

## An overview of multi-ingredient kidney stone dissolving formulations from Traditional Persian Pharmacy

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### Abstract

Kidney stone, as a third important urinary tract disease, is a common disease affecting 10-15% of the world population. Effective medical treatment for the disease is not yet well established. On the other hand, there is an increasing global demand to manage and control various diseases with natural medicine and medicaments originating from Complementary and Alternative Medicine (CAM). Traditional Persian medicine (TPM), as one of the most popular schools in CAM, suggests numerous clinical interventions for kidney stones. This review provides various related compound formulations for kidney/bladder stones from the standpoints of Persian scholars. These remedies have been cited in a series of traditional pharmaceutical manuscripts of Persian medicine, namely *Qarābādin* or prescription. More than fifty multi-ingredient formulations for kidney/bladder stones have been found by reviewing five main Persian pharmacopeias. Various dosage forms have been reported for the management of kidney/bladder stones, such as *Majoon* (confection), *Sharāb* (syrup), *Jawārish* (semisolid confection), *Qors* (Tablet), and *Safoof* (oral powder). Considering the positive pharmacological or biological activities of the constituents of filtered formulations, many of those can be re-formulated and either experimentally or clinically evaluated to be introduced as new natural remedies in this field.

**Keywords:** Kidney stone, Complementary medicine, *Qarābādin*, Traditional pharmacy.

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### 1. Introduction

The kidney stone is caused by an abnormal accumulation of crystalline substances in the kidneys. This complication is a third important urinary system disease that imposes a great deal of financial burden on the American treatment system. Kidney stone has a high incidence, affecting 10-15 % of the world population. The prevalence

of kidney stones is more in American men (12%) as compared with American women (5%) (1-4).

Studies from other Western countries show that kidney stones are uncommon before the age of 20; the incidence rises between the ages of 20 and 30 years and remains relatively constant until the age of 70 (5). On the other hand, the incidence of nephrolithiasis in children aged  $\leq 18$  years was found to be 18.5 per 100,000 children in 2007, while it was 7.9 per 100,000 in 1996 (6). Studies suggest that the development of kidney stones

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from 1970 to 2000 was approximately constant, but the incidence is growing in men and decreasing in women (7).

Nephrolithiasis is a painful and costly medical condition that begins with solute supersaturation, crystal formation, and aggregation, followed by retention in the collecting system and further growth. Kidney stones are associated with hypertension and chronic kidney disease (6). Although the pathology of the disease is still unclear, the effect of factors such as gender, age, diet, the concentration of  $\text{Ca}^{+2}$  in the urinary tract, and pH have been confirmed (8).

Medical conditions that are associated with an increased risk of kidney stone formation include hyperparathyroidism, hyperthyroidism, sarcoidosis, gout, malabsorption (inflammatory bowel disease, ileal resection or bypass), cystic fibrosis, renal abnormalities (medullary sponge kidney, distal renal tubular acidosis, and anatomical abnormalities) (9). Prospective studies have shown stone recurrence rates of between 26% and 53% after ten years. Risk factors for recurrence include: presenting with a first stone at a younger age, family history, stone number, and gouty arthritis (5).

Besides non-pharmacological therapies such as lowering sodium, oxalate, and animal protein intake, pharmacotherapy should be considered. Common medicines include Thiazide diuretics for hypercalciuria management, Potassium citrate for the management of hypocitraturia, and abnormal urinary tract acidity. Allopurinol is also used to control hyperuricemia and hyperuricosuria (9). Extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy, ureteroscopy, laser therapy, and surgery are other ways to manage kidney stones. Disadvantages of current medicaments include high costs, invasiveness, side effects, and disability to alleviate the sharp pain associated with kidney stones (10-12).

As mentioned, kidney stone is a lifestyle-related disease prevalent in developed countries, and effective medical treatment for the disease is not yet well established (13). On the other hand, there is an increasing global demand to manage and control various diseases with natural medicine and medicaments originating from Complementary

and Alternative Medicine (CAM) (14, 15).

Moreover, traditional medical systems are effective for many chronic disorders. Traditional Persian Medicine (TPM) is an old medical system with indigenous knowledge derived from Chinese, Indian, and Egyptian traditional medicine (16, 17).

TPM pharmacopeias have valuable information on treating urinary tract diseases such as kidney stones. Muhammad Ibn Zakaria Razi wrote a book on kidney and bladder stones and described his method of diagnosing and treating calculi (18,19). Avicenna dedicated a remarkable part of his encyclopedia "*The Canon of Medicine*" to kidney and bladder disease. He believed that foodstuffs, dairy products, sour fruit, unclear water, and dark juices could increase the risk of kidney calculi. The term "*Mofatet Hasat*" refers mainly to compounds used to treat kidney stones in TPM pharmacopeias (20).

