

Effect of Ginger Hydro Alcoholic Extract on Oxalate Renal Stone in Rats

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Abstract: *Nowadays, biotechnology of medicinal plants is a modern sub-branch of biotechnology and pharmacy that has gradually become the focus of attention of pharmaceutical and traditional medicine specialists which results to major changes and jumps in production of science. Since herbal medicine is one of the oldest therapies in Middle East and Chinese tradition, herbal medicines, owing to less side effect levels compared to chemical treatments, have long been used for preventative and therapeutic treatment, as well as the attention of medical professionals. Herbal medicine is totally based on plant parts like roots, leaves, etc., there are various manners of using herbs in different traditions such as soaking into the water, boiling, chewing, etc.. The present study intends to investigate the effect of ginger hydro alcoholic extract on kidney stone (oxalate type). [1] We initially divided the rats into five groups which includes control group, 2 doses of Ginger extract, treating by regular medication and not treating. By injecting peritoneal of sodium oxalate solution to the rats after about 7 to 10 days, and by observing the oxalate crystals in the urine samples taken from the kidneys and physical signs of kidney stones like decrease in volume of urine, Zingiber officinalis rhizome, which was used as a herbal remedy, was extracted and injected into the rats with different doses. As results of injection on a regular basis, we observed treatment in rats with kidney stone. According to the dosage, the pace of treatment was different in samples. So, low dose can be used for minor problem in a long term and high dose can be use for major level of kidney stone which is working more efficiently with a higher speed of treatment. [2],[3]*

Keywords: *Ginger, Hydro Alcoholic Extract, Kidney Stone, Oxalate, Rat*

I. INTRODUCTION

According to researches, it has been proven that chemical drugs and other existing methods (including treatment with ultrasonic waves, chemical drugs, etc.) are associated with side effects, and researchers seek to find drugs that have the least side effects. The review of the articles in the world scientific journals suggests that in most studies, the impact of different materials on the function or tissue of the organs is measured. It is also noteworthy that European and American researchers consider traditional medicine, while we are keen on market chemical drugs. [4] Considering the above-mentioned and medical value that Abu Ali Sina has established in Iran and is recognized globally, and considering that most treatments in advanced countries are therapies in which less chemicals are used, we conclude that the best medicine with less side effects is in the herbal medicine group. Therefore, we decided to investigate the effect of an herbal drug on kidney stone.

Considering that kidney stones have different types, and according to antimicrobial, anti-inflammatory and anti-inflammatory properties of ginger, ginger is a good candidate for the herbal remedy in the project. [2]

Ginger (Latin name Elecampane) with its scientific name as Zingiber officinale was used in the past by Romans, Greeks, and Celts to eliminate gastrointestinal complications, and in Iran, it was also used to treat asthma, bronchitis, Chills, chest pain, cough, diphtheria, emphysema, burns, fever, hay fever, parasites, pneumonia, respiratory problems, tuberculosis, wheezing and pertussis. [1], [4], [5]

Ginger rhizome is a complex chemical compound. The volatile oil of this plant contains monopenenes (such as camphon, beta-flandron, travertine and germanium), diterpan lactones (such as galanolactone) and sesquiterpenoids (such as alpha-zinybirin and r-curcumin). Ginger spicy taste is due to various gingerols, including 6-gingerol. (Figure 1). [6]



Fig. 1: Zingiber officinalis rhizome as a powder and the real rhizome

As mentioned, kidney stones have different types that are referred to below:

Oxalate and calcium phosphate stones are among approximately 80% of kidney stones, calcium oxalate, struvite stones are after calcium stones, uric acid stones contain approximately 4% of kidney stones, and cysteine stones accounts for approximately 1% of kidney stones (Figure 2). [2]

