

**REVIEW ON PHARMACOLOGICAL ACTION OF NAGRADI*****GHANVATI & SWADANSTRADI KASHAYA IN RENAL CALCULUS***

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**ABSTRACT**

Renal calculi are one of the most common urinary tract diseases. Very often patients suffering from renal calculi are reluctant to surgery but it's not a complete treatment, they look for medical management whether allopathic and homeopathy but in ayurveda good result as compare than other because of proper diet guideline. Male-female ration is 2:1 the peak incidence is observed 2<sup>nd</sup> & 3<sup>rd</sup> decade of life. In developing country bladder stone are common particularly in children. In developing country the incidence of childhood bladder stone is low, renal calculi in adult are more common. If people are having stone, but lack of awareness of the symptoms and not taken proper medication and lifestyle, there may be a chance to increase the size of kidney stone which may leads to urinary tract infections, organs damage/failure may also associate with others chronic diseases. There may be particles like sand anywhere in the urinary tract or large round stone in the bladder. In ayurveda *Nagradi ghanvati & Swadanstradi Kashaya* given by Acharya Chukradutta which has rich properties of *Tikta*(Bitter), *Kashaya*(Astringent) *Rasa*, *Ushana*(Hot) *Veerya*, *Katu*(Pungent) *Vipaka* and *Kapha-Vata shamaka*. Due to above property both medicine is play effective role in management of Renal calculus. Aim of this article is to provide knowledge about pharmacological action of *Nagradi ghanvati & Swadanstradi Kashaya* in Renal Calculus.

**Keywords:** Calculi, *Nagradi ghanvati*, *Swadanstradi Kashaya*

**INTRODUCTION:** Urinary calculi (Stone) consist of aggregates of crystals containing small amount of proteins and glycoprotein's. It is surprising that stone and nephro calcinosis are not more common, science some of the constitutions are present in urine in concentration which is exceed their maximum solubility in water. However urine contains proteins, glycol saminoglycans, pyrophosphate and citrate, which help to keep otherwise insoluble salt in solution.<sup>1</sup> Stone may form at any level in urinary tract, but most arise in the kidney. Urolithiasis is a frequent clinical problem affecting 5% to 10% of Americans in their life time. Men are more prone then women are and the peak age is

between 20 & 30 years. Many of the inborn errors of metabolism, such AS Gout, cystinuria, primary hyperoxaluria provide good examples in hereditary disease characterize by excessive production and excretion of stone-forming substance.<sup>2</sup> Most stone are composed calcium salts or magnesium, ammonium, phosphate – the latter secondary to urea-splitting organism. Most calcium stones are idiopathic. In patients with hyperthyroidism or those who ingest largest large amount of calcium or vitamin- D or in patients which are dehydrated or immobilized, hypercalciuria promote stone formation. Recent studies suggest that calcium stone may be initiated

by cholesterol deposits in the vasa recta at the tip of the renal papilla due to repeated vascular injuries, which eventually reodes in to the calyx, forming a stone nidus.<sup>3</sup> Pain is the main symptoms, pain may be associated with profuse sweating and vomiting. Heamaturia may be complained of either during or after an attack. Pyuria is some time noticed with increase number of white cells may be found in urine even in the absence of infections.<sup>4</sup> In ayurveda acharya charaka is described in *Trimarmiya* chapter<sup>5,6</sup>. The word *Ashmari* is derived in ayurveda is *Ashmanam rati iti ashmari*<sup>7</sup>. It is a disease of *Mootravaha samsthana*, it is not a surgical disease because of Hippocrates motioned in book “I will not cut for the stone, but I leave this to be done by practitioners of this work” and Hippocrates adamantly stated that wounds of the bladder were lethal. Acharya shushrut clearly mentioned it is not completely treat by a surgical procedure in<sup>8</sup> and also ask about *Ashmari* it is a like *Yama*<sup>9</sup> so for that purpose Chakradutta described a formulation *Nagradi Ghanvati* & *Swadanstradi Kashay* for all type of *Ashmari*.<sup>10</sup> which has a rich property to dilute the responsible minerals in urine, splitting stone, anti-inflammatory, antispasmodic, antifungal and antibacterial and play very effective role to treat the disease. The aim of this article is to evaluate the efficacy of *Nagradi Ghanvati* & *Swadanstradi Kashay* in Renal calculi.