As mentioned, Pharmaceutical manuscripts of TPM encompass many mono/poly herbal medications for kidney/bladder stones which should be considered. This investigation aims to gather and study the effectiveness of critical multi-ingredient formulations used for kidney/bladder stones from five main Persian pharmacopeias.

## 2. Methods

Five main *Qarābādin* textbooks of TPM have been studied in this study. These books, known as encyclopedias, included a list of multi-ingredient preparations containing mineral, animal, and herbal materials with pharmaceutical and medical applications (21). Studied pharmacopeias include *Qarābādin-e-Kabir* (Aghili Shirazi/1772 AD) (22), *Qarābādin-e- Salehi* (Ghaeni Heravi/ 1765 AD) (23), *Qarābādin-e-Ghāderi* (Ahmadshah Arzani/1714 AD) (24), *Qarābādin-e-Azam* (Hakim Azam Khān/ 1853 AD) (25), and *Canon of medicine* (Avicenna/ 1025AD) (20). The search was done using the keywords: "*Mofatet Hasat*," "*Sange Gordeh*," and "*Sange Masane*". This review excluded a list of formulations with ingredients mentioned in the Urdu language, those containing unsafe minerals, and animal ingredients.

## 3. Results and discussion

The multi-ingredient formulations for kid-

ney/bladder stones are reported in Table 1. The traditional name of the formulations, ingredients, scientific names, and processes involved in formulation preparation are listed. Moreover, the formulation application for kidney or bladder stones has been reported. According to traditional pharmacopeias, formulations used in bladder stones can also be used in kidney stones. But those used in kidney stones are not useful for bladder stones (20, 23).

Various traditional formulations are reported for kidney/bladder stones, including *Majoon* (confection), *Sharāb* (syrup), *Jawārish* (semi-solid confection), *Qors* (Tablet), and *Safoof* (oral powder). Among reported formulations, some of the ingredients have been evaluated for kidney stones separately before, including *Lapis judaicus*, *Tribulus terrestris*, *Foeniculum vulgare*, *Cucumis sativus*, *Apium graveolens*, *Cucumis melo*, and *Cucurbita pepo*.

The Randomized and double-blinded clinical trial showed that *Lapis judaicus* could significantly reduce the kidney stone size in the group receiving 2 grams of *Lapis judaicus* powder in hard capsules for ten weeks, compared with the control group. Moreover, it has been mentioned that *Lapis judaicus* did not affect blood urea nitrogen (BUN), serum creatinine (sCr), alanine aminotransferase (ALT), or aspartate aminotransferase (AST) (26).

We could find several multi-ingredient formulations containing *Lapis judaicus*, including *Hajrul yahood Majoon* (Jews' Stone confection), *Davā* (medicine) for Kidney stone, *Hajrul yahood safoof* (Jews' Stone oral powder), and oral drop for kidney and bladder stone as listed in Table 1.

It has been reported that aqueous extract of *Tribulus terrestris*, could decrease oxidative stress induced by hyperoxaluria. Moreover, it could reduce oxalate, calcium, and phosphate secretion

