Herbal medicines for urinary stone treatment. A systematic review

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Herbal medicines for urinary calculi

Summary of findings tables

2 Summary of findings

Herbal medicines compared with citrate or placebo for urinary stones

Patient or population: patients with urolithiasis
Settings: outpatient
Intervention: any medicine based on herbal extracts or any preparation based on any part of medicinal plant, fruit or seed.
Comparison: various formulations of citrate preparations, placebo

Outcomes	Illustrative comparative risks (95% CI)	
	Assumed risk	Corresponding risk
	Control	Experimental
Comparison: herbal medicine (experimental) versus citrate (control) **Outcome: mean stone size variation at 3 months (mm)**	The stone size decrease ranged across control groups from -3.93 to -1.26	The mean stone size difference in the experimental group vs control was: 0.42 mm (higher) (95% CI 0.23 to 0.60)
Comparison: herbal medicine (experimental) versus citrate (control) **Outcome: mean concentration variation of urinary calcium at 3 months (mg/24h)**	The concentration variation ranged across control groups from -1.56 to 1.59	The mean concentration difference in the experimental group vs control was: 13.11 mg/24h (higher) (95% CI -11.69 to 37.92)
Comparison: herbal medicine (experimental) versus citrate (control) **Outcome: mean concentration variation of urinary urate at 3 months (mg/24h)**	The concentration variation ranged across control groups from -104.7 to 16.05	The mean concentration difference in the experimental group vs control was: 42.52 mg/24h (higher) (95% CI 19.44 to 65.19)
Comparison: herbal medicine (experimental) versus citrate (control) **Outcome: mean concentration variation of urinary oxalate at 3 months (mg/24h)**	The concentration variation ranged across control groups from -1.93 to 0.6	The mean concentration difference in the experimental group vs control was: -0.30 mg/24h (lower) (95% CI -2.39 to 1.79)
Comparison: herbal medicine (experimental) versus placebo (control) **Outcome: mean concentration variation of urinary calcium at end of therapy (mg/24h)**	The concentration variation ranged across control groups from -1 to 148.8	The mean concentration difference in the experimental group vs control was: -41.76 mg/24h (lower) (95% CI -142.85 to 59.31)
Comparison: herbal medicine (experimental) versus placebo (control) **Outcome: mean concentration variation of urinary urate at end of therapy (mg/24h)**	The concentration variation ranged across control groups from -16 to 88.7	The mean concentration difference in the experimental group vs control was: 21.79 mg/24h (higher) (95% CI -28.61 to 72.19)
Comparison: "Cystone" (experimental) versus placebo (control) **Outcome: mean stone size variation at 3 months (mm)**	The stone size decrease ranged across control groups from 0.07 to 1.06	The mean stone size difference in the experimental group vs control was: 4.95 mm (lower) (95% CI 9.18, 0.67)
Comparison: "Cystone" (experimental) versus placebo (control) Fraction of patients with stone clearance at 3 months	**89.28 per 1000**	**553.57 per 1000** (232.128 to 1515.96)

CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

No conflict of interest declared.

Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
//	151 (3)	⊕⊕⊝⊝ **low** [limitations in the study design and reporting biases are sufficient to lower confidence in the estimate of effect]
//	151 (3)	⊕⊝⊝⊝ **very low** [(i) high proportion of information from studies at high ROB – especially reporting and study design biases – and (ii) unexplained heterogeneity and inconsistency of results substantially lower the confidence in the estimate of effect]
//	151 (3)	⊕⊝⊝⊝ **very low** [(i) high proportion of information from studies at high ROB – especially reporting and study design biases – and (ii) unexplained heterogeneity and inconsistency of results substantially lower the confidence in the estimate of effect]
//	151 (3)	⊕⊝⊝⊝ **very low** [(i) high proportion of information from studies at high ROB – especially reporting and study design biases – and (ii) unexplained heterogeneity and inconsistency of results substantially lower the confidence in the estimate of effect]
//	97 (2)	⊕⊝⊝⊝ **very low** [(i) high proportion of information from studies at high ROB – especially reporting and study design biases – and (ii) unexplained heterogeneity and inconsistency of results substantially lower the confidence in the estimate of effect]
//	97 (2)	⊕⊝⊝⊝ **very low** [(i) high proportion of information from studies at high ROB – especially reporting and study design biases – and (ii) unexplained heterogeneity and inconsistency of results substantially lower the confidence in the estimate of effect]
//	112 (2)	⊕⊕⊕⊝ moderate
RR 6.19 (2.60 to 14.74)	112 (2)	⊕⊕⊕⊝ **moderate**

Table 1.
Summary of the characteristics and design of the studies included in the present review.

