Chapter

Impact of Vitamins and Minerals Enriched Flora in the Management of Calciphytoliths: A Special Focus on Vitamin E

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Abstract

Calciphytoliths (calcium oxalate calculi) have a great influence on human health and are a disease with a high likelihood of recurrence at a rate of more than 10% within a year. Plant flavonoids, saponins, and tannins are reported to be Litholytic by inhibiting calcium oxalate crystals or by their calcium channel blocking activity. Vitamins and minerals containing flora completely prevent deposition of oxalate by preventing pre-oxidation injury and restoring renal tissue antioxidants. So vitamin therapy also might protect against oxalate calculi deposition in the human kidneys. The present chapter discusses the impact of vitamins especially vitamin E, calcium, and low oxalate-containing plants for the management of various urinary or kidney disorders.

Keywords: calciphytoliths, prevention, vitamin E, vitamin C, calcium supplement, medicinal plants

1. Introduction

1.1 Urinary stones - kidney stones

1.1.1 Definition

Urinary stones are solid masses composed of a collection of small crystals which are formed and present in the urinary tract, due to the agglomeration of some components in the urine under certain physicochemical conditions. The urinary stone disease has a great influence on human health and is a disease with a high likelihood of recurrence (or recurrent at a rate of more than 10% within a year).

Most urinary stones are formed in kidneys (80%), then migrate in the urine stream to other places of the urinary tract. When a stone appears at any part of the urinary system, it means a urinary stone disease. Thus, urinary stones include kidney stones, ureteral stones, bladder stones, and urethral stones.

According to research, among cases of urinary stones on average, kidney stones (**Figure 1**) account for the highest proportion (40%), ureteral stones account for 28%, bladder stones account for 26% and urethral stones account for 4% (**Figure 2**).

1.1.2 Epidemiological characteristics

Urinary stone is a common disease in the world. The Urolithiasis prevalence in countries varies from 2–12% of the population, particularly with higher data as in the study of Albuquerque (Brazil), the rate of urinary stones is up to 14% and in 2014, nearly 4–15% of the population has urinary stone problems globally.

The incidence of urinary stones is related to age, gender, race, geographical environment, and eating habits [1].

Regarding gender, epidemiological studies showed that kidney stones are less common in women (6%) than in men (12%). The sex ratio ranges from 5: 1 in Japan to 15: 1 in Iran, but the likelihood of developing kidney stones is increasing in both

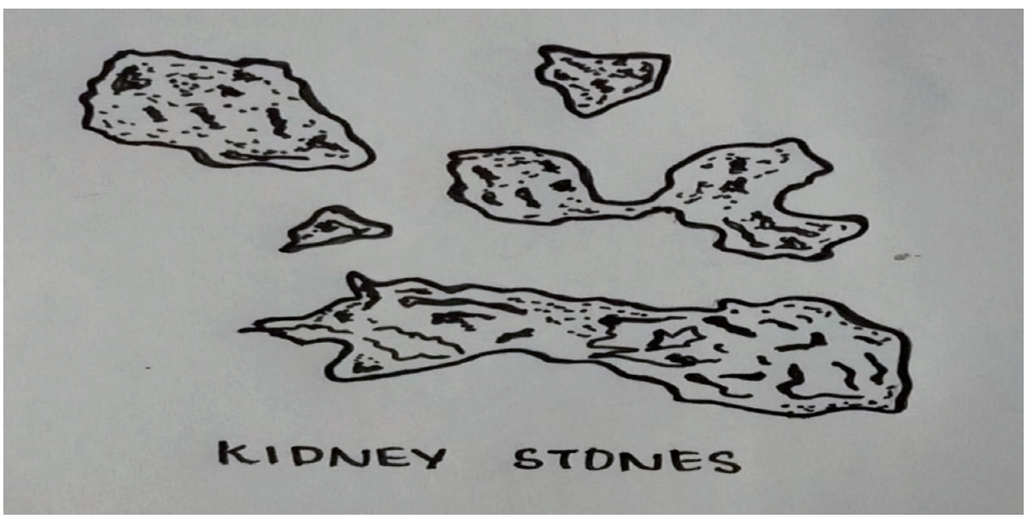

Figure 1.
Kidney stones.

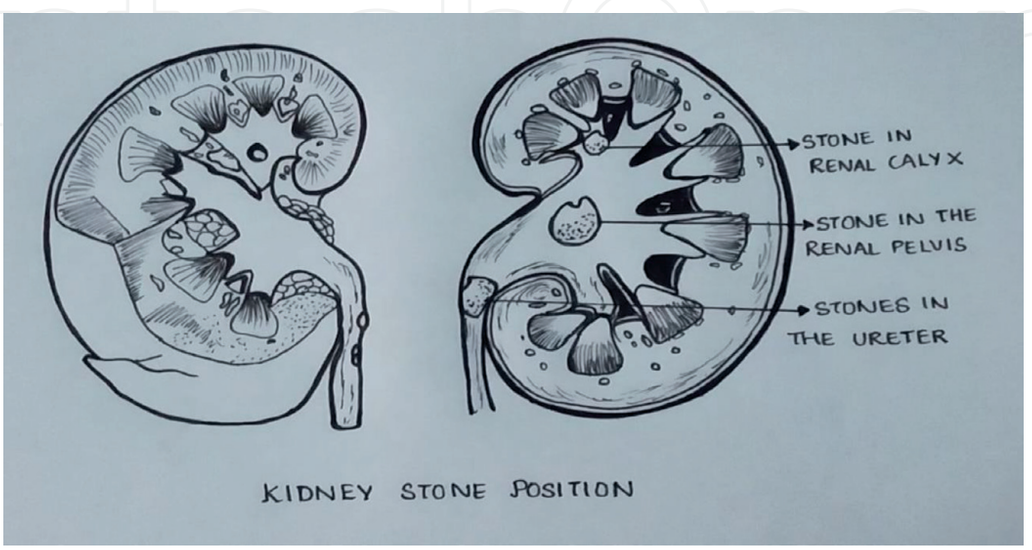

Figure 2.
Kidney stone position.

genders [2]. The risk of kidney stones increases in men in their 40s and continues to increase until the age of 60s. Several studies show that white-skin people and men are at higher risk of urinary stones than other ethnic groups.

The incidence of Urolithiasis is usually low among black-skin Americans but higher in Asian countries, typically in Thailand and India [3]. The regions with the highest percentage of kidney stones are called the "Stone Belt" in Humberger and Higgins maps. Vietnam is a country located in the "Stone Belt" of the world with a high incidence (40–60% of the total number of patients treated in the Urology department and has its special characteristics of stone disease including coming late to the hospital when the stones have enlarged; there are many serious complications such as urinary tract infections or kidney failure.

In India, about 12% of the population has Urolithiasis, of which 50% may suffer kidney loss or kidney damage. The incidence of Urolithiasis is prevalent in the North of India (nearly 15% of the population), while this disease is less commonly found in the South [4].

People who live in rocky areas, where the climate is hot and dry, are more likely to get urinary stones [5]. The incidence of urinary stones has been increasing globally. Dietary changes, as well as the effects of global warming, can be the major drivers of this trend [6].

1.1.3 Classification of urinary stones

Based on the composition of stones, kidney stones are classified into 2 groups with 6 common types including inorganic stones (Calcium, Oxalate, Phosphate) and organic stones (Cystine, Struvite, and Uric acid). Each type has different causes as well as different methods of treatment. Stones often exist as a mixture of chemical components.

A collaborative study in France involving 51,747 stones, in mid-January 2001 and December 2004 by many laboratories showed that Calcium oxalate (CaOx) is the most common ingredient accounting for 71.8% of stones. Calcium phosphate accounts for 13.6% and Uric acid accounts for 10.8% of the total stones.

Among the types of kidney stones, CaOx is the most common type. Calcium oxalate stones have two types including calcium oxalate monohydrate (whewellite) and calcium oxalate dehydrates (weddellite). The incidence of whewellite is 78% while that of weddellite is 43% [7]. Whewellite is highly capable of agglomerating, tightly binds to renal tubular epithelial cells, and retained forming stones. Whewellite accounts for 39% in men and 37.4% in women. Weddellite does not agglomerate into stable masses, does not attach to renal tubular epithelial cells and is easily swept with urine, and difficult to form urinary stones.

In Vietnam, all stone samples analyzed have two or more components, of which the most common component is calcium oxalate (90.7% of incidence), followed by calcium phosphate, struvite, ammonium urate, and cysteine.

In India, calcium oxalate stones are found to be the most important component of Urolithiasis. Calcium oxalate stones make up 80% of the analyzed stones. Calcium phosphate stones account for 15–25%, while 10–15% is mixed stones. The others are struvite with 15–30%, cystine with 6–10%, and uric acid stones with 2–10%.

It was observed that urinary stones in England, Scotland, and Sudan are mainly composed of a mixture of calcium oxalate and calcium phosphate. Meanwhile, uric acid stones in the upper urinary tract are quite common in Israel. In Saudi Arabia, calcium stones make up the majority (84.6%), uric acid stones account for 12.8% [8].