**Table 1.** The multi-ingredient formulations for kidney/bladder stones (TPM manuscripts).

No.	The traditional name of formulations	Kidney/Bladder Stone	Ingredients (Natural)	Process	Ref.
1	<i>Ābzān</i> (Sitz bath)	Bladder	<i>Crambe maritima</i> (Leaf)+ <i>Medicago sativa</i> (Seed)+ <i>Mentha pulegium</i> (Leaf)+ <i>Carthamus tinctorius</i> (Flower)+ Pigeon droppings	Mixing-Boiling	(22, 23)
2	<i>Ābzān</i> (Sitz bath)	Bladder/kidney	<i>Matricaria chamomilla</i> (Flower)+ <i>Melilotus officinalis</i> (Flower)+ <i>Rosa damascena</i> (Flower)+ <i>Althaea officinalis</i> (Flower)+ <i>Cucumis melo</i> (Seed)+ <i>Adiantum capillus-veneris</i> (Aerial parts)+ <i>Dolichos biflorus</i> (Seed)+ <i>Pimpinella anisum</i> (Seed)+ <i>Physalis alkekengi</i> (Fruit)+ <i>Artemisia vulgaris</i> (Aerial parts)+ <i>Viola odorata</i> (Flower)+ <i>Ipomoea tricolor</i> (Seed)+ <i>Asparagus officinalis</i> (Root)+ Scorpione oil	Mixing-Boiling	(25)
3	<i>Amrūsia</i> (diuretic formulation)	Bladder/kidney	<i>Helleborus niger</i> (Flower)+ <i>Commiphora myrrha</i> (Resin)+ <i>Cinnamomum cassia</i> (Bark)+ <i>Carum carvi</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Piper longum</i> (Fruit)+ <i>Saussurea costus</i> (Root)+ <i>Laurus nobilis</i> (Leaf)+ <i>Acorus calamus</i> (Rhizome)+ <i>Crocus sativus</i> (Flower)	Mixing with honey	(23)
4	<i>Aragh-e-Ānānās</i> (pineapple distillate)	Bladder/kidney	<i>Ananas comosus</i> (Fruit)+ <i>Pimpinella anisum</i> (Seed)+ <i>Allium cepa</i> (Bulb)+ <i>Nicotiana rustica</i> (Leaf)+ <i>Tribulus terrestris</i> (Fruit)	Mixing - distillation	(25)
5	<i>Balsan oil</i> (Commiphora)	Bladder/kidney	<i>Commiphora opobalsamum</i> (Resin)+ <i>Trachyspermum ammi</i> (Aerial parts)	Mixing	(23)
6	<i>Davā</i> (Medicine for kidney stone)	Bladder/kidney (specially in children)	<i>Tribulus terrestris</i> (Fruit)+ <i>Physalis alkekengi</i> (Fruit)+ <i>Cucurbita maxima</i> (Seed)+ <i>Prunus cerasus</i> (Fruit)+ <i>Portulaca oleracea</i> (Aerial parts)+ <i>Lapis judaicus</i>	Mixing	(23)
7	<i>Davā</i> (Medicine)	Bladder/kidney	<i>Hyoscyamus niger</i> (Seed)+ <i>Carum carvi</i> (Seed)+ <i>Commiphora myrrha</i> (Resin)+ <i>Ruta graveolens</i> (Aerial parts)+ <i>Crocus sativus</i> (Flower)+ <i>Cinnamomum iners</i> (Bark)+ <i>Piper album</i> (Fruit)+ Yellow sulfur	Milling-mixing with honey- put for 1 year	(20)

Table 1. Continued.

