuretic potential for managing urinary lithiasis. These drugs include formulations prepared from Varuna (Crataeva nurvala), *Gokshura* (Tribulus terrestris), and *Kulattha* (Dolichos biflorus). Four studies assessed interventions using a classical medicine, Varuna decoction [15-16,20,23]. Varuna was also included as a constituent in the intervention arm in four RCTs conducted on proprietary medicine [14,29,30,32]. *Kulattha* [18,19] and *Shigru* [21,27] were each assessed in two RCTs. The effect of Kshara was assessed in three RCTs [23-25], and potassium citrate was used as a comparative intervention in two studies [19,31].

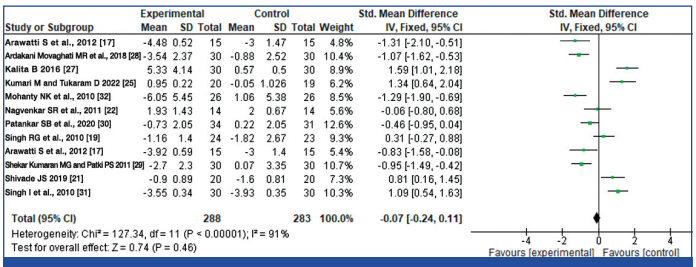
Outcome: The analysed outcomes of the studies comprise favourable changes in the number of stones (reduction or expulsion), a decrease in stone size, changes in haematuria, dysuria, and pain relief. Only the results obtained at the end of the trial period were disclosed, and no study provided follow-up data after the intervention period was completed. However, all RCTs found statistically significant improvements in the intervention group over the control group. None of the RCTs noted an adverse events in any intervention group. [Table/Fig-6a-e] shows how interventions affect outcomes.

Authors	Intervention	Jadad score	Stone size for inclusion criteria (mm)	Relief in pain	Haematuria	Dysuria	Other assessment criteria
Patankar S et al., 2008 [14]	Herbmed (Varuna and Banana stem)	6.5	2 groups (5-10 and >10)	≠	(-)	(-)	
Rani M et al., 2014 [15]	Varuna Guda	6.5	<15	✓	✓	✓	
Gupta SK et al., 2014 [16]	Varun and Boerrhavia decoction	6.5	4-10	✓	(-)	(-)	Stone clearance time
Arawatti S et al., 2012 [17]	Gokshuradi Kashaya	3.5	<8	✓	✓	✓	
Jangle VM et al., 2012 [18]	Kulatthadi Yog	5.5	1-10	(-)	(-)	(-)	Burning micturition and urine frequency
Singh RG et al., 2010 [19]	Kulatth	5.5	<5	(-)	(-)	(-)	Serum-creatinine, urea, calcium, uric acid
Arawatti S et al., 2012 [20]	Varuna decoction	6.5	<8	✓	✓	✓	
Shivade JS 2019 [21]	*Shigru* Kwath	4.5	<6	✓	✓	✓	Burning micturition
Nagvenkar SR et al., 2011 [22]	ShwadastradiGhan Vati (*Gokshura*+varuna)	6.5	<10	≠		≠	Burning micturition
Saini DP et al., 2018 [23]	VarunadiKwath&Yavakshar	3.5	<10	≠	≠	≠	Burning micturition
Sheshashye B et al., 2013 [24]	Yavaksharadi Yog	2.5	-	≠	≠	≠	
Kumari M and Tukaram D 2022 [25]	Palash Kshar&AshmariharKwath	6.5	<10	✓	✓	(-)	Burning micturition and urine frequency
Thasineku S et al., 2020 [26]	*Gokshura*di Guggul	5.5	<10	✓	Data incomplete	✓	Burning micturition
Kalita B 2016 [27]	*Shigru* Root Kwath	4.5	<20	✓	✓	(-)	Burning micturition, Strangury
Ardakani Movaghati MR et al., 2018 [28]	Nigella sativa seed	9	>5	(-)	(-)	(-)	BUN, S. creatinine, urine pH, S. calcium
Shekar Kumaran MG and Patki PS [29]	Cystone	9	5-12	✓	✓	✓	Urine frequency, pain episodes, painful micturitions
Patankar SB et al., 2020 [30]	Subap plus (Craetevanurvala+Musa paradisica+A. aspera+H. vulgare)	9	4-9	(-)	(-)	(-)	Stone density, surface area
Singh I et al., 2010 [31]	Potassium citrate	8	<8	✓	(-)	(-)	S. calcium, urinary oxalate, urinary citrate and serum electrolytes
Mohanty NK et al., 2010 [32]	Cystone	8	5-10	≠	≠	≠	(-)

[Table/Fig-5]: Major findings (outcome indicators) of studies included in the review.
≠ Data provided as % relief, hence not included in metanalysis; ✓ Data extracted and used for metanalysis; (-) Not mentioned

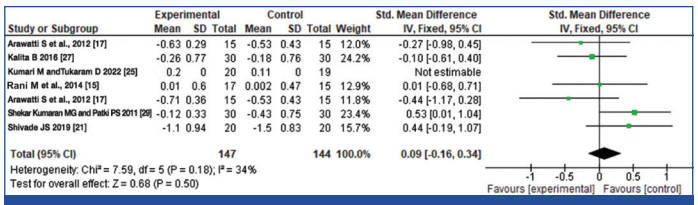


[Table/Fig-6a]: Effect of intervention on a number of stones.

