💊 Kidney Stone Removal and Inhibitory Substances by Theoretical Efficacy

The following information is a synthesis of the provided list, categorized by its theoretical efficacy in eliminating, reducing, or removing renal calculi [1]. The citation markers within the text (e.g., [74]) refer to the source indices from the original document, and all statements are supported by the primary source [1].

I. Direct Removal of Existing Stones (Highest Efficacy)

These procedures physically remove existing kidney stones [1].

1. **Percutaneous Nephrolithotomy (PCNL):** Removes kidney stones via simple extraction, chemical dissolution (chemolysis), or ultrasonic lithotripsy [74, 75, 77, 78, 80]. This technique boasts high success rates, low residual stone rates, and fast recovery, regardless of the stone's size or composition [74, 75, 77, 78, 80]. [1]
2. **Extracorporeal Shock Wave Lithotripsy (ESWL):** A non-invasive technique using shock waves to fragment upper urinary tract stones, considered the first-line method [79, 85]. It can be used as a monotherapy or combined with percutaneous procedures for larger staghorn calculi [79, 85]. [1]
3. **Ureteroscopy:** Removes or ultrasonically fragments lower urinary tract stones via visualization [79]. [1]
4. **Chemolysis:** A method for stone removal mentioned in the context of PCNL [74]. [1]

II. Strong Inhibitors/Dissolvents (Significant inhibition on stone formation and growth)

These substances show significant inhibitory effects on the formation and growth of calculi [1].

Rank	Substance/Compound	Key Mechanism/Effect	Citations
1	**L-cystine diamides** (e.g., LH708)	Potent L-cystine crystallization inhibitors, 70 times more effective than L-CDME, used for cystinuria [33]. [1]	[33]

2	**N-acetylcysteine**	The most effective cystine-binding thiol agent in studies for delaying crystallization and modifying crystal morphology; also inhibits crystallization [41]. [1]	[41]
3	**Cpd-42** (Novel RIPK3 inhibitor)	Protects kidneys from injury and inflammation caused by calcium oxalate nephrocalcinosis by targeting RIPK3-mediated necroptosis; reduces crystal deposition and improves renal function, superior to Darapladib [25]. [1]	[25]
4	**URO-5** (Herbal compound)	Significantly reduces calcium oxalate crystal number, promotes its excretion, promotes dihydrate crystal formation, and inhibits nucleation and aggregation; also aids in tissue repair and is non-toxic [70]. [1]	[70]

5	**Empagliflozin** (SGLT2 inhibitor)	Significantly reduces calcium phosphate (CaP) relative supersaturation (RSRs) in non-diabetic adults with calcium stones and uric acid (UA) RSRs in UA stone patients [48]. Also reduces renal calcium oxalate deposition, urinary oxalate concentration/excretion, and renal inflammation in hyperoxaluria rats [46]. [1]	[48, 46]
6	**Quercus dentata Thunb. leaves extract (QDWE)**	Inhibits calcium oxalate crystallization, improves ethylene glycol-induced calcium oxalate kidney stones, and promotes the conversion of harmful calcium oxalate monohydrate (COM) to thermodynamically unstable calcium oxalate dihydrate (COD) [44]. The polysaccharide component (QDP) shows more significant	[44]

		inhibition in vitro [44]. [1]	
7	**Gallic acid (GA) & Methyl gallate (MG)**	Inhibit calcium oxalate crystal formation in vitro (GA 44-57%, MG 48.35%), reduce aggregation/precipitation, and inhibit the formation of the more harmful monohydrate type [14, 15]. [1]	[14, 15]
8	**Obcordata A (OA)**	A polyoxypregnane glycoside that acts as a NOX4 inhibitor, reducing reactive oxygen species (ROS) by inhibiting NOX4 expression, offering cytoprotective and antioxidant effects to prevent kidney stones [4]. [1]	[4]
9	**Sulfated Polysaccharides (SPs) from *Caulerpa cupressoides var flabellata***	Modify calcium oxalate crystal morphology, size, and surface charge to resemble crystals found in healthy individuals, showing anti-urolithiasis potential [5]. [1]	[5]
10	**Melatonin**	Inhibits oxalate-induced	[10]

		renal cell endoplasmic reticulum (ER) stress and apoptosis by activating the AMP-activated protein kinase (AMPK) pathway, enhancing antioxidant capacity, and lowering ROS levels [10]. [1]	
11	**Mitochondrial ROS scavengers** (e.g., Mito-Tempo)	Reverse renal damage and inflammation caused by kidney stones by protecting mitochondrial function [42]. [1]	[42]
12	**Umbelliferone (Umb)**	Attenuates kidney stone-induced renal autophagy via the PI3K/AKT pathway, thereby reducing inflammation and damage [47]. [1]	[47]
13	**Phillyrin**	Significantly reduces calcium oxalate-induced HK-2 cell apoptosis and oxidative stress, inhibits oxidative stress and renal crystal	[54]