8	<i>Davā</i> (Medicine)	Bladder/kidney	<i>Cucumis melo</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Helleborus niger</i> (Flower)+ sugar	Mixing	(24)
9	<i>Davā</i> (Medicine) for kidney/bladder stone	Bladder/kidney	<i>Corylus avellana</i> (Seed)+ <i>Prunus dulcis</i> (Seed)+ <i>Cucumis melo</i> (Seed)+ <i>Carum carvi</i> (Seed)+ <i>Conium maculatum</i> (Aerial parts)+ <i>Crocus sativus</i> (Flower)+ <i>Cucumis sativus</i> (Seed)+ <i>Hyoscyamus niger</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)	Mixing with honey-tableting	(20)
10	<i>Davā-e-Mofatet-Hosāt</i> (Anticalculi Medicine)	Bladder/kidney	<i>Cucumis melo</i> (Seed)+ <i>Cucumis sativus</i> (Flower)+ <i>Cichorium intybus</i> (Seed)+ <i>Amygdalus communis</i> (Seed)	Mixing	(24)
11	<i>Davā-ol-kebrit</i> (Sulfur medicine)	Bladder/kidney	<i>Stachys lavandulifolia</i> (Flower)+ <i>Hyoscyamus niger</i> (Seed)+ <i>Carum carvi</i> (Seed)+ <i>Commiphora myrrha</i> (Resin)+ <i>Ruta graveolens</i> (Aerial parts)+ <i>Saussurea costus</i> (Root)+ <i>Papaver somniferum</i> (Seed)+ <i>Crocus sativus</i> (Flower)+ <i>Cinnamomum cassia</i> (Bark)+ <i>Piper album</i> (Fruit)	Mixing with honey	(23)
12	<i>Davā-ol-kebrit</i> (Sulfur medicine)	Bladder/kidney	<i>Apium graveolens</i> (Aerial parts)+ <i>Helleborus niger</i> (Flower)+ <i>Juniperus sabina</i> (Fruit)+ <i>Asarum Europaesum</i> (Root)+ <i>Trachyspermum ammi</i> (Aerial parts)+ <i>Hyacinthus orientalis</i> (Flower)+ <i>Foeniculum vulgare</i> (Seed)+ <i>Amygdalus communis</i> (Seed)+ <i>Cucumis melo</i> (Seed)	Mixing-solve in wine	(24)
13	<i>Ghatūr</i> (oral drop) for kidney and bladder stone	Bladder/kidney	<i>Tribulus terrestris</i> (Fruit)+ <i>Raphanus sativus</i> (Rhizome)+ <i>Cucurbita pepo</i> (Seed)+ <i>Physalis alkekengi</i> (Fruit)+ <i>Dolichos biflorus</i> (Seed)+ <i>Adiantum capillus-veneris</i> (Aerial parts)+ <i>Lapis judaicus</i> + <i>Scorpiones</i> oil	Mixing-boiling	(23)
14	<i>Habb-e-Mofatet-Hosāt</i> (Anticalculi pill)	Bladder/kidney	<i>Commiphora simplicifolia</i> (Resin)+ <i>Raphanus sativus</i> (Rhizome)+ <i>Helleborus niger</i> (Flower)+ <i>Pimpinella anisum</i> (Seed)+ <i>Prunus dulcis</i> (Seed)+ <i>Cinnamomum cassia</i> (Bark)+ <i>Lycopodium clavatum</i> (Aerial parts)+ <i>Peganum harmala</i> (Seed)+ <i>Gentiana cruciata</i> (Seed)+ <i>Lagoecia cuminoides</i> (Aerial parts)+ <i>Hyoscyamus niger</i> (Seed)+ <i>Capsicum annum</i> (Fruit)+ <i>Acorus calamus</i> (Rhizome)	Mixing with wine	(24)
15	<i>Hab-ol-Ghotan Majoon</i> (Levant cotton confection)	Bladder/kidney	<i>Gossypium herbaceum</i> (Seed)+ <i>Cinnamomum verum</i> (Bark)+ <i>Urtica dioica</i> (Leaf)+ <i>Pastinaca sativa</i> (Root)+ <i>Zingiber officinale</i> (Rhizome)+ <i>Saussurea costus</i> (Root)+ <i>Linum usitatissimum</i> (Seed)+ <i>Pistacia lentiscus</i> (Leaf)	Mixing with honey	(23)
16	<i>Hajrul yahood Majoon</i> (Jews' Stone confection)	Kidney	<i>Cucurbita pepo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Cucumis melo</i> (Seed)+ <i>Physalis alkekengi</i> (Fruit)+ <i>Lapis judaicus</i>	Mixing with Angbin	(23)
17	<i>Hajrul yahood Majoon</i> (Jews' Stone confection)	Bladder/kidney	<i>Physalis alkekengi</i> (Fruit)+ <i>Asarum europaesum</i> (Root)+ <i>Lagoecia cuminoides</i> (Aerial parts)+ <i>Cucumis melo</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Daucus carota</i> (Aerial parts)+ <i>Carthamus tinctorius</i> (Flower)+ <i>Cucumis sativus</i> (Seed)+ <i>Citrullus lanatus</i> (Fruit)+ <i>Cucurbita pepo</i> (Seed)+ <i>Pimpinella anisum</i> (Seed)+ <i>Lapis judaicus</i>	Milling-mixing with honey	(25)
18	<i>Hajrul yahood Majoon</i> (Jews' Stone confection)	Bladder/kidney	<i>Cucumis sativus</i> (Seed)+ <i>Physalis alkekengi</i> (Fruit)+ <i>Lapis judaicus</i>	Mixing with honey	(24)
19	Hazelnut formulation	Bladder/kidney	<i>Cucurbita pepo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Cucumis melo</i> (Seed)+ <i>Portulaca oleracea</i> (Aerial parts)+ <i>Althaea officinalis</i> (Flower)+ <i>Amygdalus communis</i> (Seed)+ <i>Papaver somniferum</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Corylus avellana</i> (Seed)	Milling-mixing	(22)

Table 1. Continued.