FIRST AUTHOR/ YEAR (reference n.)	STUDY DESIGN	DURATION THERAPY/ DURATION FOLLOWUP	OUTCOMES (CONSIDERED IN THIS REVIEW)	TOTAL PATIENTS RANDOMIZED	EXPERIMENTAL TREATMENT (n. randomized)	CONTROL (n. randomized)	CONTROL (n. randomized)	DROPOUTS Experimental/ control/Total
Brardi 2012 (13)	Prospective, randomized, open-label	5 months / no follow-up off-treatment	Stone number reduction, stone size reduction, urinary urate, oxalate, calcium concentration variation, adverse effects	50	Agropyrum repens extract (200 mg/day) plus potassium citrate (48 mEq/day [5224 mg/day]), plus allopurinol (300 mg/day) plus amiloride-hydrochlorothiazide (5+50 mg/day) plus pyridoxine (300 mg/day)(N=25)	Potassium citrate (48 mEq/day [5224 mg/day]), plus allopurinol (300 mg/ day) plus amiloride-hydrochlorothiazide (5+50 mg/day) plus pyridoxine (300 mg/day)(N=25)	//	0/0/0
Ceban 2012 (14)	Prospective, randomized, open-label	1 month / no follow-up off-treatment	Rate of spontaneous elimination of calculi, adverse effects	237	"standard medication"("common anti-inflammatory, analgesic or spasmolytic treatment") plus Canephron coated tablets [powdered Centaurii herba (18 mg), Levistici radix (18 mg) and Rosmarini folium (18 mg)], 6 tablets/day (N=135)	"standard medication"("common anti-inflammatory, analgesic or spasmolytic treatment") (N=102)	//	0/0/0
Erickson 2011 (16)	Prospective, randomized, double-blind, cross-over (second phase: open-label)	6 weeks / no follow-up off-treatment	Cystine stone burden reduction, adverse effects	10	"Cystone" tablets [Didymocarpus pedicellata 130 mg, Saxifraga ligulata 98 mg, Rubia cordifolia 32 mg, Cyperus scariosus 32 mg, Achyranthes aspera 32 mg, Onosma bracteatum 32 mg, Vernonia cinerea 32 mg, Shilajeet (tar-like rock exudate?) 26 mg, Hajrul yahood bhasma (fossilized stone?), 32 mg], 4/day plus "existing kidney stone treatment program" (N=5)	Placebo tablets, 4/day plus "existing kidney stone treatment program" (N=5)	//	0/0/0
Erickson 2011a (15)	Prospective, randomized, double-blind, cross-over (second phase: open-label)	6 weeks / no follow-up off-treatment	Stone burden reduction, adverse effects	10	"Cystone" tablets [composition: see above] 4/day plus "existing kidney stone treatment program" (N=5)	Placebo tablets, 4/day plus "existing kidney stone treatment program" (N=5)	//	?/?/1 (allocation unknown)
Kobayashi 2008 (17)	Prospective, randomized, open-label in post-lithotripsy patients	therapy "until stone clearance achieved"	Percentage of stone-free patients	102	Choreito [Mushrooms Polyporus umbrellatus and Wolfiporia extensa, plant Alisma orientale], 7.5 g/day plus diclofenac on-demand (N=30)	Tamsulosin, 0.2 mg/day plus diclofenac on-demand (N=38)	No fixed medication; diclofenac on-demand (N=34)	0/0/0/0
Lin 2013 (18)	Prospective, randomized, open-label	1 month / no follow-up off-treatment	Urinary calcium and urate concentration variation, adverse effects	39	Dried extract [Rhizoma alismatis, Poria cocos Wolf, Polyporus umbellatus Fries, Rhizoma Atractylodis Macrocephalae and Ramulus Cinnamomi Cassiae; the weight of each is in a ratio of 4:3:3:3:2] 2 g, thrice daily (N=20)	Placebo, 2g thrice daily (N=19)	//	6/5/11
Micali 2006 (19)	Prospective, randomized, open-label	"a minimum of 90 days" / 90 days follow-up	Percentage of stone-free patients, adverse effects	150 post-lithotripsy	Phyllantus niruri extract, 2 g/day (N=78)	No medication (N=72)	//	0/0/0
Mohanty 2010 (28)	Prospective, randomized, double-blind	6 months / interim control at 3 months, no follow-up off-treatment	Stone clearance, stone size reduction, adverse effects	52	"Cystone" tablets [composition: see Erickson 2011] 3/ day plus diclofenac 50 mg on-demand (N=26)	Placebo tablets, 3/day plus diclofenac 50 mg on-demand (N=26)	//	0/0/0
Nishiura 2004 (20)	Prospective, randomized, double-blind	3 months / no follow-up off-treatment	Stone number reduction, stone size reduction, urinary citrate, urate, oxalate, calcium concentration variation	69	Phyllantus niruri extract, 450 mg thrice/day (N=33)	Placebo [Chicorium sativum extract, unknown dosage] (N=36)	//	Unknown
Patankar 2008 (21)	Prospective, randomized, double-blind	3 months / no follow-up off-treatment	Stone size reduction, adverse effects	77	Crataeva magna, 250 mg plus Musa paradisiaca, 250 mg, twice/day plus diclofenac on-demand (Group A [Stone size 5-10 mm], N=23; Group B [Stone size >10 mm], N=24)	Placebo plus diclofenac on-demand (Group A [Stone size 5-10 mm], N=8; Group B [Stone size >10 mm], N=6)	//	Unknown