1.1.4 Causes and mechanism of formation of kidney stones

1.1.4.1 Causes

The generation and formation of urinary stones come from different sources that are not only caused by any group of reasons but due to a combination of factors including diet, diseases in the body, and genetic factors which together form urinary stones. Factors leading to the risk of kidney stones include

1. **Not drinking enough water** (<1,200 ml/day) makes the urine more concentrated with minerals such as calcium and phosphorus leading to the risk of kidney stones.

2. **Eating more animal protein in the diet**

High animal protein in food causes acidosis of urine, creating conditions for crystals as uric acid to crystallize to stones. Eating a lot of sodium (salty foods) causes an increase in the renal tubular sodium and this will reduce the reabsorption of calcium there. Also, studies by scientists from Ahvaz University of Medical Sciences, Iran showed that there is an intimate relationship between the consumption of purines, calcium oxalate foods, and the formation of stones [9].

3. **Genetics**

Families with a regular incidence of developing stones (an abnormal amount of calcium filtered into the urinary tract) are at higher risk of kidney stones than other families.

4. Chronic enterocolitis leads to kidney stone formation during pregnancy.

5. The increase in parathyroid activity is another reason. Hyperparathyroidism can be either a primary or secondary method, increasing calcium reabsorption from bone and leading to hypercalciuria.

6. **Improper calcium supplementation**

Pregnant women often need a supplement with a lot of vitamins and minerals, including calcium. However, calcium excess causes kidney stones. Moreover, calcium content is usually absorbed better during pregnancy. Therefore, both of these factors increase the risks. Pregnant women with urinary tract infections should discuss with their doctor for appropriate examination and treatment.

7. **Occupation**

Urinary stones are closely related to the profession of the patients. People who work in a hot environment like metallurgists, construction workers, sailors, stressed-minded workers like doctors, officers, etc. are more likely to be in the disease than those who are unskilled laborers.

8. Another reason causing kidney stones is long-term treatment with certain medication. It is believed that 1–2% of kidney stones are drug-induced. Certain medications including the antiviral drug Indinavir, Triamterene (diuretic), Sulfadiazine (an antibiotic) as well as Ephedrine and Guaifenesin are known as a cause of kidney stones [10].

Also, different reasons for stone formation purely depend on stone type such as

1. **Calcium stones**

The main reason is due to the state of oversaturated urine with calcium salts causing by the increase of calcium absorption in the intestine or the increase of calcium reabsorption in the renal tubular region. Causes that increase the concentration of calcium in the urine are hyperparathyroidism, major bone fractures, and immobilization for a long time, taking lots of Vitamin D and Corticoid, metastases of cancer through the bone, causing bone destruction. However in many cases not able to find the reason for calcium increase in urine. High level is not a determinant of urinary stone formation but a favorable factor.

2. **Oxalate stone**

This type of stone account for a high proportion in tropical countries like Vietnam and India. Oxalate is often combined with calcium to form calcium oxalate stones and 2/3 of stones in oxalate stone are due to the insoluble calcium oxalate salt. When the urine is saturated with oxalate, by eating foods and vegetables which are high in oxalate and poor in calcium, these molecules will pass through the digestive tract and be excreted as waste. When passing through the intestine, oxalate can combine with calcium to form calcium oxalate and be excreted in the waste. Having too much oxalate in the kidneys can lead to kidney stones. According to Prien, lack of vitamin B6 in the body is a cause of oxalate stones. Experiments in rats showed that vitamin B6-deficient foods produce in the renal tubule and thorn the Randall-like lesions in kidneys and oxalates are crystallized. In contrast, vitamin B6 will reduce the excretion of oxalate in urine.

3. **Phosphate stones**

A common type of phosphate stone is ammonium-magnate-phosphate (struvite stone), accounting for 5–15% of the number of stones. This type of stone has a large size, coral shape, and is in contrast.

Stones are formed as a result of a bacterial infection, especially proteus bacteria in the urinary system. This bacterium releases the urease enzyme, which breaks down urea into ammonia, making urine alkaline, resulting in a reduction in struvite solubility which facilitates stone formation.

4. **Uric acid stones**

With the increase of uric acid concentration in blood, in addition to deposition in cartilage, mucous membranes, muscle skin, the concentration of uric acid in the kidneys also increase. Uric acid deposition in kidneys is a major cause of uric acid stones, which is more common in gout patients (the result of nucleic acid metabolism disorders). Possible causes of purine metabolism increase include the intake of purine-rich foods such as pig intestine, dried fish, meat, and mushrooms. It is noted that uric acid is soluble in an alkaline environment and crystallizes in an acidic environment when urine pH is below 6. Accordingly, acidified urine is a good environment for forming stones.

5. **Cystine stones**

Stones are formed when cystine is excreted to the kidneys but less soluble making it easily be deposited. The stone is often congenital with the disorders of cystine reuptake transport and some other amino acids such as lysine and arginine in the

renal tubules and intestinal mucosa. Cystine stones are usually simple and rarely combine with other stones [11].

1.1.4.2 Mechanism and development of stones

The formation of stones in the body is a complex process, which is a result of a series of physicochemical processes including five main stages: (i) oversaturation of substances dissolved in urine (ii) nuclear formation (iii) nuclear proliferation (iv) crystallization and (v) crystals attachment to epithelial cells of renal tubules [12].

Oversaturation of substances that are capable to crystallize in urine is a phenomenon of concentration of a substance being able to crystallize in urine exceeds its solubility. There are many causes of urine oversaturation, including a change in urine pH, decrease in urine volume or metabolic disorder that increases the elimination of one or several substances through kidneys, imbalances in urine calcium excretion, hypercalciuria which is familiar or idiopathic, imbalance in oxalate excretion, reduction in urinary citrate and hyperuricemia due to purine-rich foods. It not only depends on the concentration of the stone formation substances but also depends on other factors such as urine pH, the ions representing inhibitors of the stone formation process such as citrate, pyrophosphate, magnesium, ribonucleic acid, and glycosaminoglycan.

1.1.4.2.1 Crystal nucleus formation

In oversaturated urine, free ions tend to coalesce into very small particles. The result of this process is the formation of a crystal nucleus which may be single-component or multi-component. In urine, a crystal nucleus can be formed on the structure of cellular debris and urinary crystals. The majority of urinary stones is a mixture of more than two substances. When there is a saturation of calcium or oxalate by urine when passing through the renal tubules, it will form a nucleus making COD form (which is common in the urine of healthy people) and COM form (mostly common in urinary stones).

1.1.4.2.2 Nuclear proliferation

It is the process of a nucleus which is made up of very small size continues to grow during the movement in the urinary tract, through the transferring of free ions in the solution into the crystals. This process does not cause any problems if the crystals are easily removed (as stones that are less than 5 mm in diameter). Larger stones are difficult to be excreted causing the blockage, pain, injury, and bleeding during urinary tract movement. However, this process takes a long time. Therefore in the process of moving through the nephron (5–7 minutes), the growth of crystals will not reach a large size which is enough to obstruct the renal tubules. The growth of the crystal is then explained by the aggregation of small crystals or the creation of secondary nuclei on the initial crystal surface.

1.1.4.2.3 Crystal aggregation

It is the process of linking small crystals together by chemical or electrostatic forces to form large crystals. For oxalate stones, the formation of urinary stones from COD crystals is difficult because COD crystals do not coalesce into stable masses, do not attach to the tubular epithelial cells and so they have easily swept away with urine. COM crystals are highly agglomerated and can bind tightly to tubular epithelial cells and be trapped facilitating the formation of stones.

1.1.4.2.4 Crystal attachment to kidney cells

The mechanism of this process is still unclear and explained by many different theories. The first theory is that stone crystals are formed in the kidney's lumen, where they aggregate, grow to a size large enough to block the renal tubules, and be trapped there. The second theory also states that stone crystals are formed in the renal tubules but suggests that crystals are formed by the development of apatite plaques and attached to a certain location at the surface of the tubular epithelial cells and structures present in the renal papillae also known as Randall's plaque. Various studies have confirmed the role of microscopic lesions in kidneys in the formation of kidney stones. These lesions were detected in causing urinary stones by a model that causes an increase of urinary oxalate.

1.1.5 Harmful effects

After forming, if the stone is small, it usually passes through the urine and is expelled. But if the stone is trapped somewhere in the urinary tract, it will grow larger obstructing the flow of urine, leading to stagnation and swelling above the blockage and causing many symptoms such as obstruction, infection, additional stones, and gradual destruction of kidney structure.

If urolithiasis is not monitored and treated promptly, it can lead to many serious complications such as urinary tract infections, kidney failure even death.

1.1.5.1 Common and dangerous complications

1.1.5.1.1 Obstruction is a severe acute complication

If ureters are completely obstructed, the renal pelvis dilates, and after 6 weeks the renal parenchyma may not recover. The consequence of water retention is structural damage leading to functional damage.

1.1.5.1.2 Acute renal failure

It may be occurred due to a severe obstruction (completely or near completely) on both sides of the ureters. Kidney failure occurs in the case of ureteral stones on one side but creating vasoconstriction on both sides causing anuria. Clinical manifestations are anuria, urea test, creatinine, a rapid increase of potassium (K+) in blood, and metabolic acidosis.