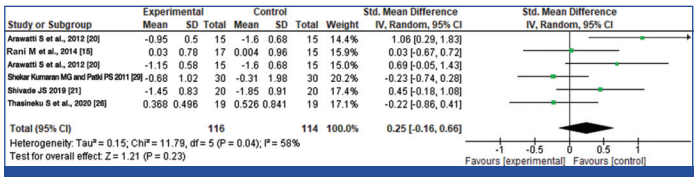


[Table/Fig-6b]: Effect of intervention on size of stones.

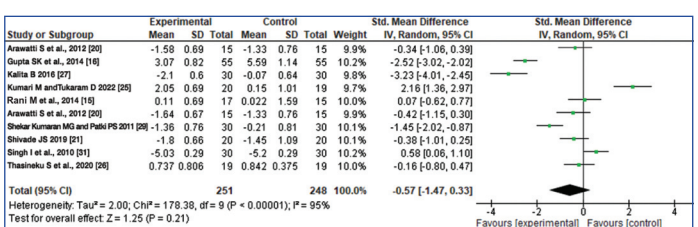
Effect of intervention on the number of calculi: Seven studies reported changes in the number of stones in the genitourinary tract, as observed by Ultrasonography (USG). These studies included 480 events (number of stones), with 261 in the treated group and 219 in the non-intervention group. The overall results of these studies using fixed-effects analysis revealed a substantial decrease in the number or size of stones in 178 cases in the group receiving the intervention, compared to only 101 events in the non-intervention category (OR: 3.03, 95% CI; 2.00, 4.61; [Table/Fig-6a]).



[Table/Fig-6c]: Effect of intervention on haematuria.



[Table/Fig-6d]: Effect of intervention on dysuria.



[Table/Fig-6e]: Effect of intervention on relief in pain.

Effect of intervention on the size of stones: The effect of interventions on the reduction in the size of stones was evaluated in 12 studies. These studies covered 571 patients, with 288 in the treated group and 283 in the non-intervention group. The overall

results of these studies using fixed-effects analysis revealed a substantial decrease in the size of stones (SMD: -0.07, 95% CI; -0.24, 0.11; [Table/Fig-6b]).

Effect of intervention on haematuria: The outcome of interventions on haematuria was analysed in seven studies, covered 291 patients, with 147 in the treated group and 144 in the non-intervention group. The overall results of these studies using fixed-effects analysis revealed a substantial results in haematuria with p=0.18 (SMD: 0.09, 95% CI; -0.16, 0.34; [Table/Fig-6c]). The heterogeneity I^2 was found to be 34%.

Effect of intervention on dysuria: The outcome of interventions on dysuria was analysed in six studies, involving 230 patients, with 116 in the treated group and 114 in the non-intervention group. The overall results of these studies using random-effects analysis revealed a highly substantial results in dysuria with p=0.04 (SMD: 0.25, 95% CI; -0.16, 0.66; [Table/Fig-6d]). The heterogeneity I2 was found to be 58%.

Effect of intervention on relief in pain: The outcome of interventions on pain relief in pain was analysed in ten studies, included 499 patients, with 251 in the treated group and 248 in the non-intervention group. The overall results of these studies using random-effects analysis revealed a highly substantial results in pain relief with p<0.0001 (SMD: -0.57, 95% CI; -1.47, 0.33; [Table/Fig-6e]). The heterogeneity I^2 was very high at 95%.

DISCUSSION

The increase in the number of urinary lithiasis (UL) cases worldwide is highly alarming. UL is a complex condition caused by physico-chemical phenomena such as saturation, nucleation process, expansion, accumulation, and retention in the kidney. Although there are several traditional therapies for UL, the recurrence of kidney stones and pharmacological side effects cannot be prevented [33]. Despite the abundance of anti-UL medicines available, treating UL with herbal plants is usually preferred. Herbal medications and medicinal plants with low toxicity and few or no adverse effects are crucial therapeutic choices for treating this disease throughout the globe [34]. This systematic review identified and analysed RCTs conducted in various parts of the world utilising therapies mentioned in Ayurvedic scriptures to treat UL.