Premgamone 2001 (23)	Prospective, randomized, single-blind	18 months / no follow-up off-treatment	Rate of size reduction per year, adverse effects	48	Orthosiphon grandiflorus tea, 2.5 g/250 ml infusion twice daily (N=24)	Sodium potassium citrate granules “5 to 10 g/ day” (N=24)	//	2/5/7
Premgamone 2009 (22)	Prospective, randomized, double-blind	14 days / no follow-up off-treatment	Adverse effects of therapy	87	Orthosiphon grandiflorus capsuled extract, 1.6-1.8 g per capsule, twice/daily plus purine-free diet (N=42)	Capsuled placebo [Ipomea aquatica Forsk, unknown dosage], plus purine-free diet (N=45)	//	6/5/11
Shekar Kumaran 2011 (27)	Prospective, randomized, double-blind	3 months, interim control at 6 weeks on-therapy / no follow-up off-treatment	Stone clearance, stone size reduction, adverse effects	60	“Cystone" tablets [composition: see Erickson 2011] 4/ day plus “pain killer” on-demand (dose? N=30)	Placebo tablets, 4/day plus “pain killer” on-demand (dose? N=30)	//	0/4/4
Singh 2010 (24)	Prospective, randomized, open-label	6 months / no follow-up off-treatment	Stone size reduction; urinary urate, oxalate, calcium concentration variations	47	Dolichus biflorus seeds, 1-2 g/day (N=24)	Potassium citrate, “10-15 ml” (concentration?), 4 times/day (N=23)	//	Unknown
Singh 2011 (25)	Prospective, randomized, single-blind	90 days, interim control at 30 days	Stone clearance, stone size reduction, urinary urate, oxalate, calcium concentration variation, adverse effects	60	Calcury tablets [Saxifraga ligulata 150 mg, Saccharum officinarium 75 mg, Boerhaavia diffusa 75 mg, Hazaral yahud pishti 37.5 mg, Yavakshar (?) 15 mg, Parmelia perlata 150 mg, Crataeva nurvala 150 mg, Tribulus terrestris 75 mg, Picrorrhiza kurroa 75 mg, Tinospora cordifolia 75 mg], four tablets daily (N=30)	Potassium citrate “syrup”, “10 ml/ day” (concentration?) (N=30)	//	0/0/0
Singh 2012 (26)	Prospective, randomized, open-label	6 months / no follow-up off-treatment	Stone size reduction, urinary urate, oxalate, calcium concentration variation	44	Celosia argentea (Sitivaraka) seeds, 10 mg/kg thrice/ daily (N=21)	Potassium citrate “0.25 ml/kg body weight” (concentration?) 4 times/day (N=23)	//	0/0/0
Upadhyay 2011 (29)	Prospective, randomized, double-blind	6 months / followed-up every 2 months on-treatment	Stone clearance, stone size reduction, adverse effects	72	UNEX (Boerhavia diffusa, 2g/capsule, Tribulus terrestris, 1g/capsule), 4 capsules/day, plus diclofenac 50 mg on-demand (N=32)	Not described in the study report. Supposedly, placebo capsules, 4/day plus diclofenac 50 mg on-demand (N=32)	//	0/0/8

Table 2.
Summary of the risk of bias assessment for the present review.