20	Hoghne (Enema formulation)	Kidney	<i>Hordeum vulgare</i> (Seed)+ <i>Triticum aestivum</i> (Seed)+ <i>Tribulus terrestris</i> (Fruit)+ <i>Adiantum capillus-veneris</i> (Aerial parts)+ <i>Althaea officinalis</i> (Flower)+ <i>Beta vulgaris</i> (Root)+ <i>Crambe maritima</i> (Leaf)+ <i>Viola odorata</i> (Flower)+ <i>Cassia fistula</i> (Fruit)+ <i>Cucumis melo</i> (Seed)	Milling-mixing-boiling	(23)
21	<i>Jawārish-e-Jālinūs</i> (semisolid confection)	Bladder/kidney	<i>Valeriana officinalis</i> (Root)+ <i>Dianthus barbatus</i> (Aerial parts)+ <i>Terminalia chebula</i> (Fruit)+ <i>Cinnamomum cassia</i> (Bark)+ <i>Alpinia officinarum</i> (Root)+ <i>Zingiber officinale</i> (Rhizome)+ <i>Piper nigrum</i> (Fruit)+ <i>Piper longum</i> (Fruit)+ <i>Saussurea costus</i> (Root)+ <i>Asarum europaeum</i> (Root)+ <i>Crocus sativus</i> (Flower)	Milling-mixing with honey	(24, 25)
22	<i>Jawārish-e-Kākanj</i> (a semisolid confection of bladder cherry)	Bladder/kidney	<i>Hyoscyamus niger</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Foeniculum vulgare</i> (Aerial parts)+ <i>Cucumis sativus</i> (Seed)+ <i>Pinus gerardiana</i> (Fruit)+ <i>Corylus avellana</i> (Seed)+ <i>Prunus dulcis</i> (Seed)+ <i>Crocus sativus</i> (Flower)+ <i>Physalis alkekengi</i> (Fruit)	Milling-mixing with water and honey	(22)
23	<i>Ma'a-ol-osūl</i> (Roots water extract)	Bladder/kidney	<i>Apium graveolens</i> (Aerial parts)+ <i>Pimpinella anisum</i> (Seed)+ <i>Cymbopogon schoenanthus</i> (Leaf)+ <i>Commiphora opobalsamum</i> (Resin)+ <i>Asarum europaeum</i> (Root)+ <i>Cinnamomum Cassia</i> (Bark)+ <i>Gentiana cruciata</i> (Seed)+ <i>Withania somnifera</i> (Root)+ <i>Peganum harmala</i> (Seed)+ <i>Vitis vinifera</i> (Leaf)	Mixing-boiling	(23)
24	Majoon (Confection)	Bladder	<i>Apium graveolens</i> (Aerial parts)+ <i>Pimpinella anisum</i> (Seed)+ <i>Daucus carota</i> (Aerial parts)+ <i>Medicago sativa</i> (Seed)+ <i>Lepidium sativum</i> (Seed)+ <i>Trachyspermum ammi</i> (Aerial parts)+ <i>Cucumis melo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Anacyclus pyrethrum</i> (Root)+ <i>Crocus sativus</i> (Flower)+ <i>Portulaca oleracea</i> (Aerial parts)+ <i>Pistacia lentiscus</i> (Leaf)+ <i>Myristica fragrans</i> (Seed)+ <i>Dianthus barbatus</i> (Aerial parts)+ <i>Piper longum</i> (Fruit)+ <i>Piper cubeba</i> (Fruit)+ <i>Liquidambar orientalis</i> (Aerial parts)+ honey	Mixing with honey	(23)
25	<i>Majoon</i> Confection for kidney/bladder stone	Bladder/kidney	<i>Cinnamomum iners</i> (Bark)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Commiphora myrrha</i> (Resin)+ <i>Piper album</i> (Fruit)+ <i>Boswellia Sacra</i> (Resin)+ <i>Daucus carota</i> (Aerial parts)+ <i>Foeniculum vulgare</i> (Aerial parts)+ <i>Lilium candidum</i> (Flower)+ <i>Papaver somniferum</i> (Seed)+ <i>Amygdalus communis</i> (Seed)+ <i>Lapis judaicus</i>	Mixing with honey	(20)
26	<i>Majoon</i> for kidney stone(Confection)	Kidney	<i>Nardostachys jatamansi</i> (Seed)+ <i>Zingiber officinale</i> (Rhizome)+ <i>Piper longum</i> (Fruit)+ <i>Cinnamomum iners</i> (Bark)+ <i>Teucrium canadense</i> (Leaf)+ <i>Asarum europaesum</i> (Root)+ <i>Daucus carota</i> (Aerial parts)+ <i>Crocus sativus</i> (Flower)+ <i>Ricinus communis</i> (Seed)+ <i>Cymbopogon schoenanthus</i> (Leaf)+ <i>Allium sativum</i> (Bulb)+ <i>Piper album</i> (Fruit)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Commiphora simplicifolia</i> (Resin)+ <i>Lilium ledebourii</i> (Flower)	Mixing with honey	(20)
27	<i>Majoon Ghobād-al Molk</i> (Confection)	Bladder/kidney	<i>Ruta graveolens</i> (Aerial parts)+ <i>Marrubium vulgare</i> (Aerial parts)+ <i>Pimpinella anisum</i> (Seed)+ <i>Phyllitis scolopendrium</i> (Leaf)+ <i>Crocus sativus</i> (Flower)+ <i>Capsicum annuum</i> (Fruit)+ <i>Cymbopogon schoenanthus</i> (Leaf)+ <i>Valeriana officinalis</i> (Root)+ <i>Commiphora simplicifolia</i> (Resin)+ <i>Cinnamomum cassia</i> (Bark)+ <i>Hyoscyamus niger</i> (Seed)	Milling-mixing-macerate in wine	(22)

Table 1. Continued.