#### AIMS & OBJECTIVES:

- (1) To get a absolute knowledge about the Renal calculi.
- (2) To study about the pharmacological effect of *Nagradi Ghanvati* & *Swadanstradi Kashay* in Renal calculi.

#### CAUSATIVE ORGANISM OF RENAL CALACULUS:

**Dietetic:** Deficiency of Vit A caused desquamation of epithelium of epithelium. The cells form a nidus around which stone is deposited. Economic conditions in place where stone are common it is evidence that the inhabitants do suffer dietary imbalance.<sup>11</sup>

**Solute and colloids:** Dehydrations leads to increase concentration of urinary solutes and tends to cause them to precipitate. It has been postulated that reductions of urinary colloids which adsorb solutes or muco proteins which calcium will also result in a tendency for stone.<sup>11</sup>

**Decreased urinary output:** The presences of citrate in urine, 300-900mg, in 24hr as citric acids, tends to keep otherwise relatively insoluble calcium phosphate and citrate in solutions.<sup>11</sup>

**Immobilization:** It is due to caste traction or quadriplegia may leads to marked loss of calcium from bone, resulting hyper calciurea. Renal calculi in immobilization patient is a result of skeletal decalcification.

**Hot climate:** May be the factor responsible for the production of urinary calculus. eg. Punjab & Rajasthan. Due to excessive fluid loss caused by perspiration and atmospheric temperature resulting concentration of urine and diminished urine output. Hotter area is more prone to stone formation so stone are more common in hot and dry areas.

**Dietary Factor:** Over or large intake of calcium and vit-D rich diet.

- **Vegetable:** It is associated with a low incidence of stone disease
- Diet rich in calcium, tomatoes, milk which lead to formation of calcium oxalate stone.
- **Vit-A deficiency:** Vit-A deficiency causes desquamation and squamous

metaplasia of the columnar epithelium of the pelvis of the kidney and these desquamated cell is form Nidus for the formation of calculi.

- Excessive intake of oxalate containing food:-Dietary oxalate are poorly absorbed and doesn't play a major role in formation of oxalate stone.

- Diet rich in calcium:- On regular diet normal urinary excretion of calcium ranges between 200 to 300 mg/day. Milk and proteins also cause increased absorption of calcium from the gut. In certain disease i.e.- myeloma, Paget's disease there is hypercalciuria which favour stone formation. In idiopathic hypercalciurea male exercise more calcium though the serum calcium is normal and serum phosphate is decreased. This may be due to the defective renal tubular reabsorption of calcium. renal tubular acidosis also causes hypercalciurea.

**Metabolic condition:** These include Hyperparathyroidism and gout.

- **Hyperparathyroidism:** Increase serum calcium level resulting in hypercalcinosi and pelvic stone. Excess parathyroid hormone result increase bone re-absorption of calcium from the bone and accounts for more than 5% of stone. Parathyroid hyperplasia or adenomas secrete excess PTH causing increase intestinal absorption of calcium, increased 1, 25- vitamin D3 and increase bone demineralization & calcium release from bone.

- **Gout:** Increase the uric acid level and cause multiple uric acid stone.