This systematic review included 19 RCTs, which assessed the effectiveness of herbal medications in patients with urinary lithiasis (UL) with 1003 participants. The studies were of good quality as assessed using Jadad scoring. The reporting of RCT methodological components was adequate in all of them. All of the studies had well-defined primary outcomes and inclusion and exclusion criteria. However, none of the studies revealed prior sample size calculation. Sixteen authors indicated their research was randomised; however, only five studies used well-defined randomisation. Only one RCT stated that the outcome assessors were blinded. Nine trials reported a total of 48 dropouts. The duration of the studies varied from four to twenty-four weeks. There were no adverse medication reactions recorded in any of the investigations. Four RCTs reported the outcome in terms of percentage or number of stones only; thus, those were excluded from meta-analysis [18,19,23,24]. Although the research evidence is insufficient to establish the significance of Ayurvedic medicine in managing UL, the outcomes are reassuring. The present review confirmed the efficacy of therapies also included in Ayurvedic teachings. Nine studies were conducted compared to placebo, while three assessed the intervention against hydrotherapy. Similarly, potassium citrate was part of two studies [19,31]. Cystone, the most widely used proprietary medicine, was evaluated against a placebo in two studies [29,32], while it was used as a control in another two RCTs [18,22].

Crataeva nurvala Duch, *Tribulus terrestris* Linn, *Achyranthus aspera* Linn, *Nigella sativa* L. (Black seed), *Moringa oleifera* Lam, *Bergenia ligulata* Wall, *Dolichos biflorus* Linn, *Ricinus communis* Linn, *Musa paradisiaca* Linn, and *Onosma bracteatum* Wall were the main constituents of interventions included in this review.

Crataeva nurvala Duch includes the active ingredient Lupeol, which is widely known for its anti-urolithiatic action via anti-oxaluric and anti-calciuric properties [35]. *C. nurvala* decoction inhibited endogenous oxalate production in experimental UL [36]. *C. nurvala* reverses increased urine excretion of crystalline components while decreasing magnesium excretion. This action could be mediated by (Na+, K+) ATPase, which affects the transport mechanism [37]. *M. paradisiaca* stem juice was reported to help dissolve phosphate-type calculi [38]. Bergenin inhibits the development of urinary crystals by affecting the crystalloid colloid balance [39]. Yavakshara has a pH of 11.73, which aids in neutralising acidic environments and preventing calculus formation [26]. *N. sativa* contains its active compound, thymoquinone, which reduces the frequency and size of calcium oxalate plaques in rat renal tubules and has a preventative impact on developing calcium oxalate deposits in rat kidneys. As a result, it may be helpful in the prevention and dissolution of renal stones [40].

Different from Western medicine, the pharmacological composition of herbal medicine is complicated, making it difficult to pinpoint the mechanism(s) of action. Most herbs contain Tannin and Saponin, which have bioactivity such as diuretic, analgesic, anti-inflammatory, and anti-oxidant qualities and are responsible for these plants' UL capabilities [32]. Chemical studies of the plants are also required to extract and study the active principles to identify the ideal lead molecule.

Many herbal medications can be harmful if used for an extended period or at improper dosages. Thus, the long-term use of herbal therapy for UL should be investigated further. Surgical methods and ESWL are now widely used in treating urinary stones. The main disadvantage of these procedures is the recurrence of stones. Although plant products and derivatives of their lead chemicals cannot replace these methods, they can help reduce the recurrence rate of renal calculi [41].

Limitation(s)

First, the research sample size needed to be increased to determine the outcome. A limited sample size may impact the trial's quality, resulting in statistical discrepancies when measuring the effect of an intervention. Nine trials were compared to a placebo, with lifestyle adjustments and food management included in all studies to account for causal dietary factors and avoid the stones' recurrence. The interventions should be compared to the indicated medications of choice to analyse their effectiveness correctly. Because therapy options for UL are inadequate, the utility of AyM as a supplementary tool for treating UL should be investigated using high-quality RCTs. The findings from these RCTs should focus on the nephro-protective properties of Ayurvedic medications, as well as attempts to collect reliable information on efficacy. There was insignificant heterogeneity (I^2=49%) in the pooled analysis of studies of the primary outcome on the size of the stone and haematuria (I^2=34%). However, high heterogeneity was observed in a pooled analysis of studies in other outcomes. This could be due to the limited amount of studies in the assessment [42]. UL is a urinary manifestation that should be evaluated subjectively for symptomatic patients to provide comprehensive patient care.

CONCLUSION(S)

Conventional medicines have been employed since the dawn of time, and a few have been investigated for their efficacy in UL. The results of these studies have been inspiring. The limited available data show that Ayurvedic drugs have positive outcomes in the treatment of UL. Further extensive and long-term evidence is required for AyM to be adopted as a treatment option for UL.

Therefore, RCTs featuring traditional Ayurveda medication ought to adhere to CONSORT rules, with a greater sample size and a targeted strategy.

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