1.1.5.1.3 Chronic renal failure

Chronic pyelonephritis is the most severe consequence of kidney and urinary stones because it is no longer able to recover due to gradual renal fibrosis.

1.1.6 Symptoms

Symptoms of kidney stones can range from asymptomatic to the frequency of mild and uncomfortable urination, then severe colic in the abdomen, hips, and lower back. When a stone passes through the ureter, it can cause hematuria, severe pain, nausea, vomiting, diarrhea, sweating, and a fast heartbeat. In severe cases, kidney stones can obstruct the urinary tract, scar, kidney infections, and kidney damage.

It was identified that pain in the lumbar region is the main symptom of ureteral stones; renal colic occurs when stones move and cause edematous inflammation and acute ureteral obstruction.

1.1.7 Treatments

The choice of treatment method depends on many factors such as the size of stones, the severity of symptoms, the degree of obstruction, kidney function, the location of stones, and whether or not the infection is present.

2. Applications of medicinal plants in the management of kidney stones

2.1 Some effects of natural medicines in the treatment of kidney stones

The use of drugs which are from herbal plants in the treatment of kidney stones is increasingly common but its majority comes from folk remedies. In recent years, there have been many studies of scientists on the treatment effects of medicinal plants for kidney stones.

Proven studies have shown the action mechanism of herbal extracts on the treatment and the relapse prevention of kidney stones, including

1. Help to erode and reduce stone size naturally.

2. An alkaline urine and inhibit the process of crystallization of stones on the urinary tract.

3. Inhibit stone formation by preventing calcium oxalate nucleation and the growth of calcium oxalate crystals, inhibiting synthesis and accumulation of the crystals.

4. Reduce the deposition of crystals on tissue and in the lumen of kidneys.

5. Enhance the concentration of inhibitors of stone formation in the kidneys to increase urine citrate excretion, reduce calcium and oxalate excretion in urine.

6. Reduce the concentration of calcium in kidney tissue and improve the state of saturation.

7. Support diuretic, analgesic, and anti-inflammatory activities.

8. Balance electrolytes and minerals and regulate oxalate metabolism helping to reduce the recurrence of kidney stones.

The antioxidant activity of medicinal plants also helps to prevent urinary cell damage. Some promising plants containing vitamin E, vitamin C, and calcium showing their antioxidant and anti-urolithic activity demonstrated through *in vivo* and *in vitro* studies are discussed below.

2.1.1 Flax

Flax (*Linum usitatissimum* L) in the genus Linum, which belongs to the Linaceae family, is an annual herb with green flowers, produces different small flat seeds

ranging from yellow to reddish-brown color. The plant is 40–70 cm tall, smooth, with only branches in the upper part. Leaves are staggered, spear-shaped, 1–3 cm long, and 0.3 cm wide with three ribs. Flowers often grow individually with 5 blue petals; petals are three times longer than sepals. The capsule has smooth walls, divided into 10 cells containing one grain in each. The grain is oval, long, pointed, glossy, and brown.

Since ancient times, flax has been grown for fiber or seeds using for medicinal purposes and as nutritional products [13]. Currently, flax is grown in more than 50 countries, mainly in the Northern Hemisphere. Canada is the world's largest producer and exporter of flaxseeds [14]. Important developing countries for flaxseed include India, China, United States, and Ethiopia [15, 16]. India ranks first among the top flaxseed producing countries in terms of area, accounting for 23.8% of total production and third in production, contributing to 10.2% of world production [16]. In India, flaxseeds are mainly grown in Madhya Pradesh, Maharashtra, Chattisgarh, and Bihar. The bark of the plant has good fiber quality and high durability, so it is used to weave cloth.

Flaxseeds, also known as Linseed, have a crunchy texture and chestnut flavor [17, 18]. Seeds with oil after refining are used for edible purposes [16]. People have been consuming flaxseeds since ancient times. In India, flaxseeds are still being consumed as food and also for medicinal purposes [19]. It has an important position among oilseeds because of its versatility. It is considered an attractive nutritional food because of its exceptionally high content of alpha-linolenic acid (ALA), high-quality fiber and protein, lignans, vitamin E, phenolic compounds, and phytoestrogen.

2.1.1.1 Chemical composition

Flaxseeds contain about 55% of alpha-linolenic acid (ALA), 30% of protein and 35% of fiber [18, 20, 21]. Flaxseed oil has alpha-linolenic fatty acid, which is an essential acid (ALA). From these facts, the body will convert to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Flaxseeds are increasingly considered by nutritionists and medical researchers due to their potential health benefits associated with bioactive components, lignan-secoisolariciresinol glycoside (SDG), and dietary fiber [22]. The composition of flaxseeds is presented in **Figure 3** [17, 23, 24]. Flaxseed oil has alpha-linolenic fatty acid, which is an essential acid (ALA). From these facts, the body will convert to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

The chemical composition of flaxseed depends on its growing environment, genetics, and processing conditions [17]. The lipid content of flaxseeds varies from 37 to 45 g/100 g of seeds as reported by various scientists [17, 20, 24]. Cotyledons are the main oil storage tissues containing 75% of seed oil [16, 18, 25].

Flaxseed oil makes up 98% of triacylglycerol, phospholipids, and 0.1% of free fatty acids [26]. On average it contains 21% protein. The majority of protein is concentrated in cotyledons [21]. The main protein segments are globulin (26–58%) and albumin (20–42%). The nutritional value and amino acid content of flaxseeds are equivalent to that of soy-bean protein [27, 28].

Flaxseed protein is rich in arginine, aspartic acid, and glutamic acid, while lysine is restricted [16, 25, 29]. A high content of cysteine and methionine improves antioxidant content, thereby reducing the risk of cancer [14]. Treatment, de-heat, and defatting conditions affect protein content. Defatted and de-heat meals are high in protein [15, 30]. Flaxseed protein exhibits antifungal properties against *Alternaria solani, Candida albicans,* and *Aspergillus flavus* [31, 32].

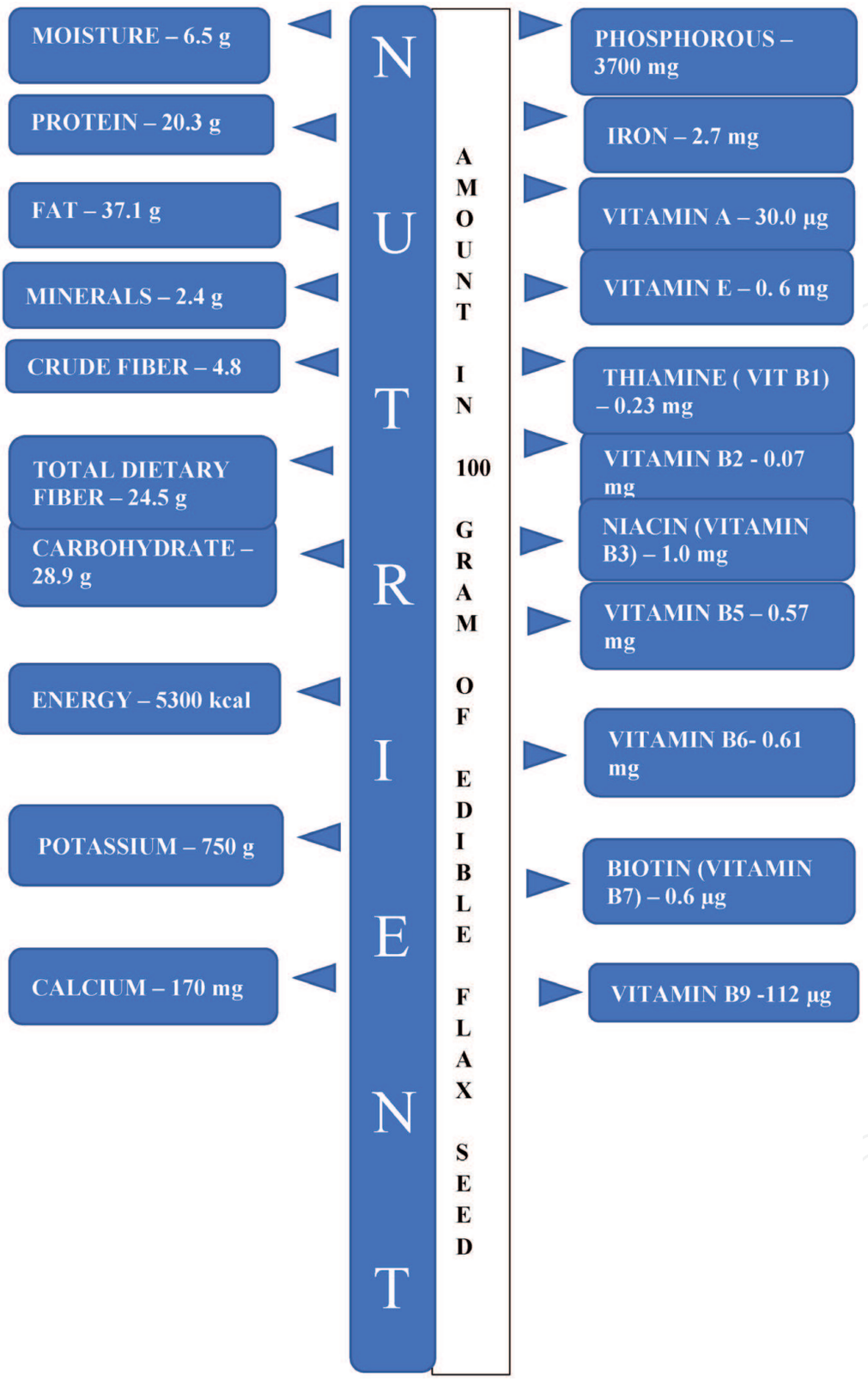

Figure 3.
Nutrient composition of flaxseed.

