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Dietary interventions on nutritional management of population with urolithiasis: a systematic review of clinical evidence

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Review Article

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Abstract

Urolithiasis (UL) is a multifactorial condition whose global prevalence has been increasing in recent years, and it is closely associated with dietary factors. Diet is one of the key elements linked to the development of UL due to the intake of many nutrients that cause metabolic alterations associated with the crystallisation process and the risk of developing urinary stones. Despite the crucial role of diet, few studies have implemented dietary interventions. In this sense, dietary modifications play a fundamental role in the prevention, control and management of UL. Thus, the aim of this systematic review is to summarise the main beneficial effects of dietary interventions in populations with UL. A comprehensive search was conducted in MEDLINE/PubMed, SpringerLink, Google Scholar, Scielo and Redalyc databases for intervention studies published up to July 2025 that reported dietary interventions aimed at preventing and controlling UL. The risk of bias and quality of studies were assessed. A total of twenty-six articles were included, focusing on dietary interventions such as controlling sodium, oxalate, calcium, citrate and protein intake, as well as low-calorie diets. In addition, foods such as lemon, orange, melon, lime, cranberry, apple juices, milk, vinegar, black seed, green bean extract, probiotics and synbiotic were also explored, which promoted significant changes in serum and urinary parameters related to UL. This review compiles evidence on dietary intervention strategies that lead to significant improvements in biochemical parameters in populations with UL (PROSPERO CRD42022361702).

Introduction

Urolithiasis (UL) refers to the presence of stones in the kidneys or the urinary tract[1]. It is a consequence of metabolic alterations and changes in urine composition that induce stone formation[2,3]. The most frequent metabolic disorders associated with UL are hypocitraturia (<320 mg/d), hypercalciuria (>300 mg/d in men and >250 mg/d in women), and hyperoxaluria (>45 mg/d)[4]. These metabolic disturbances are directly related to the composition of stones, which mainly contain calcium (70–88%), calcium oxalate (CaOx, 36–70%), calcium phosphate ($CaPO_4$, 6–20%), and mixtures of magnesium ammonium phosphate (struvite, 6–20%), uric acid (6–17%), and/or cystine (0·5–3%)[5].

UL has become one of the main health problems worldwide with increasing prevalence rates[6], which are highest in Saudi Arabia (20·1%), Spain (15·5%), Canada (12%), France (10%) and the USA (8·8%)[7,8]. Being a multifactorial disease, risk factors for stone formation include age, climate, excess body weight, diet and genetic factors[9]. Despite the existence of pharmacological and surgical treatments for UL, up to 50% of people present recurrence of the disease 5 years after the first episode[5,10,11].

Diet plays a key role in the prevention and management of UL[12,13]. Studies and guidelines currently recommend diet management as a useful treatment to reduce the risk of UL. Dietary recommendations include increased intake of water (3 L to generate ≥2·5 L urine output volume), citrates (40–60 mEq/d), calcium (1500–1200 mg/d), potassium (>2000 mg/d),

magnesium (350 mg/d) and fibre (25–30 g/d), as well as the reduced consumption of oxalate (40–50 mg/d), sodium (1000–2300 mg/d) and protein (<1 g/kg/d). These recommendations aim to avoid low urinary volume and pH, and/or regulated urinary metabolic alterations that lead to stone formation[14–17]. Nonetheless, few studies have addressed the effects of dietary interventions on stone formers. Thus, the aim of the present systematic review was to summarise the main beneficial effects of dietary interventions on individuals with UL.

Materials and methods

The present study was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Supplementary Table 1)[18]. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under reference number CRD42022361702.

Search strategy

Two authors (B.P.-H. and D.S.-E.) performed the search strategy, for which the following databases were searched for intervention studies published up to July 2025: MEDLINE/PubMed, Springerlink, Google Scholar, Scielo, and Redalyc. The search strategy included the following terms and operators: 'dietary intervention', 'diet', 'nutrition', 'alimentation', 'diet therapy', 'treatment dietary', 'dietary', AND 'kidney stones', 'urolithiasis', 'calculi', 'hyperoxaluria', 'calcium oxalate', 'hypercalciuria', 'renal stone', 'urinary calculi' NOT 'shockwave lithotripsy', 'nephrolithotomy', 'surgery', 'medical', 'antibiotic'. The search filters applied were type of article (clinical trial and randomised controlled trial) and articles in the urology or nephrology division. The included studies were evaluated following the Population, Intervention, Control, Outcomes (PICO) strategy[19] (Table 1).

Study selection

After removing duplicates, the same authors (B.P.-H. and D.S.-E.) independently screened titles and abstracts for eligibility based on the inclusion criteria. Articles that could not be eliminated by title or abstract were retrieved in full and subsequently assessed against eligibility criteria prior to final inclusion. Subsequently, potentially eligible articles (by title and abstract) were assessed by three authors (B.P.-H., D.S.-E and A.A.-N.) according to eligibility criteria and full-text data extraction was carried out.

Selection criteria

Experimental studies (randomised controlled trial) and quasi-experimental studies (non-randomised controlled studies and before-and-after studies) were included. Inclusion criteria were studies (1) performed on adult with the presence of kidney stones or identified as stone formers; (2) evaluating any dietary intervention; (3) reporting urinary parameters such as volume, pH, calcium, uric acid, urea, citrate and oxalate; (4) reporting serum parameters including pH, uric acid and calcium; and (5) studies in English or Spanish language. Exclusion criteria were (1) retrospective studies; (2) *in vitro* studies; (3) animal studies; (4) studies including healthy populations only; (5) studies restricted to children, adolescents or older adults; (6) pharmacological intervention studies; (7) surgical intervention studies; and (8) review articles.

Table 1. PICO criteria for study selection

	Criterion	Description
P	Population	Individuals with presence of kidney stones or stone formers
I	Intervention	Nutritional management of patients with kidney stones
C	Control	Any comparator or comparison: placebo, control diet or group, and before-and-after comparisons
O	Outcome	Urinary parameters such as volume, pH, calcium, uric acid, urea, citrate and oxalate. Serum parameters including pH, uric acid and calcium

Data extraction

Data extraction from all selected articles was independently performed by four authors (B.P.-H., D.S.-E., I.M.-V. and M.G.-C.). The following characteristics were recorded: (1) first author's name and year of publication, (2) country, (3) study design, (4) characteristics of the study population and sample size, (5) dietary intervention, (6) follow-up time and (7) main results. Any discrepancies were solved by J.G.R.-G., C.C.M.-M. and A.L.G.-S.

Quality assessment

The risk of bias was assessed with the Cochrane tool[20]. The following items were evaluated: adequacy of sequence generation and allocation concealment to evaluate selection bias, blinding of individuals and personnel to evaluate performance bias, blinding of outcome assessment to evaluate detection bias, incomplete outcome data to evaluate attrition bias, selective outcome reporting to evaluate reporting bias, and other potential sources of bias. The quality of study reporting was assessed with the CONSORT statement[21]. These assessments were performed independently by four authors (B.P.-H., D.S.-E., I.M.-V. and J.G.R.-G.) and any discrepancies were solved by the other researchers.

Results

Study selection

Studies included for analysis were published between the years 1996 and 2025 (Table 2). A total of 648 studies were identified, of which 27 duplicates were removed. In addition, 581 were removed after title screening, association studies, studies of other diseases, pharmacological intervention studies, and surgical intervention studies. Forty studies were identified for potential inclusion in the review. After reviewing the summary, fourteen studies were eliminated on the basis of the selected criteria. The main reasons for exclusion were studies including healthy populations ($n = 8$), association studies ($n = 1$), reporting the composition of functional foods but no dietary interventions ($n = 1$), with the use of vitamin supplementation or medical intervention ($n = 2$), not available data of urinary or serum parameters ($n = 1$), and protocol ($n = 1$). Ultimately, twenty-six articles were included in the review (Fig. 1).