		deposition in model rats, and activates the PPARγ signaling pathway [54]. [1]	
14	**Betulin**	Possesses antioxidant and anti-urolithiasis activity, inhibiting the crystallization, nucleation, and aggregation of oxalate crystals [59]. [1]	[59]
15	**Benzene sulfonamide derivatives** (SBCl and SBF)	Exhibit anti-urolithiasis potential by inhibiting stone formation complications, with antioxidant and anti-inflammatory effects [50]. SBCl performs better in antioxidant and anti-inflammatory parameters [50]. [1]	[50]
16	**Vanillin**	Shows anti-urolithiasis action in hyperoxaluria rats by reducing hyperoxaluria, hypercalciuria, and crystal count [49]. Molecular docking	[49]

		studies indicate strong binding to human CTP:phosphoethanolamine cytidylyltransferase [49]. [1]	
17	**Litiax** (Oak extract)	Inhibits stone growth and possesses anti-inflammatory and diuretic properties, which may partially inhibit bacterial proliferation [71]. [1]	[71]

III. Moderate Inhibitors/Reducers (Some inhibition on stone formation and growth)

These agents offer some inhibitory action on calculus formation and growth [1].

- **Potassium citrate compounds:** Used to stabilize urinary pH and control stone formation, particularly for patients with medullary sponge kidney (MSK) who are prone to stones [6]. [1]
- **Citrates and Magnesium:** Recognized as effective inhibitors of calcium oxalate crystals [19]. [1]
- **Penicillamine and tiopronin:** Cystine-binding thiols that inhibit cystine crystallization [41]. [1]
- **4-Aminocoumarin based Aroylthioureas** (e.g., 5i): Potent *Canavalia ensiformis* urease inhibitors, relevant to stones caused by urease-producing bacteria [7]. [1]
- **Yellow tea (flavonoids):** Reduces crystal deposition, inflammation, oxidative stress, and fibrosis in a rat model, possibly by modulating PPARγ transcription factor activity [30]. [1]
- **Incarvillea diffusa Royle extract (IDW):** Significantly reduces crystal deposition, inflammation, oxidative stress, and fibrosis by modulating the ROS-induced Nrf2/HO-1 pathway [35]. [1]
- **Rhizoma Polygonati (RP):** Improves renal function and reduces crystal deposition in a kidney stone mouse model, possessing anti-inflammatory and anti-apoptotic effects [38]. [1]

- **Clerodendranthus spicatus (Cat's Whisker):** A traditional Chinese medicine used for kidney stones and other urinary conditions, possessing antibacterial, anti-inflammatory, antioxidant, and renal protective effects; clinically proven effective for urinary system inflammation and stones [69]. [1]
- **Hesperidin:** Shows anti-urolithiasis potential in sodium oxalate-induced *Drosophila* and mouse urolithiasis models by reducing crystal deposition, improving renal function markers, and increasing urine flow [43]. [1]
- **Protosappanin B, 10-methyl-protosappanin B, and brazilin** (from *Caesalpinia bahamensis*): Show anti-calculi activity by lowering urinary calcium and oxalate concentrations [61]. [1]
- **Herbo-Mineral Medicine, Lithom:** In vitro, significantly reduces the average crystal area, Feret's diameter, and area-perimeter ratio of calcium oxalate monohydrate (COM) crystals, transforming their morphology from irregular polygons to smooth small cubic polygons [67]. In an ethylene glycol-induced rat model, it lowers urinary oxalate levels, oxidative stress, renal inflammation, and crystal deposition [67]. [1]
- **SLC26A3 (DRA) inhibitors** (e.g., 4k): DRA is an anion exchanger (Cl^-, HCO_3^-, and oxalate) [40]. Inhibiting DRA may be a potential strategy for treating calcium oxalate kidney stones by reducing urinary oxalate excretion [40]. [1]
- **Antioxidants, free radical scavengers, and inhibitors of NADPH oxidase, the NLRP3 inflammasome, and the Renin-Angiotensin-Aldosterone System (RAAS):** Considered beneficial for stone prevention, with experimental data supporting compounds like statins and Angiotensin-Converting Enzyme inhibitors [28]. [1]
- **Natural products as Nrf2 regulators:** Being explored for their renal protective roles by inhibiting ferroptosis, a process implicated in kidney stone formation [68]. [1]
- **Jinqiancao granules:** A traditional Chinese medicine containing active compounds with anti-inflammatory effects, potentially useful for kidney stone treatment [37]. [1]
- ***Drymoglossum piloselloides*, *Kalanchoe laciniata*, and *Aegle marmelos* flower extracts:** Show an ability to inhibit calcium oxalate crystal nucleation, growth, and aggregation in vitro [26]. [1]
- **Peppermint oil (*Mentha piperita L.*):** Possesses preventative and therapeutic effects against ethylene glycol-induced urolithiasis, with antioxidant, spasmolytic, and renal-protective potential [18]. [1]
- **Ammi visnaga (Al-Khillah) seeds:** Significantly reduce the incidence of experimentally induced oxalate renal calculi and exhibit potent diuretic activity [95]. [1]