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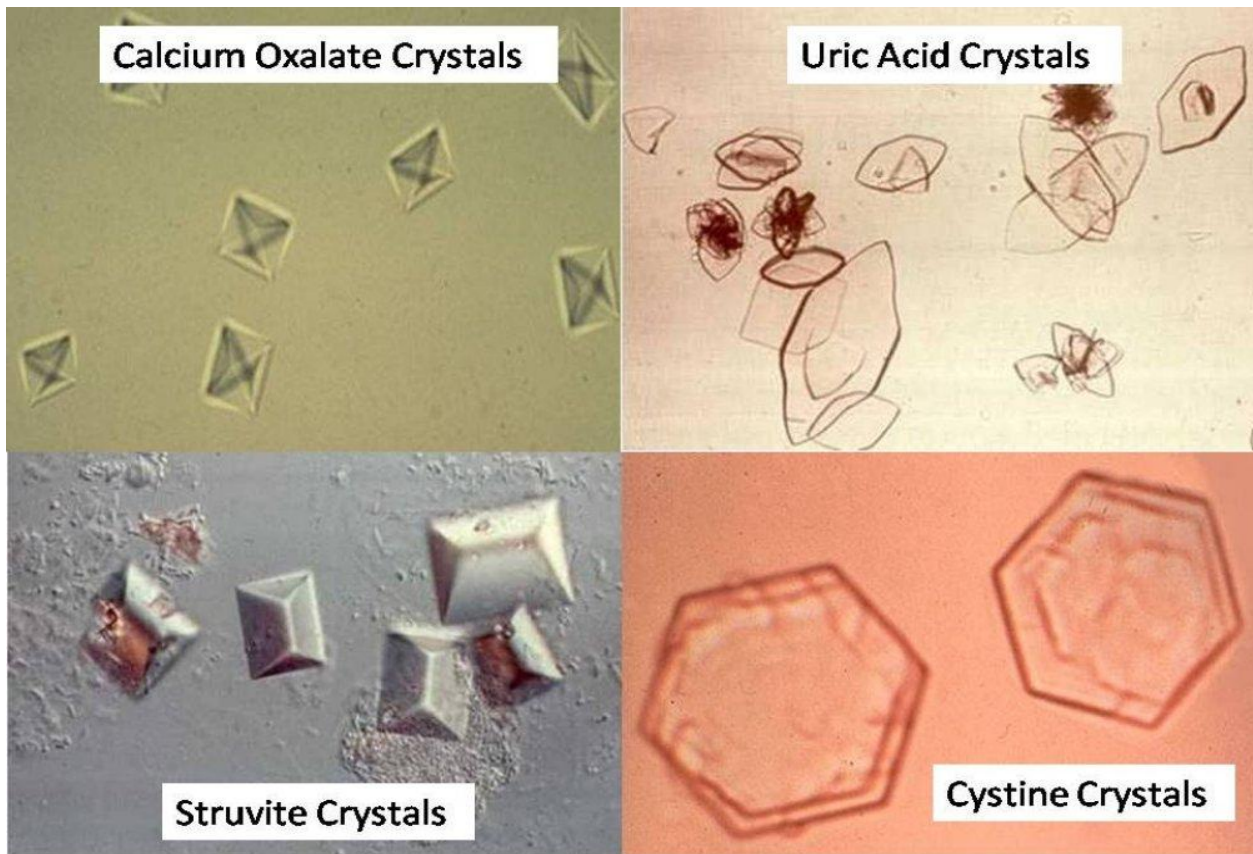


Fig. 2: Different types of kidney stones which are specified by the shape of their crystals

In this study, the rats were divided into 5 healthy, infected and treatment with market drugs (vitamin D), infected and treatment with low-dose ginger extract, and infected and treatment with high-dose ginger extract, as well as infected and without treatment. Furthermore, sodium oxalate and normal saline solution was injected into four groups of the rats (all rats other than healthy ones) peritoneally and they are infected with kidney stones, which after observing the

signs of kidney stones such as abdominal inflammation (Figure 3), pain, low mobility, change in urine color and examination of the number of urine crystals, treatment with peritoneal injection of hydroalcoholic extract of ginger was applied so that status of each rat was separately examined until improvement of the rats and elimination of kidney stone.



Fig. 3: The case of kidney stone made by injection of oxalate solution.

II. EXPERIMENTAL DETAILS

- Tested animals

Adult and male wistar rat with the scientific name *Rattus norvegicus*, with an average weight of 250 g to 275 g and a total number of 25, was tested.

Grouping of the rats is as follows:

Group 1: Healthy rats (control)

Group 2: Infected rats and low-dose treatment

Group 3: Infected rats and high-dose treatment

Group 4: Infected rats and treatment with commonly used medicines

Group 5: Infected rats and without treatment

- Required Materials

Sodium oxalate, normal saline serum (injectable salt), ethyl alcohol (ethanol), ginger powder

- Creation of kidney stones

Oxalate with a ratio of 28 mg per 1 ml of normal saline serum for each wistar rat is administered intraperitoneally. After 7 to 10 days, the clinical signs of kidney stones appeared as abdominal cavity inflammation, blurred urine, decreased urine volume and low activity, and by urine sampling and microscopic observation, oxalate crystals were seen in envelopes or two square pyramids. Then, we prepare glycogenic hydroalcoholic extract, and start the injection treatment with the preparation of the ginger extract. [2]