Populations and study design

All studies included both women and men, except for the studies of Borghi *et al.*[22], which only included men, and Aras *et al.*[23], which did not specify the sex of individuals. All study populations consisted of patients with UL and three included healthy individuals as the

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Table 2. Characteristics of the studies included in this systematic review

Author, year	Country	Study design	Population and sample size	Intervention	Follow-up	Main results
Dietary interventions of foods or functional components against urolithiasis						
Massey *et al.* 1998[27]	USA	Randomised crossover trial	Individuals with UL and hyperoxaluria (CaOx stone) $n = 21$	Interventions with: 1. Apple juice (180 mL + 4 g egg white powder) 2. Skim milk (120 mL) Three times a day	6 d and washout period (4 weeks)	Comparison of interventions *In urine* Skim milk ↓↓↓ Ox ↑ Ca
Mendonca *et al.* 2003[24]	Brazil	Randomised controlled trial*	Individuals without UL $n = 41$ Individuals with UL (CaOx stones) $n = 70$	Intervention with: 1. Milk chocolate (200 g) (Ox: 94 mg, Ca: 428 mg) 2. Dark chocolate (67 g) (Ox: 94 mg, Ca: 26 mg)	3 d	Compared with baseline *In urine* Dark chocolate: ↑ Ox **Without differences between interventions
Gettman *et al.* 2005[25]	USA	Randomised, controlled crossover trial*	Individuals without UL $n = 12$ Individuals with UL (CaOx stone) $n = 12$	Two groups: 1. Deionised water (control) 2. Cranberry juice (500 mL of each), two times a day	7 d and washout period (3 weeks)	Comparison of interventions Individuals with UL *In urine* Cranberry juice ↑ Ox ↑↑ Ca ↓↓↓ UA, pH *In serum* Cranberry juice ↓ UA Control individuals *In urine* Cranberry juice ↓ UA, pH *In serum* Cranberry juice ↓ UA
Goldfarb *et al.* 2007[28]	USA	Randomised, double-blind, placebo-controlled trial	Individuals with UL and hyperoxaluria (CaOx stone) $n = 20$	Intervention with (3 g): 1. Oxadrop ($3{\cdot}6\times10^{11}$ bacteria) 2. Placebo (corn starch)	28 d	**Without differences between intervention
Koff *et al.* 2007[44]	USA	Clinical crossover study	Individuals with UL and hypocitraturia $n = 21$	Interventions two with: 1. Potassium citrate supplementation (2160 mg potassium citrate (60 mEq/d]) three times per day 2. Lemonade (30 mL of lemon juice (real lemon) + 3/4 cup water + 1 sweetener for each serving (3 times per day (4500 mg, 63 mEq citrate/d)	5 d and washout period (2 weeks)	Compared with baseline *In urine* Potassium citrate supplementation ↑↑ Cit ↑↑↑ pH ↓ Volume **Without analysis between interventions

(*Continued*)

Table 2. (*Continued*)

Author, year	Country	Study design	Population and sample size	Intervention	Follow-up	Main results
Aras *et al.* 2008[23]	Turkey	Randomised trial	Individuals with UL and hypocitraturia (Ca stones) $n = 30$	Interventions with: 1. Lemon juice (85 mL/d, 60 mEq 4·2 g Cit + 1000 mL of ± water) 2. Potassium citrate supplement (60 mEq/d) 3. Dietary recommendations	3 months	Compared with baseline *In urine* Lemon group ↑↑ Cit ↑ Volume Potassium citrate group ↑↑ Cit ↑ Ox, pH and volume Dietary recommendations *In urine* ↑↑ Cit ↑ Volume Comparison of interventions Lemon juice *v.* dietary recommendation: Lemon juice *In urine* ↑ Cit Potassium citrate supplementation *v.* dietary recommendation: Potassium citrate supplementation *In urine* ↑ Cit
Lieske *et al.* 2010[29]	USA	Double-blind, placebo-controlled trial	Individuals with UL and mild hyperoxaluria (CaOx stones) $n = 40$	Interventions with: 1. Probiotic (Oxadrop, one packet q.d. + one placebo capsule b.i.d.) 2. Synbiotic (AKSB, one capsule b.i.d. + one placebo packet q.d.) 3. Placebo (one placebo packet q.d. and one placebo capsule b.i.d.)	5 weeks	**Without differences between intervention
Baia *et al.* 2012[30]	Brazil	Randomised trial*	Individuals with UL and hypocitraturia (CaOx stone) $n = 30$	Three different interventions: 1. Non-citrus fruit (300 mL of melon + 85 mL of water) 2. Orange juice (385 mL) 3. Lime water (75 mL of lime + 310 mL of water)	1 d	Compared with baseline *In urine* Non-citrus ↑ Cit (at 4 h) ↑ pH (at 4 h, 6 h) Orange juice ↑ Cit (at 2, 4, 6 h) ↑ pH (at 4 h) Lime water ↑ Cit (at 2, 4 h) Orange juice ↑ Cit (at 2, 4 h) **Without analysis between interventions

Table 2. (*Continued*)

Ardakani *et al.* 2018[31]	Iran	Randomised, double-arm, double-blind, placebo-controlled, clinical trial	Individuals with UL (CaOx stones) *n* = 60	Two interventions with capsules of: 1. Black seed (*Nigella sativa* L) 2. Placebo starch Two times per day (500 mg/d)	10 weeks	Compared with baseline Black seed *In serum* ↑↑ Ca *In urine* ↓ pH Comparison of interventions *In urine* Black seed ↓↓pH
Zhu *et al.* 2019[32]	China	Randomised controlled trial	Individuals with UL (CaOx stones) *n* = 79	Two groups: 1. Control: pure water (purified water) 2. Intervention group: mature vinegar (Ninghuafu®, 12·5 mEq/d acetate) (5 mL three times)	12 months	Comparison of interventions *In urine* Mature vinegar ↑↑↑ Cit ↓↓ Ca ↑↑ pH
Jalal *et al.* 2020[47]	Saudi Arabia	Randomised controlled trial	Individuals with UL *n* = 60	Two groups: 1. Control group 2. Extract of green bean (*Phaseolus Vulgaris*) group (750 g of fresh beans in 2·2 L to 2·5 L) three times per week	6 weeks	Compared with baseline *In urine* Extract of *Phaseolus vulgaris* ↑↑ Volume ↓↓↓ UA, Ca, Ox **Without analysis between groups
Benefits of diets with controlled mineral salt intake in individuals with urolithiasis						
Caudarella *et al.* 1998[33]	Italy	Randomised crossover trial	Individuals with UL (CaOx stone) *n* = 22	Interventions with different types of water-based drinks (2 L/d): 1. Control group (usual water consumed at home) 2. High Ca (380 mg/L, pH 6·1) 3. Medium Ca (123·9 mg/L, pH 7·2) 4. Low Ca (15·3 mg/L, pH 7·1)	20 d and washout period (2 weeks) between interventions	Comparison of interventions Differences between control group *v.* high Ca water *In urine* High Ca ↑ Cit ↓ Ox
Bellizzi *et al.* 1999[34]	Italy	Randomised double-blind crossover trial	Individuals with UL (CaOx stone) *n* = 18	Interventions with three types of water (2 L/d): 1. Naples tap water: (Ca 63 ± 8 mg/L) 2. Soft water: 'Fiuggi'water (Ca 22 mg/L) 3. Hard water: 'Sangemini' water (Ca 255 mg/L)	7 d and washout period (1 week)	Comparison of interventions *In urine* Hard water ↑ pH, Ca Hard water *v.* Naples tap water *In urine* Hard water ↑ UA

(*Continued*)

Table 2. (*Continued*)

Author, year	Country	Study design	Population and sample size	Intervention	Follow-up	Main results
Liatsikos *et al.* 1999[45]	Greece	Before-and-after study*	Individuals with UL and hypercalciuria *n* = 42	Intervention with a controlled diet (Ca 900–1000 mg/d, protein intake 0·8 g/kg/d, liquids 2000 mL/d)	10 d	Compared with baseline *In serum* ↑ pH ↓urea *In urine* ↓UA, Ox ↓↓↓ Urea, Ca
Borghi *et al.* 2002[22]	Italy	Randomised trial	Men with UL and hypercalciuria (CaOx stones) *n* = 120	Interventions with two diets: 1. Normal Ca (30 mmol/d) 2. Low Ca (10 mmol/d)	5 years	Comparison of interventions *In urine* Normal Ca diet ↓↓↓ Ox
Karagüelle *et al.* 2007[35]	Germany	Double-blind crossover trial	Individuals with UL (CaOx stone) *n* = 34	Interventions with two types of water (1·5 L/d): 1. Control water (mineral content 213 mg/L; content of bicarbonate (99 mg/L)) 2. Bicarbonate water (mineral content 4015 mg/L; content of bicarbonate (2673 mg/L))	3 d and washout period (1 week)	Compared with baseline *In urine* Control water ↑↑ Volume ↑ pH Bicarbonate Water: ↑↑ Volume, pH, Cit ↑ Ca, Ox Comparison of interventions *In urine* Bicarbonate Water: ↑↑ pH, Cit
Nouvenne *et al.* 2010[36]	Italy	Randomised controlled trial	Individuals with UL and hypercalciuria (CaOx stone) *n* = 210	Interventions with dietary recommendations: 1. Low-salt diet (<60 mmol NaCl) 2. Control group (Bilgewater)	3 months	Comparison of interventions *In urine* Low-salt diet ↓↓ Ox, Ca Without baseline analysis
Noori *et al.* 2014[46]	Iran	Randomised controlled trial	Individuals with UL and hyperoxaluria *n* = 57	Intervention with two diets: 1. Dietary Approaches to Stop Hypertension (DASH) 2. Low Ox (list of foods with high Ox content).	8 weeks	Comparison of interventions *In urine* DASH ↑ Cr, Urea ↑↑ Cit, pH Without baseline analysis
Kumar-Gopala *et al.* 2021[37]	India	Randomised crossover trial	Individuals with UL (CaOx stones) *n* = 60	Two interventions for breakfast with: 1. High-Ca (1340 ± 20 mg) 2. Low-Ca (90 ± 10 mg)	1 d washout period (7 d)	Compared with baseline *In urine* Low-calcium breakfast ↓↓ Ca/Cr