FIRST AUTHOR/ YEAR (reference n.)	RANDOM SEQUENCE GENERATION (selection bias)	ALLOCATION CONCEALMENT	BLINDING PATIENTS/ PERSONNEL (performance bias)	BLINDING OF OUTCOME ASSESSOR (detection bias)	INCOMPLETE DATA (attrition bias)	SELECTIVE REPORTING (reporting bias)	OTHER BIAS (study design, baseline imbalances, etc.)	ANNOTATIONS
Brardi 2012 (13)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (open-label design)	**High** (open-label design)	**Low** (apparently no missing values)	**Unclear**	**High** (sample size calculation and analysis not performed or not disclosed; baseline clinical presentation data not shown; absence of imbalances only declared in text; citrate doses slightly differ in the two treatment groups [48 vs 54 mEq/day])	//
Ceban 2012 (14)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (open-label design)	**High** (open-label design)	**Unclear** (apparently no missing values, but duration of therapy [2 to 5 years] suggests likely generation of missing data)	**High** (statistical significance of increased frequency of spontaneous stone elimination not disclosed; intergroup statistics not disclosed)	**High** (baseline data not disclosed; sample size calculation and analysis not performed or not disclosed, undisclosed proportions of patients may have received different drugs or doses of "standard medication" that might have influenced the study endpoints)	//
Erickson 2011 (16)	**Low** (randomization method disclosed; blinded table strategy is adequate)	**Low** (allocation adequately concealed)	**High** (30% of patients could guess allocation by tasting the difference between herbal medicine and placebo)	**Low** (double-blind study, assessor blinded)	**High** (pre- and pos-crossover interim data not disclosed)	**High** (interim data pre- and pos-crossover not disclosed)	**High** (sample size calculation and power analysis not performed or not disclosed, undisclosed proportions of patients may have different drugs or doses within "existing stone treatment program" that might have influenced the study endpoints; CT scans and radiological assessment were only performed at baseline and at 52 wks from baseline, when the patients had all been switched to the experimental treatment for 40 wks)	Only first phase of crossover trial eligible for evaluation in the present review
Erickson 2011a (15)	**Low** (randomization method disclosed; blinded table strategy is adequate)	**Low** (allocation adequately concealed)	**High** (10% of patients could guess allocation by tasting the difference between herbal medicine and placebo)	**Low** (double-blind study, assessor blinded)	**High** (pre- and pos-crossover interim data not disclosed)	**High** (interim data pre- and pos-crossover not disclosed; statistical analysis for calcium phosphate [hydroxyapatite] not reported; 24 hour urine supersaturation data are reported instead of 24 hour urinary excretion)	**High** (sample size calculation and power analysis not performed or not disclosed, undisclosed proportions of patients may have different drugs or doses within "existing stone treatment program" that might have influenced the study endpoints; CT scans and radiological assessment were only performed at baseline and at 52 wks from baseline, when the patients had all been switched to the exp. treatment for 40 wks)	Only first phase of crossover trial considered. No explanation was provided of how the number of participants for analysis was determined or whether analysis was per-protocol, intention-to-treat, or else. Power of the study was diminished by failure of patients to return all required 24 hour urine samples. The botanical authenticity of Cystone was not documented.
Kobayashi 2008 (17)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (open-label design)	**High** (open-label design)	**High** (visual analysis of the graph correlating stone size and expulsion time suggests the existence of missing data, not addressed in the report)	**High** (rates of adverse effects not disclosed)	**High** (sample size calculation and power analysis not performed or not disclosed; undisclosed proportions of patients may have received diclofenac, that might have influenced study endpoints)	//
Lin 2013 (18)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**Unclear** (no mention of blinding is reported, though placebo formulation preparation suggests patient blinding)	**High** (open-label design)	**Low** (apparently no missing values)	**High** (data on serum uric acid not reported; stone severity index after treatment not reported)	**High** (sample size calculation and power analysis not performed or not disclosed)	Study limitations: oxalate and citrate levels in urine not examined; short treatment period; daily urine output used as a marker of drug efficacy. Data in the two tables are dubious. Percent changes in treatment and placebo groups were compared irrespective of the statistical significance of the change.
Micali 2006 (19)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (open-label design)	**High** (open-label design)	**Low** (apparently no missing values)	**High** (rates of adverse effects not disclosed)	**High** (sample size calculation and power analysis not performed or not disclosed; stratification by stone location was not originally included in the design of the study)	//
Mohanty 2010 (28)	**Unclear** (randomization strategy not disclosed)	**Low** (the allocation was reportedly concealed)	**Low** (double-blind design)	**Unclear** (not disclosed whether outcome assessors were blinded to treatment allocation)	**Unclear** (No mention is made of how the data pertaining to the subjects in which the calculi disappeared were treated in the stone size analysis)	**High** (in describing the effects of Cystone on calculi size, it is stated that "the study showed significant reduction in the calculi size […] in the Cystone group *as compared to placebo* (increase by 10.37%). This is misleading because a) the increase was not statistically significant; b) no direct comparison was made between Cystone and placebo)	**High** (undisclosed proportions of patients may have received different doses of diclofenac, that might have influenced study endpoints)	//