2.1.1.2 Pharmacological effects and uses

Scientists are interested in flaxseed for its health benefits due to its high content of α-linolenic acid and lignans. Natural treatment agents which have the effects on lipid-lowering, antioxidant, anti-inflammatory, and antihypertensive are expected to have a protective effect on the kidneys.

For kidney stones, flaxseeds may help reduce the amount of calcium in the urine. Daily intake of organic, unrefined, and cold-pressed flaxseed oil has been shown to have good results for patients with kidney stones.

William F. Clark, Anwar Parbtani (1995) studied the impact of flaxseed on immune and renal damage models. ALA in flax constituents has been shown to have anti-inflammatory and anti-thrombotic properties, while flaxseed lignans have been reported as platelet-activating factor receptor antagonists (PAF). PAF contributes to the inflammatory response in progressive glomerulonephritis. The authors conclude that results from animal and human studies indicated that flaxseeds provide significant benefits in kidney function as well as important atherogenic and inflammatory mechanisms in the pathogenesis of lupus nephritis. Thereby, the authors recommend long-term studies with flaxseeds as a potential treatment for lupus nephritis and other forms of progressive kidney diseases [33].

According to research by the University of Manitoba and the Manitoba Children's Health Institute, Winnipeg, Man., Canada (2007), late intervention with soy protein and flaxseed oil in the diet has reduced the number of diseases related to multipurpose kidney diseases which were present in the rat. The potential benefits of antioxidant and anti-inflammatory effects on kidney disease results are continuing to be studied [34].

According to the report on "medical and dietary therapies for the prevention of kidney stones" by Zeyneplrul and Manoj Monga (2014), the main source of polyunsaturated fats in the Western diet is arachidonic acid (AA) an n-6 fatty acid found in vegetable oils and animal fats. N-6 fatty acids are involved in stone formation. The breakdown of AA leads to the formation of precursors including prostaglandin E2 (PGE2) [35].

PGE2 causes hypercalciuria because it increases intestinal calcium absorption, reduces renal tubular reabsorption, and increases bone resorption. Eicosapentaenoic acid (EPA) is an n-3 fatty acid and is a component of fish oil, as well as is found in flaxseeds. EPA undergoes the metabolism similar to n-6 fatty acids. Therefore, increasing EPA and reducing n-6 fatty acid metabolites, especially PGE2. Lower PGE2 concentration not only reduces calcium excretion through urine but also leads to the activation of nephron Na/K/2Ca transporters, leading to the increase of renal calcium reabsorption. The clinical experiment showed that consuming 1,200 mg/day of flax oil is associated with a significant decrease of calcium and oxalate concentration and an increase of citrate concentration in urine.

Research Institute for Pharmaceutical Education, Narsapur, Medak, Telangana, India (2015) conducted a study to assess *in vitro* anti-inflammatory activity of flax. Ethanolic extract showed its maximum effectiveness in dissolving calcium oxalate crystals, thereby clearly showing that ethanolic extract of flaxseed was quite promising for further research on the treatment of kidney stones [36].

Several clinical studies have realized the great potential of n-3 polyunsaturated fatty acids (eicosapentaenoic acid - EPA) found in flaxseeds, which not only work against inflammatory mediators (such as prostate E2, leukotriene B4, TNF-α, interleukin, and cytokine) but are also very helpful in reducing the risk of calcium stone formation for kidney stones. According to a study by the authors of the Department of Urology, Nagoya City University of Medicine, Japan, to determine the effect of EPA on Urolithiasis, the authors conducted a clinical study in which a high-purity EPA product is provided (at a dose of 1,800 mg/day) for 88 patients with urinary stones for 3 months (short term) and 18 months (long term). The results suggest that EPA has reduced the amount of calcium in the urine which well affects the urine composition in a way that can reduce the risk of calcium stone formation.

The Japanese authors when doing clinical research "Preventive effects for the recurrence of kidney stones", implemented high-purity EPA preparation at

1,800 mg EPA/day for 29 patients in 36.4 ± 22.0 months after treatment of kidney stones. By observing the recurrence of Urolithiasis in these patients during 8 years (before, during, and after taking the drug) and studying the preventive effects for the recurrence of kidney stones, the study results showed that prevalence of nephrolithiasis (times/year) before, during and after taking EPA are respectively 0.22283, 0.0693 and 0.11742. The incidence of Nephrolithiasis while taking EPA was significantly lower than the findings before and after using ($p < 0.05$). Thus, the results suggest that EPA may reduce the risk of calcium stone formation.

2.1.2 Plantago major

Plantago major is also known as broadleaf plantain, white man's foot, or greater plantain, which belongs to the Plantaginaceae family. It is a kind of plant that is used both as food and as a medicinal plant. *Plantago major* is native to most of Europe and northern and central Asia. It is one of the most abundant and widely distributed medicinal crops in the world.

Plantago major is a herbaceous perennial plant with a rosette of leaves. Each leaf is oval-shaped. The leaf blade is 12 cm long and 8 cm broad. There are five to seven parallel veins that diverge in the wider part of the leaf. The inflorescences are borne on stalks. Flowers are always bisexual. They are small, greenish-brown with purple stamens, produced in a dense spike 5–15 cm long on top of a stem, 13–15 cm tall, and rarely to 70 cm tall. *Plantago major* propagates primarily by seeds, which are held on the long, narrow spikes which rise well above the foliage. *Plantago major* fruits are canned fruits, containing many glossy dark brown seeds. Each fruit has 8–13 seeds. The outer shell of the seed becomes mucous in water. Each plant part of *Plantago major* has been used in many traditional medicines for the treatment of cough, diarrhea, dysentery, urinary stones. The seeds of *Plantago major* have long been used in the treatment of urinary retention and urination.

2.1.2.1 Chemical composition

Plantago major leaves contain iridoid, aucubosid, catalpol), phenolic acid, and phenylpropanoid esters of glycosides, majorosides. Leaves also contain mucus with a content of 20%. *Plantago* contains mucus which is rich in D-galactose, L-arabinose, and has about 40% uronic acid, fatty oils including 9-hydroxy-cis-11-octadecenoic acid. Besides, *Plantago major* is also rich in flavonoids including apigenin, quercetin, scutellarin, baicalein, hispidulin (5,7,4′-trihydroxy-6-methoxy-flavon), luteolin –7-glucoside, luteolin-7-glucuronide, homoplantaginin (= 7- O-D-glucopyranosyl-5,6,3', 4'-trihydroxyflavon). Besides, *Plantago major* contains many other substances such as coumaric acid, ferulic acid, caffeic acid, chlorogenic acid, carotene, vitamin K and vitamin C.

2.1.2.2 Pharmacological effects and uses

In the document of medicinal plants, Prof. Dr. Do Tat Loi also mentioned the effect of increased excretion of urea, uric acid, and salt (the components that make up urinary stones in urine) of *Plantago major* seeds. This activity was confirmed again by research done at Vietnam - Sweden hospital. The scientists found that the extract of *Plantago major* seed contains the active ingredient aucubin - 1 iridoid glycoside that works to increase the amount of urine, thereby stimulating more urine excretion, helping to enhance bacterial excretion and stones out of the urinary tract for people who have a urinary tract infection or have urinary stones.

In Japanese traditional medicine, the decoction of *Plantago major* helps to treat cough, urinary tract infection, and inflammation. In Thailand, whole plants or leaves are used for the effects of diuretic, antipyretic, laxative, anti-inflammatory, and flatulence. In Korea, *Plantago major* is used to treating liver diseases. In Haiti, *Plantago major* is used to treating nerve stutter and eye pain.

Scientists at Malaysia Kebangsaan University (2003) also found that ethanol extract of whole *Plantago major* plant significantly reduces the size of calcium oxalate crystals better than allopurinol and potassium citrate drugs, at the same time inhibits newly formed stones. Malaysian scientists (2012) conducted a study to determine the inhibitory effect of *Plantago major*'s terpenoid extract on *in vitro* crystalline calcium oxalate and compared the effects of *Plantago major* with drugs which are clinically used as zyloric and potassium. The results showed that terpenoid extract of *Plantago major* inhibited the size of calcium oxalate crystals much better than zyloric and potassium citrate in the treatment of urinary stones.

According to research by Istanbul University and Kafkas University (Turkey), *Plantago major* seed extract works against most bacteria such as *Bacillus cereus*, *Staphylococcus aureus,* and especially *Escherichia coli* (E.coli)-the main agent of most urinary infections.

Research by scientists from Mashhad University of Medical Sciences, Mashhad, Iran showed that *Plantago major* extract can improve kidney function as well as oxidative stress in cisplatin-induced kidney toxicity in rats.