### **MECHANISM OF STONE FORMATION<sup>12</sup>:**

- Crystal nucleation
- Crystal Growth
- Crystal aggregation

- Crystal cell interaction
- Endocytosis of CaOx-Crystal by Renal tubular epithelial cell
- Relationship between crystal-cell interaction and renal tubular cell injuries

### **TYPES OF RENAL CALCULI:**

Basically the renal calculi can be divided into two major groups –

- Primary Stone
- Secondary Stone

#### **PRIMARY STONE:**

**Calcium oxalate:** This type of stone is usually single and is extremely hard. It is dark in color due to staining with altered blood precipitation on its surface. It is spiky that means it is covered with sharp projection, which causes bleeding due to injuries to the adjacent tissue. This stone is popularly known as Mulberry stone. On section it shows wavy concentric laminae that means it is formed by deposition of layers of calcium, oxalate on a nidus.<sup>13</sup>

**Uric acid:** Pure uric acid calculi are rare and are not visible in X- Ray. The majority contains urates and enough calcium oxalate to render such calculi radio-opaque. These stones usually occur in multiples and so are typically faceted. The stone are of moderate hardness. Their color varies from yellow to dark brown. Surface of these stone are usually smooth.<sup>13</sup>

**Cystine calculi:** These stones usually appear in patients with cystinuria. Such cystinuria sometimes occurs in young girls. Cystine is an aminoacids rich in sulphur. Cystine calculi usually occur multiple. These calculi are soft and yellow in color. It is usually occurs due to diminished resorption of cystine by the renal tubules. Cystine crystal which are found in urine cystinuria are usually

hexagonal, white and translucent. These usually appear in acid urine.<sup>13</sup>

**Xanthine calculi:** these are extremely rare. These are smooth, round and brick red in color. On cut surface it shows lamellar appearance.<sup>13</sup>

**Indigo calculi:** it is also uncommon that these are merely academic curiosities. These are blue in color and are derived from indicant, formed by decomposition of tryptophan in the intestine and found in the urine.

#### **SECONDARY STONE:**

**Phosphate stone:** Majority of these stones are composed of calcium phosphate, though a few are composed of ammonium magnesium phosphate, known as Triple Phosphate. Such calculus is usually smooth, soft and friable. It is usually dirty white in color. This type of calculus usually occurs in infected urine and so is a secondary calculus. Urine is often alkaline. Such stone enlarges rapidly and gradually fills up pelvis and renal calyces to take up the shape of Staghorn calculus. While majority of such stone are made up of calcium phosphate a few are made up of mixture of calcium phosphate and triple phosphate.

**Mixed stone:** Phosphate stone may occur as covering of a primary stone. Such stone are known as mixed stone. The primary stone is often the calcium oxalate stone. When the urine becomes infected deposits of phosphate occur on the rough surface of calcium oxalate stone. Such stone also occur in alkaline urine.

#### **CLINICAL FEATURES<sup>13</sup>:**

- Quiescent calculus
- Pain Fixed renal pain, Ureteric colic, Referred pain
- Hydronephrosis
- Haematuria

- Burning
- Micturition
- Pyuria
- Dysuria

The location and characteristic of pain in nephro-lithiasis include the following :-

**Stone obstructive uretero-pelvic junction:** Mild to severe deep flank pain without radiation to the groin.

**Stone within ureter:** Abrupt, severe, colicky pain in the flank and lower abdomen, radiation to testicles or vulvar area, intense nausea with or without vomiting.

**Upper ureteral stone:** Radiate to flank or lumbar areas.

**Mid-ureteral Calculi:** Radiate interiorly and caudally.

**Distal ureteral stone:** Radiate into groin or testicle (men) or labia majora (women).

**Stone passes into bladder:** Mostly asymptomatic, rarely positional urinary retention.

**INVESTIGATION<sup>14</sup>:** The diagnosis of renal calculi is usually made easily from the history of finding red blood cell in urine. Investigation is also required to confirm the presence of a stone and to identify the site of stone and degree of obstruction.

- **Straight X-Ray:** About 90% of stone contain calcium and seen in plain abdominal x-ray except Uric acid.
- **Spiral CT:** Give the most accurate assessment and with identified non-opaque stone like Uric acid.
- **USG:** This may show dilatation of the ureter if the stone is obstructing urine flow.
- **Excretory Urography:** To know about the position of urine, how much obstruct and functioning capacity of kidney.

