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Chapter

Medicinal Plants for the Treatment of Nephrolithiasis

Farah Al-Mamoori and Talal Aburjai

Abstract

Nephrolithiasis (kidney stones) impacts a significant group of individuals today as a result of changing lifestyles. Over the past decade, there has been a revival of interest in the study of medicinal plants as a source of potential herbal medicine. Herbal medicine could become a new phase in the medical system for human disease management within the next few decades. In fact, a number of studies strongly suggest using medicinal herbs as one of the anti-nephrolithiatic treatments. Different bioactive substances found in plants, such as polyphenols, flavonoids, saponins, furanochromones, alkaloids, and terpenoids, may be useful in halting the development of stones. These natural resources do in fact contain bioactive compounds of many types, including phenolic acids, flavonoids, and terpenoids, which have recently been shown to have potent anti-nephrolithiatic properties. However, the outcomes of the experiments that have been conducted with these natural substances are still in the preclinical stages. Future research on clinical applications may therefore be a fruitful way to confirm the clinical utility of these medications.

Keywords: medicinal plants, herbs, kidney stones, nephrolithiasis, flavonoids, phenolic acids

1. Introduction

Nephrolithiasis(kidney stone) is an illness that affects individuals of all sexes, races, and ages and is believed to be on the rise in many countries around the world. Along with the consequences of global warming, eating patterns may be a major factor influencing these trends [1]. Around 12% of people worldwide will get kidney stones at certain time in their lives. Kidney stones raise the risk of developing chronic kidney disease by 60% and end-stage renal disease by 40%, and papillary renal cell carcinoma has also been linked to kidney stones [2].

The utilization of herbal products has recently gained more attention due to the high cost and negative side effects of instrument implantation and urinary tract surgery. Humans and even animals have long relied on medicinal plants as a significant source of food and medicine. Nowadays, a number of researchers base their studies on natural resources such as medicinal herbs and a range of antiquated techniques such as those used by Ibn Sina [3]. Medical plants alleviate kidney stone pain and inhibit lithogenesis. From the kidney, medicinal plants eliminate kidney stones. Kidney stones are frequently treated with medicinal plants (calcium oxalate, uric

acid, struvite, and cysteine). The evolution of modern civilization includes the use of herbal medicine [4].

The formation of stones may be avoided by the existence of many bioactive components found in such as polyphenols, flavonoids, phytosterols, saponins, furanochromones, alkaloids, and terpenoids. Evidence points to their potential litholytic, antispasmodic, and diuretic properties as well as an inhibitory influence on crystallization, nucleation, and aggregation of crystals as the possible causes of their therapeutic effects. These benefits may be caused by antioxidant, anti-inflammatory, or antibacterial characteristics, according to the molecular pathways involved [5]. This chapter summarizes the role bioactive compounds and mechanisms of medicinal plants in the treatment of nephrolithiasis.

2. Anti-urolithiatic plants

The various traditionally based groups of medicinal plants have been used as anti-urolithiatic drugs belonging to the families including: Amaranthaceae, Malvaceae, Meliaceae, Satavari, Oxalidaceae, Crassulaceae, Saxifragaceae, etc. Considering the presence of therapeutic activities such as anti-inflammatory, antioxidant, analgesic, diuretic, or lithotriptic activities, these plants have been used as mono or polyherbs in anti-nephrolithiatic formulations [6].

The fruits of the *Rubus idaeus* L. plant, also known as raspberries, are an abundant supply of glycosaminoglycans, citrate, and magnesium that can help prevent kidney stones. Epigallocatechin, a polyphenolic component that is widely distributed in *Camellia sinensis* L. (green tea), has been shown to be effective in treating kidney stones. It works as a potent antioxidant to reduce oxidative stress and the risk of stone development. *Petroselinum crispum* Mill. (parsley) contains large amounts of apiol and myristicin, two compounds with biological properties that are antioxidants and diuretics and are thought to be beneficial in the treatment of urolithiasis. The tree pomegranate, or *Punica granatum* L., is a common name for a fruit that contains active ingredients such as flavonoids, alkaloids, glycosides, and steroids with antioxidant and anti-inflammatory properties [7].