Table 2. (*Continued*)

Gupta *et al.* 2021[38]	USA	Randomised trial*	Individuals with UL and hyperoxaluria $n = 164$	Three interventions with: 1. Diet: low Ox diet 2. Supplementation with vitamin B6 (25 mg/d) + magnesium oxide (400 mg/d) 3. Low Ox diet + vitamin B6/magnesium supplementation	12 weeks	Compared with supplement groups *In urine* Diet ↓↓ Ox Without baseline analysis
Effects of diet recommendations on individuals with urolithiasis						
Rotily *et al.* 2000[43]	France	Randomised controlled trial	Individuals with UL (Ca stones) $n = 108$	Three interventions: 1. Control group (usual diet) 2. Low animal protein diet (<10% of total energy) 3. High-fibre diet (>25 g/d)	4 months	Compared with baseline *In urine* Control group ↓ Volume Low animal protein diet ↓ Urea, Cit High-fibre diet ↓ ↓ Volume **Without differences between interventions
Massey *et al.* 2001[39]	USA	Randomised crossover trial	Individuals with UL and normocalciuria (CaOx stone) $n = 23$	Two dietary interventions with protein of different origin: 1. Beef 2. Plant (women: 71 g/d or men: 90 g/d)	6 d and washout period (1–4 weeks)	**Without differences between interventions
Siener *et al.* 2005[40]	Germany	Before-and-after study*	Individuals with UL (CaOx stone) $n = 107$	Intervention with standardised diet in water, macro and micronutrients	7 d	Compared with baseline *In urine* ↑↑↑ Volume, pH, Cit ↓↓↓ Ca, UA
Pais *et al.* 2007[26]	USA	Clinical controlled trial*	Individuals without UL $n = 61$ Individuals with UL (CaOx stone) $n = 65$	Intervention with standardised formula diet (Ensure; Ross Labs) adjusted to caloric requirement	3 d	Comparison of groups *In urine* Individuals with UL ↓ UA Without baseline analysis
Sromicki and Hess 2020[41]	Switzerland	Before-and-after study*	Individuals with UL (CaOx stones) $n = 75$	Intervention with recommendations according to the guidelines of the European Association of Urology	3 months	Compared with baseline *In urine* ↑↑↑ Volume, Ca ↓↓↓ Ox, UA
Danilovic *et al.* 2021[42]	Brazil	Before-and-after study*	Individuals with UL (CaOx stones) $n = 41$	Intervention with low-calorie diet (16 kcal/kg BW/d) and recommendations	12 weeks	Compared to baseline *In urine* ↑↑ Volume

UL, urolithiasis; Ca, calcium; Ox, oxalate; Cit, citrate; UA, uric acid; Cr, creatinine; CaOx, calcium oxalates; BW, body weight; CHO, carbohydrate; DASH, Dietary Approaches to Stop Hypertension; MPD, moderate animal protein intake; HPD, high protein diet; NaCl, sodium chloride; q.d., once a day; b.i.d., twice a day; AKSB, Agri-King Synbiotic. *Design was assigned according to characteristics since it was not explicitly mentioned in study. **Without analysis or differences between groups in urinary volume, pH, calcium, uric acid, urea, citrate and oxalate; and serum pH, uric acid and calcium. The studies are presented in ascending order, by year of publication. Effects and differences among groups are presented with *p*-values: one arrow, $p < 0{\cdot}05$; two arrows, $p < 0{\cdot}01$; three arrows, $p < 0{\cdot}001$.

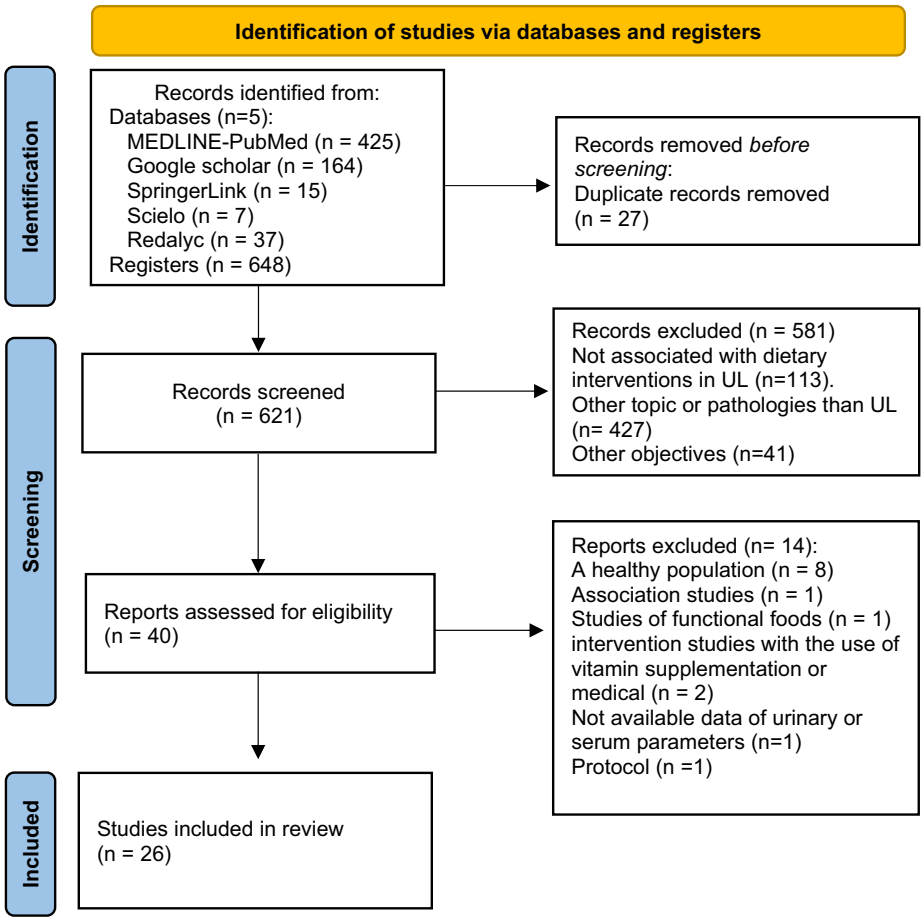

Fig. 1 PRISMA flow chart of included studies.

comparison group[24–26]. The age of individuals ranged from 20 to 60 years. Twenty studies reported the composition of kidney stones, nineteen of which specified CaOx composition[22,25–42] and two of calcium[23,43]. Eleven studies described urinary metabolic disorders including hypocitraturia[23,30,44], hypercalciuria[22,36,45] and hyperoxaluria[27–29,38,46]. The studies were conducted in the USA[25–29,38,39,44], Italy[22,33,34,36], Brazil[24,30,42], Germany[35,40], Iran[31,46], Greece[45], France[43], Turkey[23], China[32], Saudi Arabia[47], Switzerland[41] and India[37].

Characteristics of dietary interventions

Dietary interventions included reduced intake of sodium[22,23,29,33,34,36,39,40,42,45], protein[22,23,28,29,41,43,45], foods of animal origin (purines)[39,41,43], oxalates[23,27,29,38,41,46] and calcium adjustments[22,24,29,33,34,36,37,39–42,44–46]. Other interventions reported different types of water-based drinks[33–35]. Additional studies focused on dietary recommendations[37,40,41,46], a low-calorie diet[42] and the proportions of calcium and oxalate in foods[24,37]. Nutritional interventions also assessed foods or functional foods including juices from lemon[23,44], orange, melon, lime[23,46] and cranberry[25]; as well as vinegar (acetic acid)[32], apple and milk[27], black seed (*Nigella sativa* L.)[31], green bean extract (*Phaseolus Vulgaris*)[47], probiotics[28,29] and synbiotics[29].