In the study of *Plantago major* activity for urinary tract-related infectious diseases, scientists from Kaohsiung Medical Institute, Taiwan found that *Plantago major* extract is in high concentration (> 50 micrograms/ml) can inhibit inflammatory mediators such as leukotrienes, nitric oxide, prostaglandins, etc.

2.1.3 Spinach

Spinach has the scientific name of *Basella alba* L. (*Basella rubra* L.), belongs to the family of Spinach - *Basellaceae*, also known as Malabar spinach, is an ancient tropical species, often grown as a vegetable. This plant is native to South Asian countries, spreads and grows wildly in many tropical Asian countries. It is grown in Asia, Africa, South America, and also in temperate regions of Asia and Europe. Its common distribution is in Africa, the Angels, Brazil, and Asia, Japan, China, Thailand, Laos, Cambodia, and Vietnam. In Vietnam, Malabar spinach grows wildly and is planted everywhere.

Malabar spinach is a herbaceous climbing plant with wrapped, fat and viscous, and reddish stems. Plants live annually or for two years. Leaves are staggered with raw and succulent leaf-blade. Flowers are arranged in flower form and are light purple. Fruits are oval-shaped or egg-shaped. Clump roots grow deep in the soil and are suitable for loose soil. Inflorescence in flower-shape growing in spaces between leaves which are white or pale reddish-purple. Berries of Malabar spinach are small, sphere-shaped, or egg-shaped, about 5–6 mm long. They are green and turn dark purple when being ripe. Malabar spinach grows fast. Its stem can grow up to 10 m long.

2.1.3.1 Varieties of spinach

There are 3 varieties of Malabar spinach. They are

1. White Malabar spinach (also known as Green Malabar spinach)

Leaf-blade is small with a slender stem. Malabar spinach stems and leaves are pale green. The most commonly grown species is white Malabar spinach with a small leaf blade and slender stems. Its stems and leaf are pale green.

2. Purple Malabar spinach

Purple Malabar spinach has small leaves, reddish-purple stems, and veins. This is a wrapped climbing plant. The stem is fat and viscous with a 2–3 year lifespan. Leaves of purple Malabar spinach are thick, heart-shaped, and intertwined. The inflorescence is flower-shaped and white or pale reddish-purple. Berries of purple Malabar spinach are small, sphere-shaped, or egg-shaped, about 5–6 mm long. They are green and turn dark purple when being ripe. According to some Chinese medicine documents, the whole stem of Malabar spinach has a light sweet taste, a cold property which has the effects of heat dissipation, cool blood, diuretic, detoxification, and pain relief. Leaves and young stem buds of Malabar spinach are often used to stir-fry, boil, or cook soup as a cool and laxative food.

3. Large leaf Malabar spinach

Large leaf Malabar spinach is very similar to the green Malabar spinach but has different characteristics, with a larger leaf blade, the leaves are thicker, the color is darker green and the stems are fatter.

Spinach contains high amounts of vitamin A3, vitamin B3, vitamin E, saponin, and iron which are essential for general health and well-being Spinach is a wild-growing variety so it is not picky, easy to grow and take care of and grow fast with an over 10 m length of the stem.

2.1.3.2 Chemical composition

According to the documents of the United States Department of Agriculture (USDA, 2016), 100 g of edible Malabar spinach portion contains 93 g of water; 79 kJ (19 kcal) of energy; 1.4% glucid; 2.5% fiber; 0.9% ash; 1.8 g of protein; 0.3 g of fat; 109 mg Ca; 52 mg of P; 1.2 mg of Fe; 8000 IU of vitamin A; 0.05 mg of thiamin, 0.16 mg of riboflavin; 0.50 mg of niacin; 140 mg of folate; 102 mg of ascorbic acid. Besides, spinach leaves also contain aminoglycosides, several oleanane triterpenes, including *basella* saponins, betavulgaroside I, spinacoside C, and momordins. The spinach seeds contain 2 antifungal peptides and ribosome-inactivated proteins, with antiviral activity isolated from seeds.

Spinach contains many bioactive compounds such as carbohydrates, proteins, enzymes, fats and oils, vitamins, alkaloids, quinine, terpenoids, flavonoids, carotenoids, sterols, simple phenol glycosides, tannins, saponins, polyphenols, etc. It also contains Vitamin A, Vitamin E, Vitamin K, flavonoids, saponins, and β Carotene [37].

2.1.3.3 Pharmacological effects and uses

The whole plant of Malabar spinach is used to treat dysentery, esoteric defecation, cystitis, and appendicitis. Externally used for bone fractures, injuries (outside of the body), outside hemorrhage, burns. In India, people use leaves in the treatment of gonorrhea and glansitis. Leaf fluid is used to treat urticaria and constipation, especially in children and pregnant women. In Thailand, the leaves are used to treat round spots, flowers used to treat tinea diseases, roots used for laxative effect, and externally used to treat discoloration of the skin of hands, feet, and dandruff; berries used as food dyes. In Vietnam, Malabar spinach is recorded as having cold property, sour taste, heat dissipation, blood cooling, diuretic, urinary retention, dysuria, detoxification, and pain relief.

Many scientific reports indicate that sponges can be used to treat laxatives, inflammation, rubefacient, skin diseases, burns, ulcers, diarrhea, diuretics, and cancer.

Spinach leaves contain several active ingredients including flavonoids with antioxidant and anti-inflammatory properties. Spinach extract has been shown to have numerous effects such as chemotherapy, protection of the central nervous system, anti-cancer, anti-aging functions, and hypoglycemia.

For kidney stones, the Indian Institute of Pharmaceutical Sciences and Research (2020) conducted a study to evaluate the diuretic [38] and anti-diuretic activities of ethanolic extract of Malabar spinach leaves in rats that had been induced to cause kidney stones. The study results showed that ethanolic extract from Malabar spinach leaves has a significant diuretic activity by increasing the total amount of urine and the excretion of sodium, potassium, chloride, and bicarbonate, and also has significant anti-thrombotic activity by reducing high concentrations of oxalate, calcium, and phosphate in the urine and adding calcium, creatinine and uric acid in the serum. The extract of the seed's peel of Malabar spinach has properties that enhance the reducing properties of the calcium oxalate crystals. The results obtained from the studies show the potential benefits of the extract of Malabar spinach in treating and preventing the recurrence of kidney stones.

In Ayurveda, used for hemorrhages, skin diseases, sexual weakness, ulcers, and as a laxative in children. Leaves are applied to the head for half an hour before bathing to help bring about good refreshing sleep. The sap is applied to acne eruptions to reduce inflammation. Decoction of leaves used for a mild laxative effect. Pulped leaves applied to boils and ulcers to hasten suppuration. Leaf juice mixed with butter applied to burns and scalds for a soothing and cooling effect. Leaves and stems have been used as anticancer for melanoma, leukemia, and oral cancer. Roots and leaves are used for stomach pains and increase milk production. Used orally for anal prolapse and hernia. In Nigeria, used for hypertension and also used for fertility enhancement in women. In Nepal, leaf juice is used to treat dysentery, catarrh, and applied externally to boils. In Thai traditional medicine, mucilage is used as an application for bruises, ringworm, and laboring. Stem and leaves are used as a mild laxative, diuretic and antipyretic. In Cameroon, used for malaria. Herbal healers use plant extracts to enhance libido and as a remedy for infertility. In the Antilles, leaves are considered good maturative as a cataplasm. In Thai traditional medicine, mucilage is used as a topical medicine for skin irritation, bruises, ringworm, and laboring.

A study of leaves extract of *Basella alba* showed an admirable dissolving capacity of calcium oxalate crystals in both *in vitro* and *in vivo* studies. Although Malabar spinach has a rich nutrient (1/2 cup of spinach after cooking provides 190% of vitamin A and 20% of iron which the body needs), it should not be abused. Eating too much spinach makes the body absorb less because it contains a high content of oxalic acid. This is a chemical that binds calcium and iron, making it difficult for the body to absorb other important nutrients. Therefore, when eating spinach, it is better to eat with foods that are rich in vitamin C such as oranges, lemons, tomatoes, star fruit, or consuming oxalate removed spinach is much safer and useful for preventing kidney stones. Especially eating spinach cooked with star fruit will be very good for the body. Because of the content of oxalic acid and purine, eating lots of spinach converting to uric acid will increase the concentration of calcium oxalate in urine and accumulate in the body, easily causing gout or kidney stones.

2.1.4 Fenugreek

Fenugreek, also known as *Trigonella foenum-graecum* L., belongs to the family Fabaceae. The plant is about 60–90 cm tall and green. The flowers are small and white. Its seed is small and yellow-brown. Because of its preventive and curative

properties, fenugreek is used as a herb. It is native to the Middle and Near East and is widely used in the Indian subcontinent. There is even evidence that ancient Egyptians understood the benefits of Fenugreek because its seeds were found in tombs, especially Tutankhamen. The plant is grown in countries across the globe as a semi-arid crop, but most are grown and consumed in India.

Fenugreek is used as a medicinal plant (leaves) as well as a spice (seeds). Parts that are used as a medicine of Fenugreek include stems, leaves, and seeds. Fenugreek seeds are yellow or amber and generally used for dipping food, dried and pasty curry powders, commonly found in Indian cuisine. Young leaves and buds of fenugreek are also used as a vegetable, while fresh or dried leaves are used to flavor other dishes.