**Table 1- MANAGEMENT OF RENAL CALCULUS IN AYURVEDA**

No.	Drug name	Latin name	Rasa-Guna-Virya-Vipaka	Pharmacological Action
1	<i>Gokshura</i> <sup>15</sup>	<i>Tribulus terrestris</i>	<i>Madhura-Guru-Sheetamadhura</i>	<i>Mutral, Ashmarghna, Bastishotha</i>
2	<i>Varuna</i> <sup>16</sup>	<i>Crataeva nurula</i>	<i>Tikta-Laghu-Ushana-Katu</i>	<i>Mutrasankramana, Bastishoola, Agnimandya, Mutral, Ashmaribhedana</i>
3	<i>Shunthi</i> <sup>17</sup>	<i>Zingiber officinale</i>	<i>Katu-Laghu-Ushana-Madhura</i>	<i>Deepna, Pachana, Aampachaka, Agnideepka</i>
4	<i>Pashanbheda</i> <sup>18</sup>	<i>Bergenia ligulata</i>	<i>Tikta-Laghu-Sheetamadhura</i>	<i>Ashmari bhedana, Mutral, Kapghna</i>
5	<i>Kakmachi</i> <sup>19</sup>	<i>Solanum nigrum</i>	<i>Tikta-Laghu-Anushana-Katu</i>	<i>Mutral, Deepna, Kaphshamaka</i>
6	<i>Eranda</i> <sup>20</sup>	<i>Ricinus communis</i>	<i>Madhura-Snidha-Ushana-Madhura</i>	<i>Mutravishodhana, Mutravedna, Bastishoola</i>

### PHARMACOLOGICAL EFFECT OF DRUG

**(1) *Crateva Nurula*<sup>21</sup>:** The plant is known to relieve, prevent and promote the discharge of urinary stone. It has also been used in the treatment of prostate enlargement and bladder sensitivity, lupeal apentacyclic triterpene isolated from the root bark has been shown to significantly minimize the deposition of urinary stone forming constituents. Bark decoction significantly prevented the deposition of calcium-oxalate in the kidney by inhibiting the glycolic acid oxidase and lactate dehydrogenase (LDH) enzyme activity in liver which are the major oxalate synthesizing enzymes.

**(2) *Tribulus Terrestris*<sup>22</sup>:** The diuretic properties of *Tribulus terrestris* are due to large quantities of nitrates and essential oil present in its fruit and seed. The diuretic activity can also be attributed to the

presence of potassium salt in high concentration. The aqueous extract of *Tribulus Terrestris* is a positive diuresis, which is slightly more than that of frusenamide, sodium and chloride concentration in the urine were increased. The increase tonicity of the smooth muscle, which was produced by TT extract, together with its diuretic activity helped in the propulsion of stone along the urinary tract. An ethanolic extract of TT fruit is urolithiasis properties. It is inhibit the stone formation in various model of urolithiasis using sodium glyconate and ethylene glycol and also inhibit nucleation and growth of the calcium oxalate crystals as well as cyto protective role. Glycolate oxidase (GOX) is one of the principle enzyme involved in the pathway of oxalate synthesis converting glycolate by oxidation and finally to oxalate. The antiurolithic activity of TT is attributed to

its GOX inhibition. Quercetin and kaempferol, the active components of TT, were found to be non-competitive and competitive inhibitors of GOX respectively.

**(3) *Bergenia ligulata*<sup>23</sup>:** *Bergenia ligulata* calcium oxalate ( CaC<sub>2</sub>O<sub>4</sub>) crystal aggregation as well as crystal formation and prevented CaC<sub>2</sub>O<sub>4</sub> crystal deposition in the renal tubules.