Dietary interventions of foods or functional components against urolithiasis

Citrates are compounds present in various foods; their consumption has been related to beneficial effects against UL. These compounds act as inhibitors of stone formation by chelating calcium in the urine[48,49]. Eleven studies included a variety of foods containing these inhibitory compounds as a nutritional strategy for UL[23–25,27–31,44,47,50]. Three studies assessed the effect of citrates present in foods such as lemon, melon and oranges[23,30,44]. A randomised trial compared the effects of three interventions: lemon juice, potassium citrate supplementation or diet with general recommendations (for a detailed of the intervention, please refer to Supplementary Table 2) for 3 months[23]. Compared with baseline values, all groups had an increase in urinary citrate by the end of follow-up: potassium citrate supplementation (85·50 ± 44·21 to 324·70 ± 114·15 mg/d, $p = 0{\cdot}001$), lemon juice (122·6 ± 64·69 to 302·7 ± 75·14 mg/d, $p = 0{\cdot}003$) and dietary recommendations (102·70 ± 22·62 to 186·5 ± 68·92 mg/d, $p = 0{\cdot}001$). The groups with dietary recommendations showed lower levels of urinary citrate compared with the groups receiving lemon juice (186·5 ± 68·92 *v.* 302·7 ± 75·14 mg/d, $p < 0{\cdot}05$), and potassium citrate supplement (186·5 ± 68·92 *v.* 324·70 ± 114·15 mg/d, $p < 0{\cdot}01$). Furthermore, all interventions increased urinary volume: potassium citrate supplementation (1345·00 ± 486·76 to 1997·00 ± 790·33 mL/d, $p = 0{\cdot}035$), lemon juice (1455·00 ± 903·83 to 2014·00 ± 944·49 mL/d, $p = 0{\cdot}032$) and dietary recommendations (1641·00 ± 487·59 to 2118·00 ± 588·68 mL/d, $p = 0{\cdot}047$). Only the potassium citrate supplementation group showed an increase in urinary pH (from 5·9 ± 0·2 to 6·5 ± 0·3, $p = 0{\cdot}04$) (Table 2). A randomised crossover trial evaluated the effect of two interventions: potassium citrate supplementation or lemonade three times per day for 5 d. Potassium citrate supplementation increased urine citrate levels (476 ± 467 to 583 ± 430 mg/d, $p = 0{\cdot}0015$) and urinary pH (5·51 ± 0·40 to 5·89 ± 0·54,

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$p = 0{\cdot}0001$) compared with baseline[44] (Table 2). Another randomised trial included three different interventions: non-citrus fruits, orange juice and lime water, once daily at different times of the day (fasting, 2 h, 4 h and 6 h after consumption). There was an increase in urinary citrate levels for all interventions. Non-citrus fruits increased urinary citrate levels after 4 h (0·22 ± 0·10 to 0·35 ± 0·15 mg/mg creatinine/d, $p < 0{\cdot}05$), whereas orange juice showed an increase of urinary citrate levels at 2 h (0·14 ± 0·09 *v.* 0·32 ± 0·17 mg/mg creatinine/d, $p < 0{\cdot}05$) that were maintained at 4 and 6 h (0·28 ± 0·17, 0·21 ± 0·14 mg/mg creatinine/d, $p < 0{\cdot}05$). In contrast, lime water increased urinary citrate levels at 2 and 4 h (0·15 ± 0·12 to 0·39 ± 0·30 and 0·29 ± 0·21 mg/mg creatinine/d, $p < 0{\cdot}05$). Urinary potassium levels increased only with orange juice at 2, 4 and 6 h compared with baseline (0·07 ± 0·04, 0·07 ± 0·02, 0·06 ± 0·02 *v.* 0·05 ± 0·01 mEq/mg creatinine/d, $p < 0{\cdot}05$, respectively). Meanwhile, melon juice increased urinary pH levels at 4 and 6 h compared with baseline (6·72 ± 0·50 and 6·52 ± 0·50 *v.* 6·16 ± 0·75, $p < 0{\cdot}05$, respectively), and orange juice increased pH at 4 h (data not reported, $p < 0{\cdot}05$)[30] (Table 2).

Cranberry juice, vinegar, milk, apple juice, black seed, green bean extract, probiotics and synbiotics were functional foods evaluated in the included studies[24,25,27–29,31,47,50]. A clinical trial which also included individuals without UL showed the effects of consumption of cranberry juice (Ocean Spray) or deionised water for 7 d. Individuals were instructed to maintain diets of similar compositions. The results showed that cranberry juice increased urinary levels of oxalates (29·9 ± 3·0 *v.* 27·2 ± 3·7 mg/d, $p = 0{\cdot}04$), magnesium (103 ± 20 *v.* 92 ± 18 mg/d, $p = 0{\cdot}012$) and showed a higher relative CaOx saturation index (5·86 ± 0·97 *v.* 4·93 ± 1·36, $p = 0{\cdot}002$), as well as lower serum uric acid (5·5 ± 1 *v.* 5·8 ± 1 mg/dL, $p = 0{\cdot}01$) compared with deionised water in individuals with UL. Meanwhile, individuals without UL that consumed cranberry juice had decreased urinary levels of uric acid (442 ± 99 *v.* 531 ± 117 mg/d, $p = 0{\cdot}01$) and urinary pH (5·62 ± 0·56 *v.* 5·97 ± 0·37, $p = 0{\cdot}03$) compared with deionised water[25] (Table 2).

The effect of vinegar consumption was evaluated in a randomised controlled trial; the interventions included consumption of vinegar or pure water (control group = purified water) three times a day for 12 months (Table 2). Consumption of vinegar increased urinary levels of citrate (72% *v.* 19%, $p < 0{\cdot}0001$) and pH ($p < 0{\cdot}01$, data not available) compared with the control group. Also, it reduced urinary calcium (56% *v.* 19%, $p < 0{\cdot}01$) and approximate estimates of ion activity products of CaOx (50% *v.* 22%, $p < 0{\cdot}05$). The relative risk (RR) of recurrence among patients in the vinegar group was RR = 0·31 (95% CI: 0·12, 0·69, $p = 0{\cdot}0098$)[32].

The effects of substituting milk for apple juice were studied in a randomised crossover trial. The interventions included the consumption of apple juice or milk (Supplementary Table 2) for 6 d. Results showed that milk consumption generated lower urinary oxalate levels (420 ± 90 *v.* 510 ± 130 µmol/d, $p < 0{\cdot}0001$) and higher urinary calcium levels (4·74 ± 1·92 *v.* 3·87 ± 1·7, $p < 0{\cdot}05$) compared with apple juice[27] (Table 2).

Another randomised, double-arm, double-blind, placebo-controlled clinical trial evaluated the effect of black seed. The intervention consisted of capsules of black seed or placebo administered twice daily for 10 weeks. Black seed group decreased stone sizes (2·66 ± 2·72 *v.* 5·53 ± 2·91 mm, $p < 0{\cdot}05$) and urinary pH (5·19 ± 0·39 to 5·04 ± 0·19; $p = 0{\cdot}046$) with respect to placebo. Also, the black seed group increased serum calcium (9·08 ± 0·70 to 9·37 ± 0·69 mg/dL/d; $p = 0{\cdot}001$) and decreased the size of renal stones (6·20 ± 1·65 to 2·66 ± 2·72 mm; $p = 0{\cdot}000$) compared with baseline[31] (Table 2).

Another randomised controlled trial showed the effects of consumption of green bean extract or placebo three times per week for 6 weeks. Green bean extract increased urinary parameters such as volume (1962 ± 152·8 to 2005 ± 148·8 mL/d, $p = 0{\cdot}005$) and potassium (44·07 ± 3·66 to 52·15 ± 4·37 mEq/d, $p = 0{\cdot}000$), and decreased urinary calcium (205·4 ± 11·99 to 198·4 ± 12. 52 mg/d, $p = 0{\cdot}000$), oxalate (37·12 ± 5·38 to 33·02 ± 5·71 mg/d, $p = 0{\cdot}000$) and uric acid (6·88 ± 0·7 to 6·31 ± 0·58 mg/dL/d, $p = 0{\cdot}000$) compared with baseline. In addition, green bean extract reduced the size of renal stones (4·74 ± 2·15 to 2·84 ± 2·41 mm, $p < 0{\cdot}05$)[47] (Table 2).