2.1.4.1 Chemical composition

According to the study documents, fenugreek seeds contain 26.2% of protein, 5.8% of lipids, 3% of minerals including iron, calcium, phosphorus, magnesium, potassium, sodium, zinc, copper, manganese, vitamin C, folic acid, vitamins E, B1, B2, B3, 3% of fiber and 44.2% of powdered sugar. Besides, fenugreek seeds contain saponins, oil substances, flavonoids and mucus, 4-hydroxy isoleucine (amino acids that stimulate insulin secretion), and galactomannan that slow down the absorption of blood glucose.

According to a study in 2014 published in the Journal of Nutrition, fenugreek contains soluble fiber, which can reduce the glucose absorption of cells, helping to low down blood sugar. Besides, it also contains trigonelline a compound that increases insulin sensitivity, and 4-hydroxy isoleucine -an amino acid that helps stimulate insulin release in pancreatic cells, helping to control blood sugar levels automatically.

Fenugreek contains polyphenols and flavonoids that have antioxidant effects, which reduce the amount of cholesterol and triglycerides in the body. The galactomannan forms a layer of mucus in the intestines limiting the absorption of lipids and glucose.

2.1.4.2 Pharmacological effects and uses

Fenugreek seeds are commonly used in Northern Africa to prevent and treat kidney stones. In a study on an animal, it was found that fenugreek seeds significantly reduce kidney calcification and the total calcium content of kidney tissue in rats, helping to prevent kidney stones.

According to a study of King Saud University, Riyadh, Saudi Arabia on the effects of fenugreek seeds and *Ammi majus* [39] on calcium oxalate urinary stones in rats, when treated daily by oral route with fenugreek extract, it significantly reduced the amount of calcium oxalate deposited in the kidneys while the inhibitory effects obtained from *Ammi majus* grass were negligible.

In 2014, the Science University of Salahaddin, Kurdistan - Iraq region conducted a study on the effects of fenugreek in preventing the formation of kidney stones. The study result has proven its potential effects of antioxidants and Urolithiasis prevention, thus making a beneficial effect to prevent the formation of kidney stones and related free-radical complications in kidney tissues.

According to a study result on the effects of some medicinal plants used in the treatment of urinary stones of Abulcocation-Rabat University, Morocco, the extract of fenugreek seed has a good effect on dissolving cystine and carbapatite stones, probably due to the complex formation between stones and polyphenols or flavonoids in the extract [40].

3. Role of vitamins and minerals in the management of calciphytoliths

3.1 Calcium oxalate in plants

Calcium oxalate deposits in numerous plants and animal cells. Neither it excretes in urine nor retained in the form of urinary calculi. Calcium oxalate in plant sources was first described by "Leeuwenhoek" using a Simple microscope. Oxalate ranges in plants from 3 to 80%. Non-accumulating oxalate plants have less oxalic acid in them. In plants, oxalic acid is obtained from glycolate conversion. Oxidation takes place where glycolic acid is oxidase and glyoxylic acid is intermediate. Glyoxylic acid as intermediate is obtained by cleavage of isocitric acid and oxaloacetate separates in attaining oxalate and acetate.

It is present in numerous parts of plants and is considered the strongest acid present in plants. Oxalic acid as a chelating agent reacts with cations and results in the end product being oxalates. Oxalic acid is considered as the end product but in some cases, it converts to oxalate by several conditions as the alternate change in oxalate concentration. Oxalic acid acts as an "ionic balance" in plants and the formation of soluble or insoluble compounds. Oxalate in plants promotes antioxidant property. Content of oxalate more in plants results in attaining uncomfort taste but promotes plant protection from insects and animals and oxalic acid content fruits have high superoxide dismutase activity. This plays a major role in systematic resistance, programmed cell death, redox homeostasis, and anti-senescence effect in harvested fruits.

Calcium oxalate crystals form by oxalic acid interiorly present in plants and calcium obtained from the environment. Calcium oxalate occurs in many plant regions except pollen. The highest oxalic acid concentration commonly occurs in leaves and it is lowest in all other parts. It exerts its effects by binding calcium, magnesium, and other trace minerals like iron making them unavailable for assimilation. The calcium ions bind with free oxalic acid or oxalate and precipitates as insoluble crystals of calcium oxalate which may lead to hypocalcemia and urolithiasis. In the human being, <0.5% soluble oxalate in a diet may be acceptable. Plants accumulate oxalate in high proportion only during the young stage of growth and the content decreases with maturity and drying of the plant. Matured plant organs of the selected plants were discussed here which contain considerable calcium and very low amounts of soluble oxalate and also were used traditionally in treating kidney stones.

Generally oxalic acid is present in many plant families but commonly occurs in Amaranthaceae, Polygonaceae, Chenopodiaceae, Oxiladaceae, Convolvulaceae, etc. General natural products that contain oxalic acids are Sugarbeet, Spinach, Saltbush, Goosefoot, Buckwheat, Rhubarb, Mangold, Green cabbages, Tea, Chocolate, Almonds, White beans, Soyabean, Sweet potato, Ipomoea, Okra, Cocoa, Drumstick leaves, Coriander leaves, Radish leaves, etc.

3.2 Vitamins and minerals

Oxalic acid easily combines with cations to form oxalate crystals which are then excreted in urine as minute crystals. So calcium supplements given along with foods containing oxalic acid can cause calcium oxalate to precipitate out in the gut and reduce the levels of oxalate absorbed by the body by 97%. Calcium supplement like milk also has characteristics of digestive and metabolic utilization of minerals such as phosphorus, magnesium, and iron. It's calcium enrichment does not interfere in the bioavailability of the minerals but interferes with iron. So iron may not be utilized when milk is used which is an important aspect in the management of kidney stones.

A low oxalate diet is recommended for the prevention of CaOx stones, however, a recent study proved dietary oxalate had little effect on urinary oxalate excretion although vitamin C was highly correlated with urinary oxalate excretion. But high vitamin C intake can be a risk for stone formation by increasing endogenous oxalate.

A high vitamin D and protein content regimen increase hypercalciuria which lowers the pH of urine and increases uric acid level, which increases kidney stone. So consumption of deproteinized drugs is much better. All the plants discussed here contain considerable amounts of vitamin E but do not contain much vitamin D and anti-nutrient like phytates. The absorption of mineral nutrients is adversely affected by the presence of inhibitors like phytates. It is a higher calcium diet (1200 mg/day) associated with lower kidney stone formation because the higher calcium intake will bind oxalate in the gut. So calcium can bind with dietary oxalate and thus it is not absorbed. Potassium will improve hyperoxaluria and also it is a good source in the control of diuretic and hypertensive implications. Magnesium also forms a complex with oxalate and decreases oxalate in the urine, which can reduce the risk of stone formation. Hypomagnesium is not a risk factor for stone formation. Magnesium also binds with oxalate in gastrointestinal tract to reduce oxalate absorption. Citrate supplementation is one of the effective pharmacological options for preventing the recurrence of kidney stones. Calcium oxalate or calcium phosphate crystallization is antagonized by the citrate in the urine due to which recurrence of kidney stone is prevented by increased urinary citrate excretion. Potassium citrate along with thiazides are prescribed for kidney stone treatment at the same time it impaired by poor long term compliance, gastrointestinal upset and unpalatable taste. The remedy for this issue is taking potassium citrate with magnesium citrate combination. Magnesium can bind with oxalate due to which both diminishing and absorption of oxalate takes place thereby acting as a stone preventive. The binding of oxalate in urine is reduced by the binding of magnesium which results in the decrease in the recurrence of kidney stones. Patients who have diabetes, hypertension, and high blood cholesterol are often instructed to consume high oxalate foods such as fruits and vegetables. In this case, it is better to consume less and only selected fruits and vegetables to prevent kidney stones. The vitamins and mineral composition of the selected plants were given in **Figures 4** and **5** [41–56]. The plants discussed here contain all the nutrients in considerable quantities required for preventing and managing calculi forming oxalates.

3.3 Impact of vitamin E in the management of disease and calciphytoliths

3.3.1 Renal insufficiency due to vitamin E deficiciency

In rats, a combination of fat-soluble vitamin deficiency and Se or glutathione deficiency causes extreme and progressive aerophilic damage to the urinary organ's structure and function [57–59]. Furthermore, urinary organ dysfunction caused by ischemia–reperfusion damage causes 50% mortality in dietary E- and selenium-deficient rats compared to controls [60], and a-tocopherol administration increases the fatality rate by 46% after 120 minutes of heat anemia [61]. During a marked increase in the creatinine/molar creatol magnitude relationship, aerophilic urinary organ injury in nutrients E-deficient rats is depicted.

Conversion is directly mediated by chemical group radicals [62]. The living nephrons enhanced the absorption of the element and the square oxide levels multiplied within the residual cortex of rats. Dietary fat-soluble vitamin administration 11 to 16 weeks after urinary tubule reduction has been shown to attenuate glomerulosclerosis by more than 500 weeks [63]. The fat-soluble vitamin deficiencies are never seen in humans and have been delineated by sensory neurological disorders.