Nishiura 2004 (20)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**Low** (patients/personnel blinded and capsule adequately concealed)	**Low** (double-blind design)	**Low** (apparently no missing values and no dropouts reported)	**High** (rates of adverse effects not disclosed; intergroup statistics not disclosed)	**High** (sample size calculation and power analysis not performed or not disclosed; *Chicorium sativum* extract dosage not disclosed; percent changes in treatment or placebo were compared irrespective of the statistical significance of the change)	//
Patankar 2008 (21)	**Low** (randomization method disclosed; envelope method is adequate)	**Unclear** (allocation concealment strategy not disclosed)	**Low** (patients/personnel blinded and capsule adequately concealed)	**Low** (double-blind design)	**Low** (patients who did not attain the primary endpoint were left out the analysis; thus there are very likely no missing data)	**High** (rates of adverse effects not disclosed)	**High** (Baseline data not disclosed)	//
Premgamone 2001 (23)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (patients unblinded)	**Low** (assessing physicians blinded and unaware of patient allocation)	**High** (data at 18 months for citrate group not disclosed; no mention is made of how the data relating to the 6 dropped-out subjects were treated)	**Unclear**	**High** (baseline data not disclosed; sample size calculation and power analysis not performed or not disclosed, undisclosed proportions of patients may have received antibacterial treatment that might have influenced the assessed outcomes; Simply comparing ROSRPY in the treatment and control groups at each time point is not a valid statistical analysis, ANOVA for repeated measures should have been used)	//
Premgamone 2009 (22)	**High** (block randomization system allowed foreknowledge of last-in-block patient allocation)	**High** (block randomization within groups 1 and 2 performed separately)	**Low** (patients/personnel blinded and capsule adequately concealed)	**Unclear** (not disclosed whether VAS assessment supervisor was blinded to treatment allocation)	**Low** (apparently no missing values)	**High** (intergroup statistics not disclosed)	**High** (sample size calculation and power analysis not performed or not disclosed; *Ipomea aquatica* dosage not disclosed)	Adverse effects decrease or disappear with time as they overlap with baseline symptoms of disease.
Shekar Kumaran 2011 (27)	**Low** (randomization method disclosed; computer-assisted strategy is adequate)	**Unclear** (concealment declared, but allocation strategy not disclosed)	**Low** (double-blind design)	**Unclear** (not disclosed whether outcome assessors were blinded to treatment allocation)	**high**: no mention is made of how the data pertaining to the subjects in which the calculi disappeared were treated in the stone size analysis; no details are given as to whether any censoring was applied to the data pertaining to the four patients who discontinued treatment in the placebo group	**High** (number of patients complaining of GI adverse effects in the placebo arm not disclosed; intergroup statistics not disclosed; No explanation is offered for treatment discontinuation by four patients in the placebo group)	**High** (composition of experimental drug not indicated; undisclosed proportions of patients may have received different doses of diclofenac, that might have influenced study endpoints)	//
Singh 2010 (24)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (open-label design)	**High** (open-label design)	**Low** (apparently no missing values)	**High** (The Authors state that "patients who developed side effects or had deterioration of renal function were taken off the study protocol", but do not mention how many patients, in which group and what the side effects were; intergroup statistics not disclosed)	**High** (The likely reason why the observed difference in stone size in the control group is not statistically significant is the higher baseline data variability in this group; true doses of plant extract and citrate not disclosed)	Student's t test not appropriate for more than two repeated measures
Singh 2011 (25)	**Low** (randomization method disclosed; blinded table strategy is adequate)	**High** (As the patients were to be equally allocated into treatment groups, for the last patients enrolled allocation was predictable)	**High** (open-label design)	**Low** (assessing physicians unaware of patient allocation)	**Low** (apparently no missing values)	**High** (intergroup statistics not disclosed)	**High** (true doses citrate not disclosed)	//
Singh 2012 (26)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**High** (open-label design)	**High** (open-label design)	**Low** (apparently no missing values)	**High** (rates of adverse effects not disclosed; intergroup statistics not disclosed)	**High** (baseline data not disclosed; sample size calculation and power analysis not performed or not disclosed; true doses of citrate not disclosed)	//
Upadhyay 2011 (29)	**Unclear** (randomization strategy not disclosed)	**Unclear** (allocation concealment strategy not disclosed)	**Low** (double-blind design)	**Unclear** (not disclosed whether outcome assessors were blinded to treatment allocation)	**High** (no information about data from 8 patients [dropouts?])	**High** (intergroup statistics not disclosed [e.g., stone size])	**High** (baseline data not disclosed; sample size calculation and analysis not performed or not disclosed, undisclosed proportions of patients may have received diclofenac, that might have influenced study endpoints)	