A prospective randomised study, which also included healthy individuals, evaluated the effects of consumption of milk chocolate and dark chocolate for 3 d. Dark chocolate increased urinary oxalate levels compared with baseline (30 ± 10 to 36 ± 14 mg/d, $p < 0{\cdot}05$) in individuals with UL. In addition, individuals with UL and normocalciuria who consumed dark chocolate increased urinary oxalate levels (30 ± 10 to 39 ± 14 mg/d, $p < 0{\cdot}05$) compared with healthy individuals with normocalciuria who ingested the chocolate milk bar (35 ± 8 to 32 ± 12 mg/d, $p > 0{\cdot}05$). Meanwhile, healthy individuals showed no increase in oxaluria with respect to baseline, in both the chocolate milk bar (29 ± 18 *v.* 21 ± 5 mg/d) and dark chocolate groups (31 ± 7 *v.* 17 ± 5 mg/d) ($p > 0{\cdot}05$)[24] (Table 2).

Other studies evaluated the effect of probiotics and synbiotics on UL. The first study evaluated the consumption of probiotic bacteria in a randomised, double-blind, placebo-controlled trial (Table 2). The intervention consisted of the consumption of Oxadrop (Supplementary Table 2) against a placebo, for 56 d. After consumption of Oxadrop, there were no significant changes in urinary oxalate levels[28]. The second study evaluated the effect of probiotics and a synbiotic in a double-blind, placebo-controlled trial of individuals with UL and mild hyperoxaluria, for 5 weeks. Before the intervention, all groups received a standard diet for 1 week (6 d) (Supplementary Table 2). Then, individuals received the following interventions: (1) probiotic, (2) Agri-King Synbiotic and (3) placebo for 4 weeks (Supplementary Table 2). No significant changes were observed after administering the interventions[29] (Table 2).

Benefits of diets with controlled mineral salt intake in patients with urolithiasis

The control of mineral salt intake is one of the most frequent recommendations in nutritional therapy for patients with UL. Nouvenne *et al.*[36] conducted a 3-month randomised controlled trial of a low-salt diet against a control diet (Supplementary Table 2). After interventions, low-sodium diet decreased urinary excretion of calcium (−90 mg/d; 95% CI: −59, −121; $p < 0{\cdot}001$) and oxalate (−4·0 mg/d; 95% CI: −1·4, −6·6; $p < 0{\cdot}001$). Furthermore, 61·9% of patients in the low-salt diet, and 34·0% of those in the control group, reached normal urinary calcium excretion rates[36] (Table 2).

Oxalates are components in foods, that are associated with stone formation, thus it is important for the management of UL. A randomised controlled trial evaluated the effect of a low-oxalate diet *v.* a Dietary Approaches to Stop Hypertension (DASH) diet and regulated water consumption (Supplementary Table 2) for 8 weeks. The DASH diet showed the greatest changes with increases in levels of phosphorus (0·3; 95% CI: 0·1, 0·5 g/d; $p < 0{\cdot}001$), citrate (221·5; 95% CI: 117·4, 325·5 mg/d; $p < 0{\cdot}001$), pH (5·4; 95% CI: 0·3, 0·9; $p < 0{\cdot}001$), creatinine (0·23; 95% CI: 0·03, 0·43 g/d; $p = 0{\cdot}03$)

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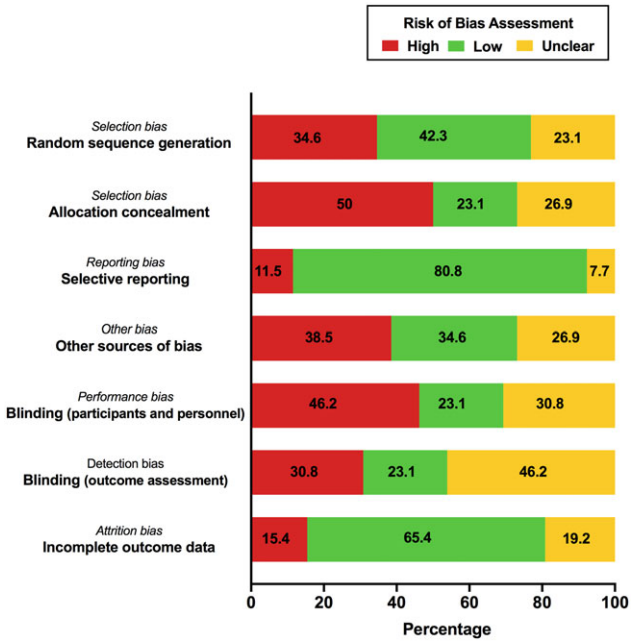

Fig. 2 Evaluation of risk of bias of included studies.

and urea (5·3; 95% CI: 1·2, 9·5 g/d; $p = 0·02$) compared with low-oxalate diet[46] (Table 2).

Other studies have focused on other minerals that can contribute to UL, such as calcium. A randomised trial conducted by Borghi *et al.*[22] compared the effects of two diets in men with UL over 5 years. The intervention consisted mainly of comparing a normal calcium diet or a low calcium diet, but other macro- and micronutrients were additionally monitored as described in Supplementary Table 2. Only 56·6% of the individuals included in the study finished the 5-year follow-up. A normal-calcium diet led to absolute changes in urinary parameters such as sodium, oxalate and relative CaOx saturation compared with a low-calcium diet (data not shown, $p < 0·05$). In addition, a normal-calcium diet had a lower risk of UL (RR = 0·49; 95% CI: 0·24, 0·98; $p = 0·04$) compared with the low-calcium diet[22] (Table 2).

Other randomised crossover clinical trial examined the effects of low and high calcium intake, followed by high oxalate intake for 1 d. The interventions included a high-calcium or a low-calcium breakfast, followed by a high-oxalate lunch 4 h later (content of oxalates in lunch not shown). The low-calcium group had lower calcium/creatinine ratios compared with the high-calcium group (0·07 ± 0·03 *v.* 0·12 ± 0·06, $p < 0·001$). In addition, crystal aggregation was lower in the low-calcium group than in the high-calcium diet group after breakfast (0·05 ± 0·07 *v.* 0·12 ± 0·09) using optical density of urine during supersaturation at 620 nm wavelength ($p < 0·001$)[37] (Table 2).

Another study that evaluated the effect of oxalates is that by Gupta *et al.*[38]. This randomised trial included three interventions: (1) low oxalate diet (D), (2) supplementation with vitamin B6 + magnesium oxide (S), and (3) low oxalate diet + vitamin B6 + magnesium supplementation (DSs) (Supplementary Table 2) for 12 weeks. The low oxalate diet showed the greatest change in urinary oxalate levels compared with the supplement groups (−15·6 (−20·1, −7·0) *v.* −7·3 (−13·8, 4·3) mg/d, $p < 0·017$)[38] (Table 2).

A 10-d before-and-after study evaluated the effect of a dietary intervention with a diet controlled primarily for calcium, protein and fluids, although monitoring of other parameters was also considered (Table 2 and Supplementary Table 2). After the intervention there was a decrease in urinary parameters such as urea (0·36 ± 0·06 to 0·28 ± 0·05 mg/d, $p < 0·0002$), uric acid (517·7 ± 122·9 to 418·6 ± 100·1 mg/d, $p < 0·04$), sodium (231·8 ± 44·95 to 175·8 ± 49·15 mEq/d, $p < 0·02$), chlorine (208·8 ± 38·5 to 156·8 ± 48·08 mEq/d, $p < 0·02$), calcium (379·64 ± 68·7 to 233·14 ± 77·1 mEq/d, $p < 0·0003$), phosphorus (780·7 ± 226·5 to 580·85 ± 185·1 mg/d, $p < 0·005$) and oxalate (0·59 ± 0. 35 to 0·29 ± 0·11 mg/d, $p < 0·02$), whereas serum pH increased (7·35 ± 0·03 to 7·37 ± 0·025, $p < 0·04$). In addition, there was a decrease in serum urea levels (34·65 ± 9·78 to 29·53 ± 5·76 mg/dL/d, $p < 0·03$) after the intervention[45].

Fluid intake is another risk factor for the development of UL[14]. However, there is little recent evidence of the types and volumes of fluids that contribute to urinary stone formation. Three of the studies included in this review evaluated different types of water intake according to their mineral salt content and determined their beneficial effects[33–35].

A randomised crossover trial evaluated the consumption of water with different calcium and other mineral contents (Supplementary Table 2) for a 20-d period. The amount of water intake was 2 L/d and only the calcium content varied. Initially, individuals maintained their common water intake at home (control), followed by water high in calcium, then by water with a moderate amount of calcium, and finally, water low in calcium (Table 2 and Supplementary Table 2). Results showed that water high in calcium increased urinary levels of citrate (675·8 ± 41·6 *v.* 537·6 ± 42·3 mg/d, $p = 0·05$) and decreased oxalate levels (23·5 ± 1·3 *v.* 27·1 ± 1·7 mg/d, $p = 0·05$) compared with the control group[33].