Group	Injection time (All injections were performed in one day)	Injection dose	Injection amount
High-dose ginger	16:10	28 mg/ml	1 MI
High-dose ginger	16:20	28 mg/ml	1 MI
Low-dose ginger	16:35	28 mg/ml	1 MI
Low-dose ginger	16:50	28 mg/ml	1 MI
Without treatment	17:00	28 mg/ml	1 MI
Treatment with market drugs	17:20	28 mg/ml	1 MI

Table of oxalate sodium injection [2],[3],[4]

- Ginger extraction

The high quality rhizome powder of ginger was prepared and mixed with ethyl alcohol (ethanol) 90% with a ratio of 1 to 3 in a dish, and we used the following molding method to extract. To prevent evaporation of alcohol and light exposure, we covered the mixture with paraffin and foil and

stored in a refrigerator for 24-48 hours, and after 48 hours, the mixture was kept, and the solution was dissolved in Ben-Marie Water bath (Fig. 4) to allow alcohol to evaporate, and at the end, a brown paste-like extract remained, and we prepared it with doses of 10mg / kg / 48h and 20mg / kg / 48h for the target groups.[3], [6], [8], [9], [11]





Fig. 4: Extraction phase. The combination of ginger and alcohol gets filtered by use of funnel and filter paper to get the pure solution with no solid inside.

- Injection

For intraperitoneal injection, the animal should be turned upside down so that the head is lower than the body and the viscera is pushed forward, the needle is palced between the groin and abdomen, and in order to make sure

we have not entered the viscera, we aspirate it before injection so that If the yellow / green colored substance is not injected into the syringe, we can perform injections to each rat in a maximum of 1 ml.[3], [8]

Group	Injection time (Sample injection hours in one day)	Injection dose	Injection amount
High-dose ginger	15:00	20 mg/ml	1 MI
High-dose ginger	15:20	20 mg/ml	1 MI
Low-dose ginger	15:30	10 mg/ml	1 MI
Low-dose ginger	15:45	10 mg/ml	1 MI

Table of ginger extract injection

III. RESULTS AND DISCUSSION

By examining and observing the urine specimens of the rats under the microscope and their clinical symptoms after injection every two days, for the third group, 30 days (15 times the injection) with a dose of 20 mg / kg / 48h, and for the second group during the a period of 54 days (27 injections) at 10 mg / kg / 48h, the following results were obtained: Group one: Healthy rats (control)

As the name suggests, we chose five healthy rats as control groups that were still healthy at the end, and no treatment was considered for them.

Group 2: Infected rats and low-dose treatment

In the treatment of this group, and with the low-dose injection as mentioned above, no improvement was made in five of the rats, and no significant changes in the oxalate crystals were observed in urine specimens in rats, but their clinical symptoms were improving.

Group 3: Mice with high dose

In the treatment of this group of five mice, one rat was eliminated due to a test error and environmental factors, and two rats were improved, and the other two rats were as in the second group.

Group 4: Infected rats and treatment with commonly used medicines

In the treatment of this group of five rats, one head was eliminated due to environmental factors, and four rats were improved.

Group 5: Infected rats without treatment

In this group of five rats, due to the presence of kidney oxalate stones as well as lack of mobility and side effects on the abdominal cavity of the rats, and lack of improvement, all of them died at different times.

Diarrhea and disinfection of ginger are one of the important factors of treatment in this research so that it effectively affects kidney stones by increasing the intake of unsaturated acids or animal protein and sugar, and decreasing its prevalence by reducing the intake of fiber and plant proteins. Consumption of low-energy foods is associated with reduced prevalence of stones. Vegetarians have a low incidence of stones. [7]

High sodium intake is associated with an increase in calcium and sodium levels and a decrease in citrate excretion, and the amount of calcium salt crystallization increases due to urinary saturation of mono-sodium urate and calcium phosphate. The rate of fluid intake and volume of urine also affect stone making. Urinary stones are polycrystalline assemblages containing crystalloid and organic matrix. The formation of stones in the urine is supersaturated, and this depends on the urine pH and the ionic strength of the concentration of soluble matter and urine composition. [10]

The composition greatly varies from one physiologic to another, and it varies from acidic in the morning urine after every meal to completely alkaline urine after each meal. As ionic strength increases, the ionic activity decreases, indicating that ion is more available. The role of the concentration of soluble materials is determined, so that by increasing the concentration of the substances, their tendency to deposition will be higher. [3], [4]