28	<i>Majoon-e-Abu Maher</i> (Confection)	Bladder/kidney	<i>Althaea officinalis</i> (Flower)+ <i>Malva sylvestris</i> (Flower)+ <i>Portulaca oleracea</i> (Aerial parts)+ <i>Cucumis melo</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Helleborus niger</i> (Flower)+ <i>Hyssopus officinalis</i> (Aerial parts)+ <i>Pimpinella anisum</i> (Seed)+ <i>Prunus dulcis</i> (Seed)+ <i>Physalis alkekengi</i> (Fruit)	Mixing with honey	(22)
29	<i>Majoon-e-Aghrab</i> (Scorpion confection)	Bladder/kidney	<i>Gentiana cruciata</i> (Seed)+ <i>Zingiber officinale</i> (Rhizome)+ <i>Capsicum annuum</i> (Fruit)+ <i>Piper longum</i> (Fruit)+ <i>Physalis al- kekengi</i> (Fruit)+ <i>Ricinus communis</i> (Seed)+ <i>Burned Scorpiones</i>	Mixing with Angbin	(23)
30	<i>Majoon-e-Balsān</i> (Commiphora confec- tion)	Bladder/kidney	<i>Commiphora simplicifolia</i> (Resin)+ <i>Raphanus sativus</i> (Rhi- zome)+ <i>Capparis spinose</i> (Flower/Seed)+ <i>Amygdalus com- munis</i> (Seed)+ <i>Cymbopogon schoenanthus</i> (Leaf)+ <i>Valeriana officinalis</i> (Root)+ <i>Cinnamomum cassia</i> (Bark)+ <i>Phyllitis scolopendrium</i> (Leaf)+ <i>Peganum harmala</i> (Seed)+ <i>Gentiana lutea</i> (Seed)+ <i>Lagoecia cuminoides</i> (Aerial parts)+ <i>Piper longum</i> (Fruit)	Milling- mixing	(22)
31	<i>Majoon-e-Ekhrāj- Sang</i> (Confection as stone remover)	Bladder/kidney	<i>Glycyrrhiza glabra</i> (Rhizome)+ <i>Hypericum perforatum</i> (Aerial parts)+ <i>Cinnamomum verum</i> (Bark)+ <i>Valeriana officinalis</i> (Root)+ <i>Crocus sativus</i> (Flower)+ <i>Apium graveolens</i> (Aerial parts)	Milling- mixing with honey	(22)
32	<i>Notūl</i> (Irrigation) for Kidney stone	Bladder/kidney	<i>Matricaria chamomilla</i> (Flower)+ <i>Rosa damascene</i> (Flower)+ <i>Melilotus officinalis</i> (Flower)+ <i>Althaea officinalis</i> (Flower)+ <i>Tribulus terrestris</i> (Fruit)+ <i>Cucumis melo</i> (Seed)+ <i>Adiantum capillus-veneris</i> (Aerial parts)+ <i>Dolichos biflorus</i> (Seed)+ <i>Glycyrrhiza glabra</i> (Rhizome)+ <i>Pimpinella anisum</i> (Seed)+ <i>Physalis alkekengi</i> (Fruit)+ <i>Trigonella foenum-graecum</i> (Aerial parts)+ <i>Viola odorata</i> (Flower)+ <i>Artemisia vulgaris</i> (Aerial parts)+ <i>Helleborus niger</i> (Flower)+ <i>Nelumbo nucifera</i> (Flower)	Boil in water	(23)
33	<i>Qors</i> (Tablet) for Bladder/kidney stone	Bladder/kidney	<i>Daucus carota</i> (Aerial parts)+ <i>Cucumis melo</i> (Seed)+ <i>Foe- niculum vulgare</i> (Aerial parts)+ <i>Commiphora myrrha</i> (Resin)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Cinnamomum verum</i> (bark)+ <i>Cinnamomum cassia</i> (Bark)	Milling- mixing- tableting	(20)
34	<i>Qors</i> (Tablet) Blad- der/kidney stone	Bladder/kidney	<i>Ricinus communis</i> (Seed)+ <i>Origanum majorana</i> (Leaf)+ <i>Ruta graveolens</i> (Aerial parts)+ <i>Hyoscyamus niger</i> (Seed)+ <i>Foenicu- lum vulgare</i> (Aerial parts)+ <i>Punica granatum</i> (Seed)	Milling- mixing- tableting	(20)
35	<i>Qors</i> (Tablet) for Bladder/kidney stone	Bladder/kidney	<i>Eruca vesicaria</i> (Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Cin- namomum cassia</i> (Bark)+ <i>Valeriana officinalis</i> (Root)	Mixing- Equal parts for tableting	(22)
36	<i>Roghan Bolūr Madani</i> (an oil)	Bladder/kidney	<i>Apium graveolens</i> (Aerial parts)+ <i>Pimpinella anisum</i> (Seed)+ <i>Cichorium intybus</i> (Seed)	Maceration	(23)
37	<i>Roghan-e- Aghrab</i> (Scorpion Oil)	Bladder	2 live Scorpions+ <i>Olea europaea</i> (oil)	Mixing- Put in sun for 40 days	(23)
38	<i>Roghan-e- Aghrab</i> (Scorpion Oil)	Bladder	<i>Rheum rhabarbarum</i> (Aerial part)+ <i>Gentiana cruciata</i> (Seed)+ <i>Capparis spinosa</i> (Flower/Seed)+ <i>Amygdalus communis</i> (Seed)+ 10 live Scorpions	Mixing - put in sun for 7 days	(24, 25)
39	<i>Roghan-e-Sodāb</i> (Rue oil)	Bladder/kidney	<i>Ruta graveolens</i> (Aerial parts)+ <i>Sesamum indicum</i> (Seed)	Mixing	(23)
40	<i>Roghan-e- Torob</i> (Radish oil)	Bladder/kidney	<i>Raphanus sativus</i> (Rhizome)+ <i>Sesamum indicum</i> (Seed) + honey	Boiling- mixing with honey	(23)