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Systematic Review Searching Record

Question title: Efficacy and safety of herbal remedies for Urinary stones

1. Literature search details

Date Restriction: None

Language Restriction: None

Database name	Dates Covered	No of references found	Finish date of search
Medline (OVID)	1946 - present	90	14/12/2015
Medline in process (OVID)	18/09/2015	2	14/12/2015
Embase (OVID)	1947 - present	100	14/12/2015
AMED (OVID)	1985 - present	53	14/12/2015
CAM Quest (Carstens-Stiftung)	From Inception	43 (11 Retrieved)	14/12/2015
CINAHL (EBSCO)	1937 - present	88	14/12/2015
BNI (ProQuest)	1994 - present	55	14/12/2015
Pubmed (National Library of Medicine)	Jan 14 - present	19	14/12/2015
Cochrane Library (Wiley)	Issue 4	33	14/12/2015
Web of Science Core Collection (Thomson Reuters)	1900 – present 1990 - present	121	14/12/2015
LILACS (Virtual Health Library)	1982 - present	25	14/12/2015
Scopus (Elsevier)	1960 - present	153	14/12/2015
OpenGrey (Native Interface)	1980 - present	37 (9 Retrieved)	14/12/2015
WHO Int.Clin Trials Registry Search Portal (World Health Orgainsation)	2009 - present	25 (8 Retrieved)	14/12/2015
ClinicalTrials.gov (U.S. National Institutes of Health)	2008 - present	1	14/12/2015
TOTAL		**845 (768 Retrieved)**	14/12/2015

Total References retrieved (after de-duplication): = 541

Search strategies

<u>Medline Search Strategy and Medline in Process (OVID)</u>

1. exp Plants, Medicinal/
2. exp Phytotherapy/
3. exp Herbal Medicine/
4. exp Drugs, Chinese Herbal/

5. exp Ethnopharmacology/
6. (herb* adj2 (remed* or medicin* or treat* or prep* or drug* or extract*)).tw.
7. Phytotherap*.tw.
8. or/1-7
9. exp Nephrolithiasis/
10. exp Kidney Calculi/
11. exp Urolithiasis/
12. exp Urinary Calculi/
13. ((kidney* or renal or urin*) adj2 (stone* or calcul* or crystal*)).tw.
14. or/9-13
15. 8 and 14
16. randomized controlled trial.pt.
17. controlled clinical trial.pt.
18. randomized.ab.
19. placebo.ab.
20. drug therapy.fs.
21. randomly.ab.
22. trial.ab.
23. groups.ab.
24. or/16-23
25. exp animals/ not humans.sh.
26. 24 not 25
27. 15 and 26

EMBASE (OVID) Search Strategy

1. exp medicinal plant/
2. exp herbal medicine/
3. exp phytotherapy/
4. exp ethnopharmacology/
5. (herb* adj2 (remed* or medicin* or treat* or prep* or drug* or extract*)).tw.
6. Phytotherap*.tw.
7. or/1-6