Another randomised, double-blind, crossover trial examined the consumption of different types of water according to calcium content to classify between tap, soft and hard water, for 7 d (more details are included in Table 2 and Supplementary Table 2). For the first period, Naples tap water was consumed, followed by soft water in the second period, and finally, with hard water, as well as with diet recommendations (Supplementary Table 2). Results showed that hard water generated the highest urinary levels of pH (6·76 ± 0·22, $p < 0·05$), calcium (152 ± 13 mg/L/d, $p < 0·05$) and calcium–citrate index (1·11 ± 33, $p < 0·05$), while also increasing urinary levels of uric acid compared with Naples tap water (355 ± 55 *v.* 223 ± 24 mg/L/d, $p < 0·05$)[34]. Similar results were found by Karaguelle *et al.*[35] in a double-blind crossover trial which included the consumption of control water or bicarbonate water for 3 d (Table 2). Control water increased urinary values of volume ($p < 0·001$) and pH ($p < 0·05$), whereas CaOx supersaturation decreased compared with baseline ($p < 0·05$). The intervention with bicarbonate water generated an increase in urine volume, pH, citrate, magnesium ($p < 0·001$), calcium and oxalate ($p < 0·05$) as well as a decrease in CaOx supersaturation ($p < 0·001$, data not shown). The comparison between interventions showed that bicarbonate water promoted an increase in urine pH ($p < 0·001$), magnesium and citrate ($p < 0·01$) compared with control water (data not shown)[35].

Effects of diet recommendations on individuals with UL

Standardised dietary recommendations have been used in the control and prevention of urinary stones. The most frequent

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recommendation for patients with UL is protein restriction. Rotily *et al.*[43] conducted a randomised controlled trial to evaluate the effect of a low animal protein diet, a high-fibre diet, or the usual diet for 4 months. At the end of the intervention period, the low animal protein diet reduced urinary levels of phosphate (31·0 ± 11 to 26·1 ± 9·3 mmol/d, $p = 0·005$), sulfate (13·8 ± 5·5 to 9·3 ± 3·5 mmol/d, $p = 0·003$), urea (387 ± 99 to 361 ± 102 mmol/d, $p = 0·03$) and citrate (3·5 ± 2·2 to 2·3 ± 1·2 mmol/d, $p = 0·04$) compared with baseline. Control diet and a high-fibre diet reduced urine volume compared with its baseline value (1·8 ± 0·6 to 1·6 ± 0·6 L/d, $p = 0·02$ and 2·2 ± 0·7 to 1·7 ± 0·6 L/d, $p = 0·002$, respectively). The low animal protein diet showed the lowest urinary phosphate levels after adjusting for sex and baseline levels (26·1 ± 9·3 mmol/d, $p = 0·04$). In addition, the low animal protein diet was subdivided into three groups according to changes in urinary urea as follows: no decrease, decrease (<50 mmol/d) and decrease (>50 mmol/d) (the upper 33rd percentile). The decrease group (>50 mmol/d) showed a reduction in urinary levels of calcium (7–5·2 mmol/d, $p = 0·004$), creatinine (13·6–11·3 mmol/d, $p = 0·02$), sulfate (16·8–8·9 mmol/d, $p = 0·03$), urate (3·8–3·2 mmol/d, $p = 0·008$) and citrate (4·5–1·9 mmol/d, $p = 0·04$)[43] (Table 2).

Another randomised crossover trial evaluated the effect of two different interventions, a diet with animal protein foods or vegetable protein foods for 6 d. Vegetable-protein-based diets increased urinary levels of sodium (3804 ± 849 *v.* 3261 ± 785 mg/d, $p < 0·01$) and potassium (2771 ± 482 *v.* 2416 ± 330 mg/d, $p < 0·01$) compared with the animal-protein-based diet[39] (Table 2).

Pais V *et al.*[26] performed a controlled trial, that also included individuals without UL (control), with a standardised formula diet (Ensure®; Ross Labs/Abbott Laboratories, Abbott Park, IL, USA) adjusted to their caloric requirements for 3 d (Supplementary Table 2). After the intervention, patients with UL had lower urinary levels of uric acid compared with individuals without UL (337 ± 64 *v.* 379 ± 76 mg/g creatinine, $p < 0·05$)[26].

Another before-and-after study implemented a standardised diet (Supplementary Table 2) for 7 d. After intervention, there was an increase in urinary volume (1940 ± 733 to 2683 ± 689 mL/d, $p < 0·001$), pH (6·13 ± 0·54 to 6·43 ± 0·36, $p < 0·001$) and citrate (2·61 ± 1·35 to 3·28 ± 1·51 mmol/d, $p < 0·001$), as well as a decrease in urinary calcium (6·64 ± 2·91 to 5·33 ± 2·09 mmol/d, $p < 0·001$) and uric acid excretion (4·00 ± 1·99 to 3·28 ± 1·14 mmol/d, $p < 0·001$)[40] (Table 2). One prospective before-and-after study evaluated the effect of dietary recommendations accordance with the European Association of Urology guidelines for 3 months (Supplementary Table 2). At the end of the intervention there was an increase in urinary parameters such as volume (2057 ± 79 to 2573 ± 71 mL/d, $p < 0·0001$), calcium (5·49 ± 0·24 to 7·98 ± 0·38 mmol/d, $p < 0·0001$) and magnesium (4·38 ± 0·14 to 5·41 ± 0·23 mmol/d, $p < 0·0001$). In addition, there was a reduction in urinary levels of oxalate (0·34 ± 0·01 to 0·26 ± 0·01 mmol/d, $p < 0·0001$), uric acid (3·48 ± 0·12 to 3·13 ± 0·10 mmol/d, $p < 0·0001$) and urinary CaOx supersaturation index (0·93 ± 0·05 to 0·73 ± 0·05, $p = 0·0005$)[41] (Table 2).

Not only specific nutrient or compounds are associated with the development of UL, the excessive consumption of macronutrients is also associated with this pathology. A before-and-after study showed the effects of a hypocaloric diet, as well as control of other nutrients described in Supplementary Table 2, for 12 weeks. After the intervention period, there was an increase in urinary volume (1559·0 ± 440·1 to 1771 0 ± 501·1 mL/d, $p = 0·007$) and CaOx supersaturation (1·2 ± 1·0 to 0·9 ± 0·7, $p = 0·021$). In addition, there was a negative correlation between urinary pH with waist circumference ($r = -0·330$, $p = 0·043$)[42] (Table 2).

Study quality assessment

Based on the risk of bias tool, there was a high risk of bias in allocation concealment, blinding (individuals and personnel) and other sources of bias. We determined a low risk of bias in selective reporting and incomplete outcome data (Fig. 2). The results of the quality of study reporting as per the CONSORT statement show that none of the studies included in this review reported all items. The following items were reported by all the studies: scientific background and explanation of rationale, specific objectives or hypotheses, interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence. The item that was not reported by 92% ($n = 24$) of the studies referred to the description of binary outcomes, presentation of both absolute and relative effect sizes (Supplementary Table 3).

Discussion

The studies included in this systematic review evaluated dietary interventions for the management of UL. To our knowledge, this is the first review of dietary interventions against UL, that included the evidence published in the last 29 years.

Strategies such as intake of vinegar, green bean extract and low-salt diets decreased urinary calcium. In addition, a decrease in urinary levels of oxalate was promoted by consumption of milk, green bean extract, calcium-rich water, low-salt diets and following the general recommendations from the established guidelines (Supplementary Table 4). However, cranberry juice, vinegar and green bean extract, as well as general dietary recommendations, result in a decrease in urine uric acid levels. Meanwhile, interventions that increased urinary citrate included potassium citrate, dietary recommendations (such as those including controls on water intake, calcium, protein, sodium, oxalates, fruits, vegetables and others), non-citric fruits (melon), juices from citric fruits (lemon, orange and lime), calcium-rich water, bicarbonate water and the DASH diet (Supplementary Table 4).

Guidelines for the management of UL recommend regular evaluations of urine and serum parameters, including calcium, oxalate, uric acid, citrate, sodium, potassium, creatinine and pH[15,17,51]. Compounds such as calcium can chelate minerals (*i.e.* oxalates), thereby preventing their absorption during bowel transit and culminating in their elimination through faeces[52,53]. Therefore, recommendations regarding the daily intake of these compounds alone or present in food should be followed. Nutritional strategies are based on the control of mineral intake (calcium, oxalate or citrates in foods) and protein intake, as well as the inclusion of foods associated with beneficial effects.