Table 1. Continued.

41	<i>Safoof Hajrul yahood</i> (Jews' Stone)	Bladder/kidney	<i>Cucurbita pepo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Cucumis melo</i> (Seed)+ <i>Tribulus terrestris</i> (Fruit)+ <i>Dolichos biflorus</i> (Seed)+ <i>Levisticum officinale</i> (Root)+ <i>Prangos pubularia</i> (Aerial parts)+ <i>Lapis judaicus</i>	Mixing	(23, 24)
42	<i>Safoof</i> (oral powder)	Bladder/kidney (especially in children)	<i>Cucumis melo</i> (Seed)+ <i>Prunus persica</i> (Fruit)+ <i>Dolichos biflorus</i> (Seed)	Mixing	(23)
43	<i>Safoof-e-Hajrul yahood</i> (Jews' Stone)	Bladder/kidney	<i>Cucurbita pepo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Cucumis melo</i> (Seed)+ <i>Portulaca oleracea</i> (Aerial parts)+ <i>Dolichos biflorus</i> (Seed)+ <i>Lapis judaicus</i>	Mixing with sugar	(24)
44	<i>Sekanjebin</i> (Oxymel)	Bladder/kidney	<i>Capparis spinosa</i> (Flower/Seed)+ <i>Apium graveolens</i> (Aerial parts)+ <i>Raphanus sativus</i> (Rhizome)+ <i>Acorus calamus</i> (Rhizome)+ <i>Urginea maritima</i> (Bulb)+ <i>Helleborus niger</i> (Flower)	Mixing with sugar & Vinegar/heat	(22, 24)
45	<i>Sharab-e-bozūr</i> (Seeds syrup)	Bladder/kidney	<i>Cichorium intybus</i> (Seed)+ <i>Pimpinella anisum</i> (Seed)+ <i>Cucumis melo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Cucurbita pepo</i> (Seed)+ <i>Carthamus tinctorius</i> (Flower)+ <i>Althaea officinalis</i> (Flower)+ <i>Glycyrrhiza glabra</i> (Rhizome)+ <i>Valeriana officinalis</i> (Root)+ <i>Pimpinella anisum</i> (Seed)+ <i>Viola odorata</i> (Flower)+ <i>Echium amoenum</i> (Flower)+ <i>Vitis vinifera</i> (Leaf)	Mixing-maceration-boiling	(23)
46	<i>Sharab-e-bozūr</i> (Seeds syrup)	Bladder/kidney	<i>Cichorium intybus</i> (Seed)+ <i>Pimpinella anisum</i> (Aerial parts)+ <i>Cucumis melo</i> (Seed)+ <i>Cucumis sativus</i> (Seed)+ <i>Cucurbita pepo</i> (Seed)+ <i>Carthamus tinctorius</i> (Flower)+ <i>Althaea officinalis</i> (Flower)+ <i>Valeriana officinalis</i> (Root)+ <i>Viola odorata</i> (Flower)+ <i>Pimpinella anisum</i> (Aerial parts)+ <i>Echium amoenum</i> (Flower)	Milling-mixing-macerateing-boiling	(24, 25)
47	<i>Sharāb-e-Hasak</i> <i>Tribulus</i> syrup	Bladder/kidney	<i>Tribulus terrestris</i> (Fruit)+ sugar (or honey)	Mixing	(23)
48	<i>Sharāb-e-Kākanj</i>	Bladder/kidney	<i>Physalis alkekengi</i> (Fruit)+ sugar	Cooking-mix with sugar	(23)
49	<i>Sharbat-e- Ejjās</i> (sour cherry syrup)	Bladder/kidney	<i>Prunus cerasus</i> (Fruit)+ sugar	Macerate for 1 day- boiling- adding sugar	(25)
50	<i>Sharbat-e- Helion</i> (Garden asparagus)	Bladder	<i>Asparagus officinalis</i> (Root)+ sugar	Boil in water- add sugar	(22, 24)

