

Treatment of Kidney Stones Using Diosgenin

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Kidney stone is a common disease worldwide. Approximately 12% of the global population suffers from this problem. Among the different diseases affecting the urinary system, kidney stone is the third most prevalent one. It is characterised by deposition of crystals/stones which are usually made of calcium oxalate.

Kidney is an organ which is responsible for purification of the blood and removal of toxic substances from it. The kidneys return the useful substances back to the blood again while the toxic substances are removed and form a part of urine. When crystals are deposited in the kidneys or other parts of the urinary system there is interference in this filtration function of the kidney. This may result in improper removal of the toxic substances from blood and level of these substances may increase in blood. Due to the obstruction, the patients may also experience severe pain in the back or abdominal area. Other symptoms can be nausea, vomiting, foul smelling urine and, frequent need to urinate but urinating very small amounts. As the disease progresses the deposited crystals may also lead to inflammation or damage to that part of the kidney tissue where they are deposited. This further worsens the situation and kidney function deteriorates even more. The damage to kidneys leads to increased excretion of uric acid, urea, and creatinine in the kidney. There is also an increase in damage to the kidneys due to free radicals derived from oxygen.

Another interesting aspect of this disease is that men are affected more as compared to women. This is because of the fact that women in their reproductive years have a higher level of estrogen. This hormone has a protective role and prevents the deposition of crystals in the kidney, while in

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men testosterone leads to aggravation of the chances of stone formation. Other factors may also be responsible for the increased prevalence of stones in one population or group as compared to the other. Citric acid prevents the formation of stones but a diet rich in oxalates may increase the susceptibility to kidney stones. Climate and lifestyle also play a significant role in stone formation. Increased atmospheric temperature (due to global warming or migration of people to urban areas) may increase the chances of formation of kidney stones. Lifestyle changes such as eating junk food has also led to increased incidence of stones in children and women.

There are currently many treatment options available for kidney stones. Allopurinol, Ibuprofen, Diuretics, Acetaminophen and Naproxen are some of the medicines which can be used. Surgical treatment may include lithotripsy which uses sound waves to break the kidney stones. However, there may be serious side effects, for example, bleeding around the kidney and in nearby organs. However, most of these treatments have side-effects of the other issue is of reoccurrence of stones. Hence, alternative therapies with less side effects are desirable.

Many drugs and active ingredients of medicines are derived from plant sources. One such natural product from plants, saponins is a class of naturally occurring plant glycosides which is characterised by their foam forming properties in aqueous solution. There are many studies which have reported that plant extracts or fractions rich in saponins have the good ability to prevent the formation of kidney stones. Saponin rich fraction from fruits of *Solanum xanthocarpum* was evaluated for their efficacy to prevent the kidney stones both *invitro* models as well as *in vivo* animal models. It was found that administration of saponin rich fraction significantly prevented the formation of kidney stones and damage to the organ caused by oxygen derived free radicals. Similarly, saponin rich fractions from the plant *Herniaria hirsuta* were also found to inhibit the formation of kidney stones both *invitro* and *invivo* animal models. Seven plants: *Verbena officinalis*, *Lithospermum officinale*, *Taraxacum officinale*, *Equisetum arvense*, *Arcostaphylos uvaursi*, *Arctium lappa* and *Silene saxifrage* were also tested to see their efficacy in preventing kidney stones. The researchers concluded that the saponin content of these plants was responsible for the beneficial effect and saponins might have a solubilizing effect on the stones. Indinavir is a drug which has had a good success rate in the treatment of HIV/AIDS but causes renal stones in patients. Two saponins, escin and glycyrrhizic acid were found to significantly increase the time taken to form the crystals by Indinavir. This further validates the beneficial use of saponins in preventing the stone formation.

Diosgenin is a saponin with beneficial effects in several conditions such as increased oxidative stress and inflammatory events. Hence, our team of researchers chose diosgenin to test its ability to prevent formation of kidney stones in animal models. Animal model of stone was created by administration of ethylene glycol (0.75%v/v) in drinking water for 28 days. Twenty-four male rats of the wistar species were divided into groups of six animals each. Group I: Given only food and water, Group II: Given only ethylene glycol 0.75%v/v in drinking water for 28 days, Group III and IV: Given ethylene glycol and diosgenin (at two different doses). After 28 days, the urine and blood samples from the animals were collected and tests were done to see if diosgenin was able to prevent the formation of stones. Different tests were done including the test of urea levels, uric acid levels, citrate levels, calcium levels, magnesium and albumin levels in the urine and serum. Kidney

histopathology was done to see the extent of damage and crystal deposition. Antioxidant enzymes analysis was done in kidney homogenate to indicate the oxidative stress. In rats administered only ethylene glycol it was found that levels of urea, uric acid and, calcium (promoters of kidney stone) were increased in urine, while the levels of citrate and magnesium (inhibitors of kidney stone) decreased. On the other hand, rats given the test drug diosgenin had a significantly decreased amount of the different promoters (urea, uric acid and calcium) while a considerable increase in levels of inhibitors (citrate and magnesium) was observed. Histopathology studies indicated that rats treated with diosgenin exhibited less damage to kidney components and less crystal deposition as compared to untreated rats. Levels of antioxidant enzymes also revealed less stress on kidneys due to oxygen derives free radicals. All these studies proved that diosgenin has a preventive effect against the formation of stones in the kidney.

Thus, diosgenin can prove to be a potential drug for treating kidney stones. Studies on animals can be extrapolated and through ethical studies on humans further validation of the drug's efficacy for use in humans can be established. The drug can have a promising role in reoccurrence of stones also as it could prevent the stones from being formed in animals.