8. exp nephrolithiasis/
9. exp Urolithiasis/
10. ((kidney* or renal or urin*) adj2 (stone* or calcul* or crystal*)).tw.
11. or/8-10
12. 7 and 11
13. crossover procedure/
14. double blind procedure/
15. randomized controlled trial/
16. single blind procedure/
17. (random* or factorial* or crossover* or cross over* or cross-over* or placebo* or assign* or allocat* or volunteer*).mp.
18. ((doubl* or singl*) adj blind*).mp.
19. or/13-18
20. 12 and 19

AMED (OVID) Search Strategy

1. exp Plants medicinal/
2. exp Herbalism/
3. exp Herbal drugs/
4. exp Drugs chinese herbal/
5. exp Phytotherapy/
6. (herb* adj2 (remed* or medicin* or treat* or prep* or drug* or extract*)).tw.
7. Phytotherap*.tw.
8. or/1-7
9. exp kidney calculi/
10. ((kidney* or renal or urin*) adj2 (stone* or calcul* or crystal*)).tw.
11. Urolithiasis.tw.
12. Nephrolithiasis.tw.
13. or/9-12
14. 8 and 13

CAM Quest (Carstens-Stiftung) Search Strategy

Key Terms: Kidney Stones

Full Text Terms: Nephrolithiasis or Urolithiasis or Kidney Stones or Kidney Calculi

CINAHL Search Strategy (EBSCO)

S12 S6 AND S11
S11 S7 OR S8 OR S9 OR S10
S10 TX ((kidney* or renal or urin*) N2 (stone* or calcul* or crystal*))
S9 (MH "Urinary Calculi+")
S8 (MH "Kidney Calculi")
S7 (MH "Urolithiasis+")
S6 S1 OR S2 OR S3 OR S4 OR S5
S5 TX Phytotherap*
S4 TX (herb* N2 (remed* or medicin* or treat* or prep* or drug* or extract*))
S3 (MH "Drugs, Chinese Herbal")
S2 (MH "Medicine, Herbal+")
S1 (MH "Plants, Medicinal+")

BNI (ProQuest) Search Strategy

(SU.EXACT.EXPLODE("Alternative Therapies") OR TI,AB(herb* NEAR/2 (remed* OR medicin* OR treat* OR prep* OR drug* OR extract*)) OR TI,AB(phytotherap*)) AND (SU.EXACT.EXPLODE("Kidney Disorders") OR SU.EXACT("Urinary System and Disorders") OR TI,AB((kidney* OR renal OR urin*) NEAR/2 (stone* OR calcul* OR crystal*)))

PubMed (National Library of Medicine) Search Strategy

#18,"Search (#8 and #16) Filters: Publication date from 2014/01/01 to 2015/12/31"
#17,"Search (#8 and #16)"
#16,"Search (#9 or #10 or #11 or #12 or #13 or #14 or #15)"
#15,"Search ((urin* stone*[Title/Abstract]) OR urin* calcul*[Title/Abstract]) OR urin* crystal*[Title/Abstract]"
#14,"Search ((kidney stone*[Title/Abstract]) OR kidney calcul*[Title/Abstract]) OR kidney

crystal*[Title/Abstract]"
#13,"Search ((renal stone*[Title/Abstract]) OR renal calcul*[Title/Abstract]) OR renal crystal*[Title/Abstract]"
#12,"Search urinary calculi[MeSH Terms]"
#11,"Search kidney calculi[MeSH Terms]"
#10,"Search urolithiasis[MeSH Terms]"
#9,"Search nephrolithiasis[MeSH Terms]"
#8,"Search (#1 or #2 or #3 or #4 or #5 or #6 or #7)"
#7,"Search phytotherap*[Title/Abstract]"
#6,"Search (((((herb* remed*[Title/Abstract]) OR herb* medicin*[Title/Abstract]) OR herb* treat*[Title/Abstract]) OR herb* drug*[Title/Abstract]) OR herb* extract*[Title/Abstract]) OR herb* prep*[Title/Abstract]"
#5,"Search ethnopharmacology[MeSH Terms]"
#4,"Search drugs, chinese herbal[MeSH Terms]"
#3,"Search herbal medicine[MeSH Terms]"
#2,"Search phytotherapy[MeSH Terms]"
#1,"Search plants, medicinal[MeSH Terms]"