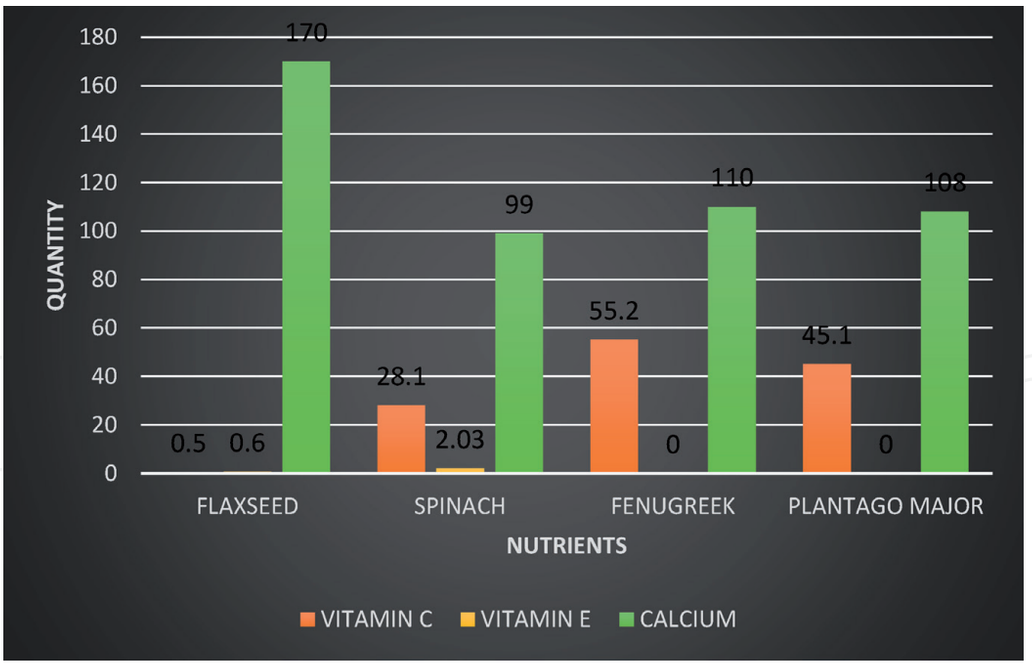

Figure 4.
Vitamins and calcium content in the selected plants (mg/100 g).

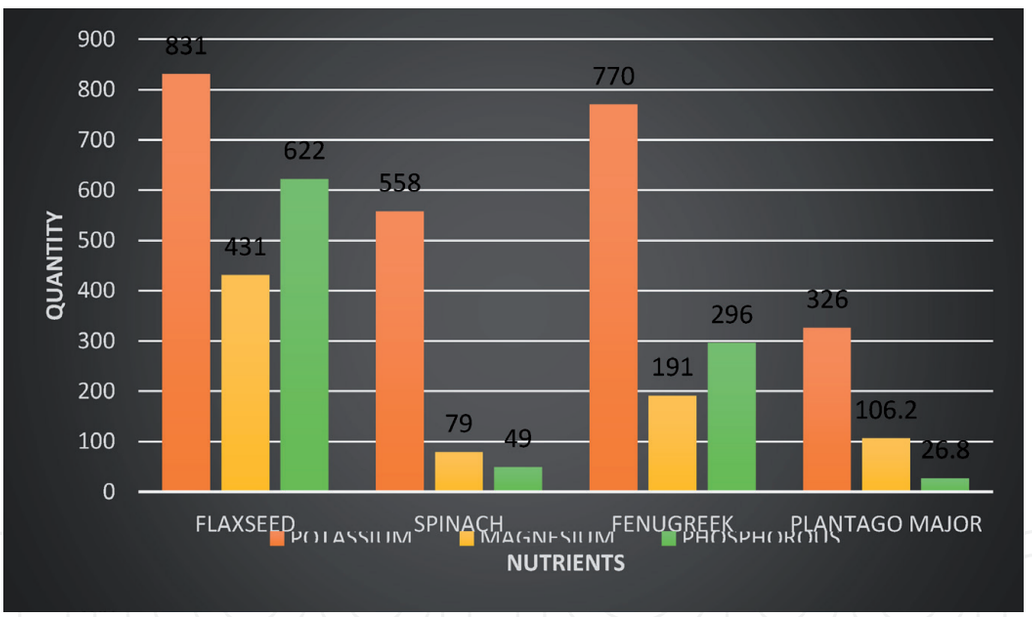

Figure 5.
Mineral content in the selected plants (mg/100 g).

It is due to diseases that hinder the streamlined absorption of fat (such as chronic disorders or abetalipoproteinemia) or, in rare highly contagious conditions, Deficit in the family of confined fat-soluble vitamins (FIVE) due to mutations in the a-tocopherol enzyme that export fat-soluble vitamins from the liver to blood [64]. If patients with permanent and high fat-soluble vitamin deficiency have urinary organ dysfunction, this is not recognized.

3.3.2 Inflammatory kidney disease

Immune globulin nephrosis (formerly known as Berger's disease) is now confirmed to be the end-stage urinary organ dysfunction in twenty-five percent of affected patients over a 25-year follow-up period [65], despite being initially

thought to be mild. It is the most common form of nephrosis on the planet. The mechanism of harm is unknown, but related medical specialty insults to the kidneys seem to be introduced as a result of immune globulin accumulation, which induces chronic oxidative stress. There are currently no lucky drugs available that may bleed down the path of the disorder, with the exception of dominant cardiovascular disease and decreased dietary macromolecule use.

The associated experimental model of early immune globulin nephrosis in rats, mild oxidant-mediated inflammation and associated structure–functional changes in glomeruli have been shown to attenuate dietary fat-soluble vitamin levels from thirty to one hundred IU/kg of a biological attack, leading to a five-fold increase in humor-soluble vitamins. Nutrition E-supplemented rats had a four-fold reduced rate of symptom, the five-hundredth decline in albuminuria, eluted urinary organ tissue lipoid peroxidation, Stabilized urinary organ plasma flow, decreased expression of fibrinogenic protein transmission protein b1 (TGFb1), and had less extreme capillary hypertrophy than control animals [66]. During the additional analysis, supported by these initial observations, Chan et al. [67] indisputably argued that a two-and-a-half to five-fold increase in fat-soluble vitamin chow supplements (i.e. 250–500 IU/kg) may further reduce plasma and urinary organ lipoid peroxidation and albuminuria, but no further change in TGFb1 RNA has been identified. The use of fat-soluble vitamin 800 IU/day is expected to be useful in patients with immune globulin nephrosis and albuminuria but one g/day and a long-term regulated, double-blind trial are currently underway to explore this risk. Twenty-nine urinary organ response injuries may also be the product of advanced immune deposition directed to the capillary basement membrane. Anti-glomerular basement membrane (anti-GBM) nephrosis is concretely caused by anti-GBM antibodies in rats. 2 stages of capillary injury square measure are obvious. The first acute (heterologous) strategy involves the attachment of antibodies to the basement membrane amid neutrophils invasion and chronic capillary inflammation. Capillary vascular square measures blocked by microthrombus that reduces the rate of filtration and plasma flow [68].

The second delayed reaction is due to the target host (autologous phase) which ends up with symptomatic, multiplied urinary macromolecule excretion, capillary cardiovascular disease, capillary wall integrity defects, protein chemical action, and macrophages aggression. Convergence of urinary organ activity and improved maintenance of the capillary structure is detected in nephrosis-controlled rats with 5 mg/100 g fat-soluble vitamin weight 3 days before management of anti-GBM protein rather than in untreated controls [69]. The amendments were marked within the capillary filtration quantity, While chronic inflammation of immune globulin {nephropathy|renal disease|nephrosis|uropathy} and anti-GBM nephrosis is not the first event of the diseased part, it is crucial for aerophilic urinary organ injury seen in these situations. Fat-soluble vitamin decreases this injury by combining its medicinal and anti-coagulant effects and its ability to strengthen membranes. Potential for therapeutic action with fat-soluble vitamins may also arise during a host of alternative urinary organ abnormalities create through medical specialty insults and chronic inflammation.

Insufficiency and extreme albuminuria are two common examples. Fx1A [70, 71] PHN coupled with lipoid peroxidation was discovered in Passive Heymann nephrosis (PHN), a gnawing animal model for human membranous nephrosis resulting from sub-animal tissue immune absorption in capillary walls following injection of heterologous protein guided against a crude, autologous annular material. Wegener's granulomatosis, for example, is caused by the expansion of anti-neutrophil living antibodies (ANCAs) against proteins expressed on the surface of activated polymorph nuclear neutrophils. Subsequent degranulation releases toxic cell-degrading enzymes, oxygen-free radicals, and pro-inflammatory substances, a method that coincides with necrotizing crescentic capillary nephrosis.