Clinical investigations have mostly focused on finding out if the stone incidence, or the frequency and size of kidney stones, has changed. Large stones shrank while little stones were destroyed. The majority of research found that herbs had diuretic properties. Typically, kidney stones are found in the ureters and renal pelvis. The most likely cause of stone passage and elimination is increased urine volume. It's unknown what led to the size reduction. As a result, even for trials with encouraging findings, we may not fully comprehend how a particular herbal remedy functions [8]. Some of the treatments have been proven to reduce urine calcium excretion and increase urinary excretion of citrate, both of which affect urinary supersaturation. Herbs impede crystal nucleation, development, and aggregation, which prevents the embryonic stone from growing in size and from being retained within the confined renal tubules. Herbal remedies boost urinary output, encouraging urine flow through renal tubules and the clearance of the developing stone before it is too large to move and obstructs the tubular lumens. They might prevent the kidneys from producing reactive oxygen species, which are known to encourage crystal attachment and their retention in the kidneys by damaging the renal epithelium [9].

3. Anti-nephrolithiatic activity of bioactive compounds

3.1 Flavonoids

Flavonols, flavones, catechins, anthocyanidins, isoflavones, dihydroflavones, and chalcones can be produced from the thousands of plant chemicals known as flavonoids. Vegetables, fruits, nuts, spices, herbs, red wine, tea, and other foods and beverages also contain varying levels of these chemicals. One of the major classes of polyphenols is flavonoids, which have a wide range of pharmacological functions and have antioxidant effects [10]. Several flavonoids have shown renal protective properties against various nephrotoxic agents that often cause acute kidney injury (AKI) or chronic kidney disease (CKD), such as gentamycin, alcohol, nicotine, lead, or cadmium. Hemodialysis patients observed vasculoprotective benefits of cocoa flavanols in humans [11].

Many flavonoids such as quercitin, hyperoside, rutin, diosmin, and apigenin have been investigated for their probable potential to inhibit the formation of kidney stones. **Table 1** summarizes the main findings regarding the anti-nephrolithiatic activity of flavonoids [12–16].

3.2 Terpenoids

Naturally occurring pentacyclic triterpenes of plant origin can have a wide range of pharmacological effects. Lupeol and botulin(pentacyclic triterpenes) were similarly effective in reducing tissue damage brought on by crystal-induced renal peroxidative alterations as evaluated by malondialdehyde. The two substances may work by inhibiting calcium oxalate crystal aggregation and boosting the body's defensive mechanisms to provide protection against oxalate-induced toxic symptoms and free radical generation [17]. Moreover, childhood nephrolithiasis or urolithiasis has benefited significantly from the use of essential oil preparations of terpenic, which contain pinene (31%), camphene (15%), borneol (10%), anethol (4%), fenchone (4%), and cineol (3%). The majority of essential oil preparations are sold in the Middle East under the brand name Urinex (Pharco Co.) [18].

Compounds	Study type	Results	References
Quercetin	*In vivo*	Reduced damage due to hyperoxaluria. Reduced oxalate stone formation	[12]
Quercetin and hyperoside	*In vivo*	Reduced the number of crystal deposits Increased superoxide dismutase and catalase levels	[13]
Rutin	*In vivo*	Decreased calcium and oxalate in the urine Less tissue damage and fewer number of calcium oxalate deposits in kidney of animal	[14]
Diosmin	*In vivo*	The average volume of calcium oxalate in the nephrolithiasis+diosmin rats was -63% lower than in the rats with untreated nephrolithiasis..	[15]
Apigenin	*In vivo*	Reduced calcium levels in kidneys Enhanced renal function	[16]

Table 1.
Anti-nephrolithiatic activity of flavonoids.

3.3 Furanocoumarin

The impact of two furanochromes (khellin and visnagin) on ethylene-glycol-induced hyperoxaluria in rats was only discussed in one study elaborated by Vanachayangkul et al. [19]. In this work, khellin and visnagin effectively reduced the incidence of calcium oxalate (CaOx) crystal deposition in rats with nephrolithiasis at doses of 5 and 10 mg/kg/day. The authors of this study hypothesized that khellin and visnagin interfere with calcium blocking activity rather than citrate reabsorption, despite the fact that these two substances did not influence urine parameters (pH, citrate, calcium, and oxalate) in this investigation [19].