and reduce BUN, uric acid, and sCr (2).

Another study suggests that *Tribulus terrestris* contain an antilithiatic protein having a molecular weight of ~60 kDa similar to Carotenoid cleavage dioxygenase 7 (CCD7). An EF-hand (a helix-loop-helix structural domain in a large family of calcium-binding proteins) domain was identified in CCD7. The EF-hand domain is a characteristic feature of calcium-binding proteins. It has a role in retinol synthesis, which is transported by retinol-binding protein, a protein found in the kidney stone matrix. As a result, it should be noted

that this protein might be responsible for preventing the adhesion of calcium oxalate crystals to kidney cells and the formation of kidney stones (27).

Another study suggests that *Foeniculum vulgare* can inhibit the formation of oxalate stones in animal models. Results of the study in rats confirm the inhibitory effect of *Foeniculum vulgare* on calcium oxalate renal stone formation. This inhibitory effect is attributed to preventing the supersaturation of calcium oxalate. Moreover, the plant's free-radical quenching capacity against oxalate-mediated tissue injury was confirmed (28).

*Cucumis sativus* is also traditionally used to prevent kidney stone formation (29). It has been reported that the hydroalcoholic extract of *Cucumis sativus* exerts dose-dependent anti-urolithiatic action. An increase in urine volume and a decrease in calcium, phosphate, and oxalate levels were observed. Normalizing the levels of sCr, BUN, and uric acid was reported in animal studies. Furthermore, it has been indicated that *Cucumis sativus* could prevent nucleation and aggregation of stone-forming components (30).

*Apium graveolens* is reported to improve urination and is used in South Africa for kidney stones. Results of a study in the rabbit model suggest that *Apium graveolens* could decrease calcium deposition from renal parenchyma and reduce BUN, sCr, as well as serum sodium with a non-significant reduction in serum potassium. Moreover, it showed a significant diuretic effect that accentuates urinary calcium excretion (31).

It has been mentioned that ethanol extract of *Cucumis melo* seed showed significant scavenging activity in nitric oxide radical Scavenging Assay (32). It has been reported that *Cucumis melo* is commonly used for renal problems in Pakistan. This property might be due to flavonoids, alkaloids, terpenes, and vitamin E (due to its antioxidant potential) content. Diuretic properties, urinary tract anti-ulcer properties, anti-histaminic, anticholinergic, and antispasmodic properties of *Cucumis melo* are all involved in renal protection (33).

It has been reported that the methanol

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extract of *Cucurbita pepo* significantly inhibited various steps of calcium oxalate crystal formation such as nucleation, aggregation, growth, and dissolution in a dose-dependent manner. Moreover, it can normalize the raised levels of oxalate, calcium, sodium, phosphate, and uric acid. Restoring histopathological alterations, and elevating the reduced magnesium levels, urine volume, and pH are other mechanisms that prevent stone formation by *Cucurbita pepo*. These protective effects might be due to the beta-tocopherol, stigmasterol, and squalene content found in *Cucurbita pepo* (34).

As mentioned, some of these herbal medicines were previously evaluated for kidney stones, and the results were noticeable. Thus, synergistic effects might be observed in dissolving kidney stones by combining these herbal medicines as a multi-ingredient formulation.

## 4. Conclusion

This study provides various compound formulations to manage and control kidney stones. These medicines can be re-formulated and either experimentally or clinically evaluated to be introduced as new natural remedies in this field. Therefore, it is recommended to consider the most reported formulations in Pharmacopias as a candidate for further studies and clinical trials.

## Conflict of Interest

None declared.

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