3.3.3 Aging kidneys

The age-related improvements in the excretory organ function and the anatomy area are correlated with lipid peroxidation and oxidative stress. Excretory organ aging is characterized by gradual glomerulosclerosis, capillary filtration, and constriction. Old (13-month old) rats on an impact diet containing fifty IU/kg E have a three-fold increase in F2 isoprostane agent, a 60-percent decrease in capillary vessel filtration, and an increase in advanced glycosylation end product (AGE) compared to young animals (3–4 months of age) on a basic diet. Supplementing the old with a high E (5000 IU/kg) diet for an additional nine months, the liquid body substance level of the inhibitor increased by thirty percent and specifically improved the capillary vascular filtration rate by fifty percent, suppressed the initiation of F2 isoprostanes and amplified each glomerulosclerosis and AGE receptor expression, as well as decreasing the activation of excreting. It has been envisaged that a 40% decline in albuminuria seen in aged nutrients E-treated animals at twenty-two months compared to old controls may well be related to higher retention of capillary vessel permeability, a parameter that reduces with age [72].

3.3.4 Oxidative stress in kidney failure

There is a significant amount of evidence to support the involvement of oxidative stress in progressive urinary organ impairment. Mononucleate leukocytes in patients with chronic renal disease (CRF) area are additionally prone to lipid peroxidation of the membrane compared to those confined to healthy controls [73] and therefore red cells in patients with E-depleted quality area unit nutrient analysis [74–77]. Bochev et al. [78] stated that the development of nephropathy from chronic insufficiency to discontinued azotemia in the qualitative analysis was related to a lower blood inhibitor capacity; An increase in polymorphic nuclear blood cells due to aerophilic activity was correlated with an abnormally high level of lipid peroxidation. Penchant et al. [79] reported that in patients with advanced CRF, a very low macromolecule diet (0.3 g/kg per day) accompanied by essential amino acids and keto acids and vitamins, as well as E (a-tocopheryl acetate, 5 mg/day), A (7.5 mg/day) and A (7.5 mg/day) was found. Sixty-one of the E levels in this patient cluster ranged from thirty-eighth to fifty-six of the management values [79] suggesting that although the sweetening was achieved, and a key red blood cell E deficiency persisted. Accumulated lipid peroxidation of red cell membranes and associated E deficiency contribute to their shortened half-life in circulation and the next anemia associated with pre-dialysis pathology seen in CRF. Thanks to dietary restrictions, CRF patients are also deficient in inhibitor vitamins and micronutrients. This is often markedly true for immediate post-hemodialysis in that the full inhibitor capacity falls from a pre-dialysis level of 1.54 to 1.38 mmol/L post-dialysis [80]. These rapid, degraded, standing inhibitor episodes could lead to windows that are usually vulnerable to general lipid peroxidation and subsequent aerophilic changes in transmitted lipoproteins, atherogenicity, and therefore distinctive upset and high blood pressure associated with CRF. In healthy plasma, salt and albumen account for seventy-five percent of full inhibitor activity in vitro, while ascorbate (vitamin C) and E account for 100 percent of full inhibitory action (a-tocopherol) [81].

Total post-dialysis inhibitors fall significantly, leading to a loss of soluble ascorbate and salt. Ha et al. [80] advised that water-soluble vitamin supplements up to one g/day should be routinely administered in qualitative analysis to reduce this temporary lack of soluble inhibitor capability. Although E is the major lipid-soluble inhibitor in plasma, the amount of nutritional inhibitor carotenoids (lutein, lycopene, a-and b-carotene) is also crucial for the effectiveness of lipoproteins from

aerophilic changes, and there are also inequalities within the traditional level of this category of antioxidants throughout CRF. Of these compounds, carotenoid is the most impacted at physiological levels and its plasma concentration is significantly reduced in post-dialysis CRF patients (0.17 mmol/L) compared to healthy controls (0.44 mmol/L). The carotenoid deficiencies may additionally contribute to the associated obstructed plasma defense inhibitor system and make up one for dietary therapeutic intervention in addition to E.

3.3.5 Effective dose of vitamin E in renal failure treatment

Normalizing the standing inhibitor of CRF patients with dietary E victimization would be a cost-effective and straightforward therapeutic target. In healthy individuals, the common daily allowance of E is 8 mg (12 IU) for girls and 10 mg (15 IU) for men (1 mg = 1.5 IU) supported common levels needed to prevent symptoms of deficiency [82]. The Plasma pool-turnover is fast (1.4 ± 0.6 pools/day) [83] and therefore the traditional transmitted plasma varies among eleven. 5 and 35.0 m [84] and giant oral doses (1500–3200 IU/day) occur together to be safe, with minor and well-tolerated duct appearance effects [85] although current levels will only be increased by 2 to 4 times the standard quantity. (The higher limit is limited by the viscus E enzyme, which preserves the plasma levels within the slime, with excess tocopherols being excreted in the digestive juice.) [86]. Vitamin E has been tested in humans with some success in the treatment of system diseases involving oxygen-free radicals and aerophilic stress in their clinical expression, as well as Friedreich's neurological disease (400 IU/day) [87]. Alzheimer's disease (2000 IU/day) [88]. Parkinson's disease (3200 IU/day) [89]. the first stages of Huntington's disease (3000 IU/day) [90] and dyskinesia (800–160 IU/day) [91–93].

The best dose of E for preventing human failure is also between 300 and 700 IU per day. (This is a healthy 'therapeutic variance,' meaning that the nutrient levels needed to prevent long-term muscular disease caused by aerophilic stress are below the edge for aspect effects.) Suha et al. [77] discovered that giving chronic dialysis patients 300 mg/day (450 IU/day) E for one month resulted in critical dialysis. Low doses of E, such as 100 mg/day (150 IU/day), have been shown to provide critical defense against the risk of upset, which is a major complication of CRF [94]. Dietary E supplements that boost plasma levels could be beneficial for sluggish people. E medical care may also be cost-effective in alleviating chronic kidney disease and standing pathophysiology.

Impaired plasma inhibitor arms are characterized by chronic kidney disease and standing pathology. Besides, E medical care is considered to be a method of correcting the position of plasma antioxidants and attenuating disorders related to kidney disease. In conclusion, the mixture of E and antioxidants protects against HLP-induced salt uropathy. Calculus disease has been known to be the leading disease of life in every human and animal. Calculus could destroy the excretory organ of hollow epithelial tissue, leading to impaired excretory organ function. Aerophilic stress in chronic inflammatory conditions, anti-glomerular basement membrane kidney disease, focal segmental glomerulosclerosis, rhabdomyolysis (myoglobin acute excretory organ failure), diabetic uropathy, and toxic poisoning compounds such as transition metals, weed killers, and medicines such as cyclosporine A and cisplatin all aggravate the progression to failure. E inhibitor membrane (5–007-tocopherol) is considered to be the possible therapeutic intervention that will make it easier to weigh reduce the level of decrease in excretory organ activity under these conditions. The impaired plasma inhibitor arm is indicative of chronic kidney disease and standing pathology. E medical care is also thought of as a method of correcting the status of plasma antioxidants.

4. Discussion and conclusion

Kidney stone disease has been identified together as a major disease in every human and animal. Calculus (stone) may harm the excretory hollow epithelial tissue of the organ, resulting in the impaired excretory activity of the organ. The most important of human excretory organ stones is the metallic element salt, which relates to the metallic element and the metabolism of salt in the tissue and urinary tract system [95–97]. CaOx stone also had a high incidence and recurrence rate in animals and iatrogenic aerobic stress [98]. Several previous studies have shown that increased aerobic stress has been associated with the formation of CaOx crystal and stone. As a result, intrusion with aerobic damage could also play a key role in stopping the continuous formation of stones and the resulting excretory organ pathology. Antioxidant supplement (Vit E) reduces metabolic stress, salt excretion, and crystal formation of CaOx in hyperoxaluric rats receiving antifreeze (EG) [99]. In hypertensive and hyperoxaluric patients, oral supplementation of Vit E at four hundred mg/day for 9 months may normalize the organic chemistry and kinetic properties of Tamm-Horsfall supermolecules that impede CaOx crystal aggregation [100].

Also, overproduction of antioxidants avoided metallic element salt accumulation by preventing peroxidant injury and preserving excretory organ tissue antioxidants and glutathione oxidation–reduction balance. Antioxidant medical aid may therefore protect against the accumulation of metallic element salt stones within the human circulatory organ [101].

It is reportedly stated that oxygen-free radicals square measure essential for the pathology of multiple chronic disorders as well as renal failure. Enhanced element radical generation and/or compromised inhibitor weaponry leads to chronic oxidative stress that markedly worsens several things. Three excellent concerns were jointly endorsed by the likelihood of delaying the regression to kidney disease through inhibitor action. Restoration of capillary membrane integrity is important for urinary organ activity, and the biomembrane square measure is protected from aerophilic deterioration by the fat-soluble vitamin lipotropic inhibitor, primarily within the species of a-tocopherol [102].

In summary, although the use of herbal medicine in the treatment and prevention of urinary stones recurrence has been proven and promising, further studies are needed to understand disease physiology, the action mechanism of herbal medicine to develop an effective and safe lithophytic agent. At the same time, it is necessary to identify the mechanism of action for the discussed vitamins containing plants, thereby assessing the dosage, controlling herbal quality, and investigating their interactions and side effects. Vitamin E plants may completely prevent deposition of oxalate by preventing pre-oxidation injury and restoring renal tissue antioxidants. So vitamin E therapy also might protect against oxalate calculi deposition in the human kidneys.

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