There is evidence that the regulation of calcium intake is important for the development of UL. For many years, calcium intake restriction (<400 mg/d) has been recommended for individuals with UL[54]. However, recent studies have showed that insufficient dietary calcium intake (in food) reduces its intestinal availability, and results in higher urinary excretion[55]. Current studies on calcium intake are still controversial since it has been suggested that an adequate calcium intake is 1000–1200 mg/d. Massey L *et al.*[27] sought to study the effects of the reduction in calcium intake by substituting milk (772 mg/d) for apple juice (354 mg/d), finding that milk reduces urinary oxalate levels in patients with UL and hyperoxaluria. These results are similar to those

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reported by Caudarella *et al.*[33] and Bellizzi *et al.*[34] who studied calcium intake restriction through water-based beverages. The results showed that only high-calcium water (380 mg/L) decreased urinary levels of oxalates. However, Bellizzi *et al.*[34] found that the intervention with high-calcium water (255 mg/L) increased urinary levels of calcium in individuals with hypercalciuria. Thus, it is also important to consider biochemical alterations in patients with UL to adapt the diet according to their individual needs. Other studies have controlled daily calcium intake not only through specific foods or water. Liatsikos *et al.*[45] and Borghi L *et al.*[22] found that consumption of calcium (30 mmol/d or 1200 mg/d) leads to a decrease in urinary levels of oxalate and uric acid. This is according to the daily recommended intake of calcium (1200 mg/d). In fact, a 5-year follow-up study showed that a normal-calcium diet (30 mmol/d) reduced urinary sodium and oxalate, with patients having a lower risk of UL (RR = 0·49; 95% CI: 0·24, 0·98; $p = 0·04$) than those on a low-calcium diet (10 mmol/d or 400 mg/d). Although studies have shown that normal calcium intake generates beneficial effects, one study found that a low-calcium breakfast (90 ± 10 mg) generated a decrease in urinary calcium compared with a high-calcium breakfast (1340 ± 20 mg)[37]. However, this might be due to the amount of calcium ingested all at once, which cannot be compared with the daily intake throughout the day. Beneficial effects of adequate calcium intake are based on its availability in the bowel to chelate minerals such as oxalates, thereby decreasing their absorption and favoring greater excretion through faeces, which decreases the risk of urinary stone formation[54].

Sodium is among the minerals that have been related to UL. For instance, Nouvenne *et al.*[36] showed that a low-salt diet intervention (60 mmol NaCl) decreased oxalates and calcium levels in urine. Excessive sodium intake increases calcium levels and urinary pH, favouring the crystallisation of compounds such as CaOx[56]. Urinary stones consist of mixed components and are determined by the fluctuation of diverse minerals. Bicarbonate serves as a buffer in such fluctuations, regulating concentrations of minerals, and hence decreasing stone formation. In fact, Karagüelle *et al.*[35] showed that consumption of mineral water increased urinary levels of citrate. This is important in the management of hypocitraturia, which is one of the most important metabolic alterations in UL. Thus, studies have focused on regulating citrate levels through interventions with isolated compounds or foods that contain it. Foods that contain citrate include oranges, limes, lemons and cranberries[57]. Baia *et al.*[30] and Aras *et al.*[23] showed an increase in urinary citrate levels after consumption of 385 mL of orange juice or 85 mL of fresh lemon juice. Conversely, Koff *et al.*[44] showed that an intervention with 30 mL of lemon juice did not cause changes in urinary citrate. The differences in these results could be due to the lower amount of lemon juice intake, which was almost half of that reported by Aras *et al.*[23]. Cranberry also contains citric acid, a citrate salt related to increased urinary citrate and delayed stone formation. In the study by Gettman *et al.*[25], the consumption of 1000 mL/d of cranberry juice increased urinary pH and oxalate levels. This contradictory result may be explained by the ability of citric acid to promote increases in urinary citrate only in the presence of an alkaline environment. This condition is primarily influenced by minerals such as potassium, which is found in foods such as oranges and grapefruit. Even though cranberry juice contains citric acid, its potassium content is low[58]. In fact, the combined intake of these two minerals has been shown to have beneficial effects. Moreover, Koff S *et al.*[44] and Aras *et al.*[23] showed that potassium citrate supplementation generated an increase in urinary pH and citrate levels. The beneficial effect of citrate at the urinary level is attributable to the chelation of calcium ions, which forms a soluble salt and decreases the availability of calcium to form CaOx compounds.

Many studies have referred to the role of oxalates as promoters of crystallisation and the formation of urinary stones. Oxalates are dicarboxylic acids (HOOC–COOH) derived from endogenous metabolism and diet[59]. Oxalates are present in various foods and are known as 'antinutrients' owing to their ability to generate insoluble complexes with minerals such as calcium and magnesium, hence promoting their accumulation[60]. In this sense, dietary strategies have sought to reduce the consumption of foods with a high oxalate content. One such food is chocolate, which is why its restriction should be considered in dietary recommendations for individuals with UL. In fact, Mendonca *et al.*[24], showed that consumption of dark chocolate (94 mg oxalates + 26 mg of calcium) increased urinary levels of oxalate. Even when this study only showed the effect of controlling a single food high in oxalate without controlling calcium intake, there have been other studies evaluating interventions based on diets with restricted oxalate intake, with potentially conflicting findings. The studies of oxalate intake restriction by Sromicki J and Hess (2020) (oxalate-rich products) and Gupta *et al.*[38] 2021 (foods that contain >50 mg of oxalate per 100 g in a serving per day) showed reductions in urinary oxalate levels. Nonetheless, Noori *et al.*[46] did not observe such changes by restricting oxalates, although patients were put on a DASH diet, which did cause an increase in urinary citrate. A DASH-style diet has been associated with a significant UL risk reduction (RR: 0·69; 95% CI: 0·64, 0·75)[14]. These results may be explained by the fact that studies of oxalate reduction did not directly restrict oxalate intake, as only recommendations based on food lists of oxalate content per serving were used. To this extent, the content of oxalates in foods may vary depending on the way they are consumed since there are different processes with the ability to reduce the content of oxalates, such as boiling (30–87%) and steaming (5–53%)[61]. Such factors could have affected the amount of oxalate ingested, thus warranting caution with the interpretation of results. Under these considerations, oxalate intake restriction is an important keystone in the management of UL, as shown by the recommendation of the Academy of Nutrition and Dietetics that limits dietary oxalate intake to amounts lower than 50 mg/d[62].

Animal protein has been related to urinary alterations due to its purine content[63,64]. Studies showed that elevated consumption of animal protein is associated with glomerular hyperfiltration; increased urinary levels of calcium, oxalates and uric acid; as well as a reduction in citrates and urinary pH, which cause low-grade metabolic acidosis through increased tubular reabsorption of citrates and decreased urinary excretion, ultimately leading to a higher risk of having uric acid and CaOx stones[12,16,50,65,66]. Despite these attributions to proteins of animal origin, Massey *et al.* showed that there were no differences in individuals with UL who consumed plant-derived or animal-derived proteins in a 6-d randomised crossover trial[39]. Therefore, the quantity of protein may be more important than the type, or both factors could play a role and should be further investigated. In fact, Liatsikos *et al.*[45] and Rotily *et al.*[43] found that interventions based on a low animal-protein diet (<10% of total energy) or low protein intake (0·8 g/kg/d) generated a decrease in urinary levels of oxalates and urea. For these reasons, interventions consisting of standardised diets that control not only the consumption of minerals but also protein, water and calory intake have generated a decrease in urinary levels

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of calcium and uric acid, as well as an increase in urinary volume and citrates, all of which reduce the risk of developing stones[26,40,42].

Intervention studies to date have focused on the presence of compounds in foods that generate beneficial effects. For instance, specific foods such as green bean extract, black seed, vinegar, probiotics and synbiotics have been studied owing to their content of polyphenols, acetic acid, dietary fibres or probiotics. Green bean extract and black seed contain polyphenols, which have been associated with beneficial effects, namely diuretic, antioxidant and anti-inflammatory properties[67]. In fact, green bean extract generates a reduction in urinary levels of uric acid, calcium and oxalates[47]. Similarly, black seed modulates urinary parameters such as calcium and pH which prevent the formation of CaOx stones[31]. These effects could be related to the presence of polyphenols. On one hand, its antioxidant properties can reduce oxidative stress which contributes to renal damage. On the other hand, its anti-inflammatory activity suppresses nuclear factor-kappa B (NF-kB) activation, the production of prostaglandin E2 and cytokines, all of which have a role in diuretic activity in UL[67].