The effect of animal protein differs from plant protein, so that the prevalence of kidney stones in vegetarians is half that of the general population. Restricting animal proteins in the diet can be beneficial in reducing formation or recurrence of kidney stones. Animal proteins cause stones due to increased calcium, oxalate and uric acid in the urine, and lowering citrates and urine PH. [5]

Using a glass of boiled water per hour will dilute salts in the urine and cause faster and easier disposal of stones in patients with the disease. Ginger also has diuretic properties. [10]

Protein can become oxalate and repel through urine. In addition, protein boosts calcium excretion. Therefore, oxalate and calcium both go out of the urine together and this causes the formation of kidney stones. Experiments performed on kidney stones indicated that the most common kidney stones are calcium and oxalate, and parathyroid gland disorders or excessive consumption of protein causes increasing calcium secretion in the urine and possibly increases the risk of kidney stones. The researchers concluded that a special plant sterol called stigarmosterol could inhibit enzyme activity and eventually form the protein plaques found in ginger. [5], [6], [9]

Ginger produces heat in the body and, by increasing circulation and sweating, it repels toxins faster than the body, thereby reducing the amount of toxins in the blood. [1], [10]

Studies have shown that ginger has the same effect as non-steroidal anti-inflammatory drugs (mefenamic acid and ibuprofen).

The materials in ginger prevent accumulation of blood platelets and dilutions of the blood. They are beneficial for the gland and increase the secretion of the hormone cortisol from the glands. Cortisol prevents plasma leakage by reducing the permeability of the capillaries in the tissues, reducing inflammation and healing of wounds more quickly. [6],[11]

Cortisol also plays a role in the metabolism of protein and lipids, maintaining normal blood pressure, muscle resistance, increasing stomach acid, absorbing water and sodium in the kidneys, and lowering lymphocytes in the blood. [6]

High-fat and high-cholesterol diets can increase the incidence of kidney stones, and ginger is one of the lowering cholesterol levels in the blood. [10]

Consumption of potassium, magnesium, vitamin C, B6 and D is effective in the treatment of kidney stones. Ginger is rich in vitamins C, D and B, minerals such as potassium and calcium, magnesium, copper and zinc. [9]

Naturally, the amount of uric acid excreted in the urine should not exceed 10-40 mg per day; only 10% of this amount is derived from the diet, the rest is the result of the internal metabolism. Abnormal digestive disorders associated with malabsorption are the most common cause of elevated urinary excretion of oxalate, since unbonded fat bonds calcium to the intestine, resulting in increased oxalate absorption. Ginger helps digestion and absorption of food by increasing salivary secretion and digestive enzymes. [3]

Insoluble fiber reduces calcium excretion from the urine. It also increases the movement of the intestine, therefore there will be little time to absorb calcium. High-protein diet is associated with increased calcium excretion, oxalate and urate. In fact, high consumption of animal protein with its acidic load (1 milliliter of hydrogen per gram of protein) increases calcium excretion. Therefore, some researchers recommend plant diets to people susceptible to kidney stones. Increasing dietary fiber reduces the risk factors for rock formation, especially calcium stones, which are found to be sufficient in ginger. [10]

Research has shown that ginger has crucial role in dilution of blood, and diluted blood is less toxic. Researchers have discovered a very small type of bacteria living in some people that plays an important role in the formation of stones. Bacteria in kidney stones can have a pathogenic role and also have a protective role. Struvite stones are associated with frequent urinary tract infections, since urease degrading bacteria increase urine pH, and the body does not have the ability to excrete bacteria contained within the stones. [4] Oxalobacter formigenes is an anaerobic bacterium colonized in the intestine and converts oxalate into formaldehyde and carbon dioxide. Non-colonization of the oxalobacter formigenes makes the individual susceptible to oxalate stones.

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Early studies on oral administration of oxalobacter formigens have indicated that up to 90% reduction in urinary oxalate levels in healthy subjects and patients with primary hyperoxaluria. Other properties include ginger, anti-inflammatory, antiemetic, antimicrobial, antioxidant, cardiomyostomy and stimulant of the immune system. [5]

Note - Although the use of ginger usually does not have side effects, its excessive use can cause partial heat stroke.

IV. CONCLUSION

In conclusion, this study shows that by injection of hydro-alcoholic ginger extract on a regular basis, the case of kidney stone can be solved as Ginger has got beneficial effects and uses as a herbal medication in a traditional medicine. This extract has the most effective results by dose of 20 mg/ml which has taken a period of a month to treat the kidney stone. This study can be improved by using ginger extract as part of diet and see how effective will it be.

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