Cochrane Library (Wiley) Search Strategy

#1	MeSH descriptor: [Plants, Medicinal] explode all trees
#2	MeSH descriptor: [Phytotherapy] explode all trees
#3	MeSH descriptor: [Herbal Medicine] explode all trees
#4	MeSH descriptor: [Drugs, Chinese Herbal] explode all trees
#5	MeSH descriptor: [Ethnopharmacology] explode all trees
#6	(herb* near/2 (remed* or medicin* or treat* or prep* or drug* or extract*)):ti,ab,kw
#7	phytotherap*:ti,ab,kw
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7
#9	MeSH descriptor: [Nephrolithiasis] explode all trees
#10	MeSH descriptor: [Urolithiasis] explode all trees
#11	MeSH descriptor: [Kidney Calculi] explode all trees
#12	MeSH descriptor: [Urinary Calculi] explode all trees
#13	((kidney* or renal or urin*) near/2 (stone* or calcul* or crystal*)):ti,ab,kw

#13 #9 or #10 or #11 or #12 or #13

#14 #8 and #14

Web of Science Core Collection (Thomson Reuters) Search Strategy

9 #8 AND #4

8 #7 OR #6 OR #5

7 TS=((kidney* or renal or urin*) NEAR/2 (stone* or calcul* or crystal*))

6 TS=(Urolithiasis)

5 TS=(Nephrolithiasis)

4 #3 OR #2 OR #1

3 TS=(Ethnopharmacolog*)

2 TS=(Phytotherap*)

1 TS=(herb* NEAR/2 (remed* or medicin* or treat* or prep* or drug* or extract*))

LILACS (Virtual Health Library) Search Strategy

(tw:(herb* OR erva* OR hierb* OR phytotherap* OR fitoterapia) OR mh:("Herbal Medicine" OR "Phytotherapy" OR "Drugs, Chinese Herbal" OR "Ethnopharmacology")) AND (mh:("Kidney Calculi" OR "Nephrolithiasis" OR "Urinary Calculi" OR “Urolithiasis) OR tw:(kidney stone* OR kidney calcul* OR kidney crystal* OR calcul* renais OR pedra renal OR pedra* rin OR cristal renal OR calcul* renal* OR calcul* fisica OR cristal rinon* OR urin* calcul* OR urin* crystal* OR pedra urin* OR piedra urin* OR cristal urin*)) AND (instance:"regional") AND (db:("LILACS"))

Scopus ((Elsevier) Search Strategy

(((TITLE-ABS-KEY (herb* W/2 (remed* OR medicin* OR treat* OR prep* OR drug* OR extract*))) OR (TITLE-ABS-KEY (phytotherap*)) OR (TITLE-ABS-KEY (ethnopharmacolog*))) AND ((TITLE-ABS-KEY (nephrolithiasis OR urolithiasis)) OR (TITLE-ABS-KEY (kidney* W/2 (stone* OR calcul* OR crystal*))) OR (TITLE-ABS-KEY (urin* W/2 (stone* OR calcul* OR crystal*))) OR (TITLE-ABS-KEY (renal W/2 (stone* OR calcul* OR crystal*))))) AND (((TITLE-ABS-KEY (clinical trial*)) OR (TITLE-ABS-KEY (research design*)) OR (TITLE-ABS-KEY (comparative stud*)) OR (TITLE-ABS-KEY (evaluation stud*)) OR (TITLE-ABS-KEY (controlled trial*)) OR (TITLE-ABS-KEY (follow up stud*)) OR (TITLE-ABS-KEY (prospective stud*)) OR (TITLE-ABS-KEY (random*)) OR (TITLE-ABS-KEY (placebo*)) OR (TITLE-ABS-KEY (single blind*)) OR (TITLE-ABS-KEY (double blin*))))

OpenGrey (Native Interface)

((herb* OR Phytotherap*) AND (Kidney* OR Renal OR Urin*))

WHO Int.Clin Trials Registry Search Portal (World Health Orgainsation) Search Strategy

herb* AND kidney*

herb* AND urin*

ClinicalTrials.gov (U.S. National Institutes of Health) Search Strategy

(herb OR phytotherapy) AND (kidney stone OR Kidney calculi OR kidney calculus OR kidney crystal OR renal stone OR renal calculi OR renal calculus OR renal crystal OR Nephrolith OR urolithiasis OR urinary stone OR urinary calculi OR urinary crystal)

2. Any further comments:

Results on databases with no export facility or poor search interfaces were screened and only references that were relevant to the topic were retrieved. Results on Urinary Tract Infections were not retrieved.

All databases have been searched as far back as they will go and an RCT filter has been applied where appropriate.