Beneficial effects on UL were shown after intervention with mature vinegar, which is a sorghum and Daqu vinegar that has undergone a fermentation process and matured for months. Mature vinegar consumption increases urinary citrate and pH, while also decreasing urinary calcium and calcium oxalate crystals in individuals with UL. These beneficial effects could be associated with the presence of acetate. In both *in vitro* and animal model studies, acetate promoted epigenetic changes through acetylation of histone H3 in renal tubular cells, which increased gene expression of microRNAs that suppress the expression of the cotransporter involved in modulating urinary excretion of citrate and calcium, suggesting a beneficial effect in UL[32].

Current evidence has shown that the gut microbiota plays an important role in different diseases, including UL[68,69]. Previous studies reported that modifications in the gut microbiota affect the intestinal–renal axis, thereby exerting direct effects on the development of UL[69,70]. In fact, there are studies that have shown differences in the diversity and composition of the gut microbiota of patients with UL, as compared with control individuals[70–72]. During UL, an increase in abundance of *Bacteroides*, *Enterobacteriaceae*, *Firmicutes* and *Pseudomonas*, as well as a decrease in *Bifidobacterium*, *Prevotella* and *Faecalibacterium* have been reported[70,73,74]. These modifications in gut microbiota are related to changes in the production of its metabolites such as short-chain fatty acids (SCFA) that include butyrate, propionate and acetate[75]. The SCFA are crucial for maintaining gut barrier function, decreasing permeability of the gut and systemically improving inflammatory responses and reducing renal CaOx, thereby impacting kidney stone disease[76,77]. In addition, one of the mechanisms that could explain the role of the gut microbiota in the development of UL is that the gut microbiota modulates the absorption of nutrient transporter expression, such as the modification of oxalate transport by SLC26A6, involved in stone formation, potentially altering the risk of UL[78,79], as well as possibly altering metabolic pathways, according to Zhu *et al.*, who showed that vinegar acts as a factor that alters the composition of the gut microbiota, and this alteration in turn impacts metabolic pathways such as thiamine metabolism, glycerol phosphate shuttle, biotin metabolism, phosphatidylcholine biosynthesis and membrane lipid metabolism in rats with hyperoxaluria[68]. A recent *in vitro* study showed that probiotic bacteria may improve oxalate-degrading processes[80,81]. Although *Oxalobacter formigenes* has been extensively studied in relation to UL, specifically in oxalate degradation, it appears to have promising potential for prevention. However, it has not yet been determined whether its colonisation directly affects kidney stone formation[82]. Nonetheless, Goldfarb *et al.*[28] and Lieske *et al.*[29], who evaluated interventions with lactic bacteria in individuals with UL, did not observe differences. This association has been more consistent in animal studies, which have shown that modulation of the gut microbiota a by specific probiotics such as *O. formigenes* and the use of specific strains of *Lactobacillus* (*L. fermentum* TY5, *L. fermentum* AB1 *and L. salivarius* AB11) may be an effective strategy for the management of hyperoxaluria and the prevention of UL[83,84]. However, there is still controversy about the effectiveness of the use of probiotics in UL.

Despite the changes in the gut microbiota in the UL, as well as the possible molecular mechanisms proposed for their explanation, it is important to consider that there are many factors involved, from technical methodological aspects, such as how to analyze and sequence samples, to individual heterogeneity. These challenges are of great relevance for the development of individualised strategies and the application of interdisciplinary research. Therefore, further studies are required to establish their relationship in a more conclusive manner.

General recommendations for managing UL have included water intake (2000–3000 mL/d), protein intake (0·8 g/kg/d) and specific dietary recommendations based on metabolic alterations such as hyperoxaluria, for which reduced consumption of oxalate is recommended (50–100 mg/d), accompanied by an energy intake of 16 kcal/kg body weight/d, normal amounts of calcium (1200 mg/d) and increased vegetables and fruits (at least three servings of both). A DASH diet, consumption of milk, vinegar, green bean extract and cranberry juice have also been recommended. In cases of hypocitraturia, non-citric fruits (melon) and citrate-containing foods, such as lemons, limes or oranges, are encouraged. For hypercalciuria, maintenance of a normal calcium diet (30 mmol/d) and a low salt diet (<60 mmol) are suggested.

Dietary management of UL requires considering multiple factors, making it essential for these recommendations to be comprehensive rather than focusing on individual dietary components. Thus, it would be essential to carry out studies that examine in greater detail the chemical composition of foods, both in terms of micronutrients and macronutrients, and their beneficial effects on UL. In this sense, the effects of food on UL can be considered according to the acid load of the diet that plays an important role in maintaining the optimal body acid–base balance. Thus, dietary acid load caused by certain diet components can disturb and induce a low-grade metabolic acidosis state, which is related to the development of pathologies such as UL. In general, an animal-based diet causes metabolic acidosis; meanwhile, a plant-based diet, with a restriction or exclusion of animal products, is associated with a reduced dietary acid load[85]. Nonetheless, despite the existence of many guidelines for the management of urolithiasis, a comprehensive and standardised dietary approach that considers the various associated urinary metabolic disorders has not always been developed in detail.

While this review primarily addresses individual dietary factors related to UL, it is important to acknowledge the need for a more integrative perspective in dietary management of UL. Future research and clinical practice would benefit from the development of comprehensive, standardised dietary guidelines that simultaneously consider multiple nutritional components. These should include not only fluid intake, calcium, oxalate and protein but also

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other relevant dietary elements that may influence stone formation. An integrative approach would allow for more precise, individualised recommendations and could enhance the effectiveness of prevention strategies for patients at risk of recurrent UL.

The present review has some limitations, such as the heterogeneity of the interventions included, which cannot be compared with each other. The studies included some dietary interventions, so it is difficult to elucidate which component has a more significant impact on UL, and it does not allow us to know the nutrient to which the beneficial effect can be attributed. However, through this information it is possible to obtain an overview to provide more accurate recommendations and manage nutrient intake more effectively, with the evidence generated so far. Even so, it is essential to highlight the complexity of these interventions, given the chemical composition of some foods and the interactions between different nutrients, which makes it difficult to have evidence about the effect of isolated nutrients or interventions focused on the modification of a single factor. It is important to consider that metabolic alterations and the composition of urinary stones could allow the establishment of nutritional strategies according to the excess or lack of nutrients.

Based on the above, it is important to note that further clinical studies are needed to generate knowledge about a specific type of nutrient or food to establish the possible mechanisms through which beneficial effects are generated in the UL. The generation of this information is of utmost importance since it will be considered for developing guidelines regarding public health, particularly in those countries where UL is highly prevalent.

Another limitation is that the present review only includes studies in the adult population. However, it is important to highlight that in the paediatric population, almost half of the cases of UL are associated with genetic alterations, which would imply more complex treatments than dietary intervention[86]. While in older adults with UL, it has been reported that there are increases in the risks of surgery due to the complexity of the stones, which is associated with homeostatic calcium regulatory processes affected by age-related natural hormonal changes and not by the type of diet consumed[87]. Another limitation is that not all the included studies had a control group; this is why it should be emphasised that future studies should have greater methodological rigor by adding a control group and employing randomisation and blinding to reach more robust conclusions while minimising bias in the studies. Additionally, the CONSORT-based assessment showed that most of the studies adequately reported their scientific rationale and objectives and provided interpretations consistent with their findings. However, 92% did not clearly describe binary outcomes or present effect sizes. The omission of this information limits the understanding of the impact of the intervention, hinders comparability between trials, reduces the reproducibility of results and may prevent studies from being considered in clinical guidelines. Another limitation is that almost 50% of the included studies have interventions lasting between 1 and 12 months, and only two studies evaluated outcomes beyond 1 year. This predominance of short- and medium-term evaluations limits the ability to draw conclusions about the long-term sustainability and clinical relevance of dietary interventions to prevent the recurrence of UL. However, although long-term follow-ups are essential for assessing the persistence of beneficial effects, these types of studies present significant challenges, such as lack of adherence, increased costs, participant retention and logistical complexity, which may explain their limited representation in the current evidence. Therefore, these changes should be considered as part of the population's lifestyle rather than as part of a protocol to ensure that the benefits will continue for populations with UL.

Conclusions

This systematic review summarises the results of dietary interventions in populations with UL published over the last 29 years. The reviewed studies reveal that dietary interventions can have a significant impact on the prevention and management of UL. The most common interventions include adjustment in sodium, protein, oxalates and calcium intake, as well as consumption of beverages such as lemon juice, vinegar and water with different mineral contents. Functional foods and components such as cranberry juice, black seeds, and green bean extracts showed beneficial effects in reducing urinary parameters associated with urinary stone formation. However, some approaches, such as consumption of probiotics and synbiotics, were found to show no significant changes in urinary oxalate levels. Furthermore, control of salt and oxalate intake, along with increased fluid intake, are key strategies to improve urinary health and reduce the risk of UL recurrence.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954422425100188

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