IV. Prophylactic/Supportive Measures (Reduce stone risk)

These measures primarily focus on reducing the risk of stone formation [1].

- **Dietary carotenoids** (α-carotene, β-carotene, β-cryptoxanthin, lycopene, and lutein/zeaxanthin): Higher dietary intake is associated with a lower prevalence of kidney stones, with β-carotene showing the greatest effect [32]. [1]
- **Coffee intake (Trigonelline):** Moderate coffee consumption correlates with a lower risk of kidney stones [36]. Trigonelline in coffee is found to prevent stone formation [36]. [1]

- **Prophylactic water and diet control:** Essential for stone-prone individuals [6]. [1]
- **Increased water intake and physical activity:** Highly important preventative measures for cystine stones [41]. [1]
- **Horse gram:** An underutilized pulse crop traditionally believed to treat kidney stones [56]. [1]
- **Achyranthes aspera Linn. (Prickly Chaff Flower):** The whole plant is traditionally used for kidney stone treatment [57]. [1]
- **Traditional Mayan Medicine plants** (e.g., *Annona muricata L., Carica papaya L., Ipomoea batatas (L.) Lam., Lantana camara L., Sechium edule (Jacq.) Sw., Tagetes erecta L., and Zea mays L.*): Used for kidney-related ailments, including stone elimination [63]. [1]
- **"Palo azul" (*Cyclolepis genistoides D.Don*) and "pitoreal" (*Ephedra antisyphilitica Berland. ex C.A.Mey.*):** Medicinal plants used in Mexican rural communities for urinary tract infections and kidney stones [64]. [1]
- **Stigma maydis (Corn Silk):** Used for centuries to treat kidney stones [65]. [1]
- **Gypsophila species:** Traditionally used to treat kidney stones [66]. [1]
- **Dietary Phytate:** May be beneficial in inhibiting calcium oxalate kidney stone formation [62]. [1]
- **Rice-bran products** (Inositol, IP6, rice oil, ferulic acid, γ-oryzanol, phytosterols, tocotrienols, RICEO): Show potential in preventing hypercalciuria and kidney stones [90]. [1]
- **Crataegus oxyacantha (Hawthorn):** Historically used for kidney stones, though its current use is primarily for cardiovascular conditions [94]. [1]

Substances to Avoid (Potential Stone Promoters)

Exposure to these substances may promote kidney stone formation [1].

Substance/Compound	Key Mechanism/Effect	Citations
Organotin compounds (OTs)	Increase kidney stone prevalence, inhibit H^+/K^+-ATPase, increase ROS, and lead to renal tissue damage [2]. [1]	[2]
Melamine	Stabilizes the heterogeneous nucleation of calcium crystals, promotes uric acid +	[29]

	calcium phosphate ($\text{UA} + \text{CaP}$) crystal formation, and reduces the efficacy of traditional remedies like hydroxycitrate [29]. [1]	
Volatile Organic Compounds (VOCs) (e.g., AMCC, 3,4-MHA, MA, DHBMA, HMPMA, 2HPMA, Benzene, Ethylbenzene, m/p-Xylene, 2,5-Dimethylfuran, Furan)	Positively correlated with an increased prevalence/risk of kidney stones [34, 45]. [1]	[34, 45]
Perchlorate, Nitrate, and Thiocyanate	Elevated urinary levels of nitrate and thiocyanate are associated with an increased risk of kidney stone disease (KSD) [51]. [1]	[51]
Per- and polyfluoroalkyl substances (PFAS) (e.g., PFDA, PFDE, PFHxS n-PFOS, Sm-PFOS)	Positively associated with kidney stone risk [53, 55]. [1]	[53, 55]
Uropathogenic *Escherichia coli*	Can promote crystal formation [19]. [1]	[19]
Proteus mirabilis	Primarily promotes infectious urinary stone formation by producing urease [52]. [1]	[52]

This response was generated by a Flash 2.5 (Large Language Model Variant).

Would you like to search for the specific mechanism of action for any of the listed inhibitors?