3.4 Phenolic acids

The potent pharmacological effects of phenolic acids include antioxidant, antibacterial, anticancer, antiviral, anti-inflammatory, antimutagenic, antirheumatic, antipyretic, antiseptic, anthelmintic, neuroprotective, and hepatoprotective properties [20].

Many phenolic acids such as ferulic acid, gallic acid, caffiec, and rosmarinic acid have been investigated for their probable ability to inhibit the formation of kidney stones. **Table 2** summarizes the main findings regarding the anti-nephrolithiatic activity of phenolic acids [21–24].

3.5 Tannins

Green tea contains a polyphenolic hydrolyzable tannin called gallotannin. At non-toxic concentrations, gallotannin dramatically reduced the development of CaOx monohydrate crystals and their attachment to MDCK I kidney epithelial cells. Additionally, gallotannin decreased the amount of reactive oxygen species (ROS) and malondialdehyde (MDA) produced by human primary renal epithelial cells and increased the activity of the antioxidant enzyme superoxide dismutase (SOD) in response to oxalate [25]. Catechin has proven successful in inhibiting renal papillary calcification and the growth of CaOx monohydrate papillary calculi, which may be related to its stimulation of SOD activity [26].

3.6 Saponins

The saponin-rich fraction made from the fruits of S. xanthocarpum prevented the nucleation and aggregation of calcium oxalate crystals in artificial urine solution in

Compounds	Study type	Results	References
Ferulic acid	*In vivo*	Inhibition of renal stone formation and oxidative stress. Increased lipid peroxidation	[21]
Caffeic acid	*In vivo*	Regulation of the changed biochemical parameters Reduction of calcium oxalate deposits.	[22]
Gallic acid	*In vivo*	Inhibition approximately 44-57% of the total calcium oxalate crystals formation,	[23]
Rosmarinic acid	*In vivo*	Decreased tubular dilatation, Bowman's capsule enlargement, degradation of the tubular epithelium, and localized glomerular necrosis.	[24]

Table 2.
Anti-nephrolithiatic activity of phenolic acids.

vitro, and it inhibited the pathological changes brought on by lithogenic treatment, such as polyuria, damage to renal function, oxidative stress, and crystalluria in rats with urolithiasis caused by EG [27].

3.7 Alkaloids

Evidence indicates that alkaloids can enhance urine production and Na^+ and K^+ excretion in a manner similar to that of a typical diuretic (hydrochlorothiazide). Additionally, it has been demonstrated that berberine therapy lowers the Ca^{2+} level of urine. Due to the excess calcium being the main requirement for crystal precipitation and one of the key risk factors for stone production, this has a lot of significance to urinary supersaturation [28].

4. The mechanistic insight of polyphenols in oxalate nephrolithiasis

4.1 Antioxidant

Due to the presence of flavonoids and vitamins, some plant extracts suggested to prevent nephrolithiasis, such as the FHE employed in this study, have a strong antioxidant potential. By preventing lipid peroxidation and papillary tip epithelium damage caused by hyperoxaluria, these substances may prevent the formation of calcium oxalate crystals in the kidney. This in turn may prevent heterogeneous calcium oxalate crystal nucleation on damaged cells or cellular debris, which leads to the development of kidney stones [24].

4.2 Diuretic

It has been frequently observed that polyphenols have diuretic properties. Traditional diuretics include extracts from the fruits of *Opuntia ficus indica*, *C. sinensis*, and *Hibiscus sabdariffa*. By flushing out the salt deposits, the diuretic action increases the amount of fluid going through the kidneys. Therefore, an increase in urine volume reduces salt saturation and prevents the crystals from precipitating at physiological pH [29].

4.3 Conclusions and perceptions

This chapter reveals the results obtained from the available literature about the bioactive components of medicinal plants such as flavonoids, terpenoids, tannins, saponins, etc. The majority of this research was exploratory, conducted on animals, and is insufficient for the creation of medicinal products. To evaluate the effectiveness and toxicity of these plants, extensive preclinical and clinical investigations are still needed. Future research on clinical applications may therefore be a profitable way to confirm the clinical utility of these medications.

Conflict of interest

"The authors declare no conflict of interest."

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