**(4) *Zingiber Officinalis*<sup>24</sup>:** In Shunthi [Zingiber officinalis] has a rich phyto chemical compound that scavenge free radicals {H<sup>+</sup>,OH, Uric acid, Lactic acid} produced. In biological system for the purpose of energy production but some free radicals which generated during the process of oxidation are essential. In advanced production of free radicals result in oxidative stress that can lead to DNA damage. The Anti-oxidative properties of Ginger is undoubtedly protect human against many chronic disease. 6-Shogaol has exhibited the most potent anti-oxidant and anti-inflammatory properties in Ginger which can be attributed to the presence of alpha, beta unsaturated Keton moiety. Extract of *Zingiber officinalis*. Ethanol & Acetaminophen. In Ethanol combination of vitamin-E this is protection is mediated by Renal anti-oxidant defense And Acetaminophen induced liver damage so it is also useful in preventing Acute liver injuries. Particularly fresh Ginger methanol extract of drug were found to have better antioxidant action then the n-hexane extract.

**DISCUSSION:** Urinary calculi consists of aggregate of crystals containing small amount of proteins and glycoprotein. Acute loin pain radiating to the groin together with hematuria is typical of ureteric obstruction most commonly due to calculi, different type vary in frequency

around the world, probably as a consequence of dietary and environmental factor, but genetic factor may also contribute. According to Acharya Chukradutta *Nagradi Ghanvati* & *Swadanstradi Kashay* play very effective role in *Ashmari* because of rich properties like *Mutrasankramana*, *Bastishoola*, *Agnimandya*, *Mutral*, *Ashmaribhedana*, *Deepna*, *Pachana*, *Aampachaka*, *Agnideepka*, *Kapghna*. In *Nagradi Ghanvati* 42.8% drugs are *Tikta Rasa*, 28.5% drugs are *Kashaya rasa* and 14.5%-14.2% drug are respectively *Madhura* and *Katu rasa*. 36.3% drug are *Laghu Guna*, 60% drug are *Ushana veerya*, 60% drug are *Katu vipaka* and 33.3%-33.3% drug are *Kaph-vata Shamak* or *Tridoshaja shamaka*. In *Swadanstradi Kashaya* 33.3% drugs are *Kashaya Rasa*, 16.6% drug are *Tikta rasa*, 75% drugs are *Ushna veerya*, 60% drugs are *Kapha-Vata Shamaka*. According to all above properties both medicine have majority of *Tikta*, *Kashaya Rasa*, *Ushana Veerya*, *Katu Vipaka* and *Kapha-Vata shamaka* properties. Due to *Deepan-pachana*, *ushana veerya*, *Katu vipaka* durgs are prevent the formation of intermediately product like H<sup>+</sup>, OH<sup>-</sup>, ions free radical within the blood stream as well as *Shunthi* is *Uttam Aampachaka*, in Ayurveda Lactic acid, Uric acid, Keton bodies are correlated with *Aama*. so both medicine are useful to increase the *Jathragni* (Digestive fire) and metabolism which helpful to digest food material and prevent the formation of *Ama* which is responsible for Stone formation.

**CONCLUSION:** The contents of *Nagradi Ghanvati* & *Swadanstradi Kashaya* has rich chemical constituents in *Shunthi* (Zingiberene, Zingiberol, Olioresin, Gingerin, Gingerol, Shogaol,). *Varuna* (Lauric, Stearic, Undecylic, Oleic and

linolenic acids, alcohol (root), Betulinic acid, Diosgenin,  $\beta$ -sitosterol, Alpha-beta ionones (bark), 1-stachydrine (leaves). *Gokshura* (Saponin Kaempferol, Rutinoside- $\beta$ -sitosterol, Sigmasterol, Amin acids (root), alkaloid, larmine, neotigogenin) *Pashanbhedha* (Bergenin, o-glycoside,  $\beta$ -sitosterol, Catechin-3-gellate and Afzelechin). *Kakmachi* (Riboflavin, nicotinic acid, vitamin-C,  $\beta$ -karotin, steroide glycol-alkeloid, a-b- solanigrine). *Erand* (Albumin ricin, Ricinine, Absolute alcohol, Glyceal acitic acid, Raicin oleic acid). All above chemicals and most of them are amino acids which is very helpful absorptions of calcium and alcohol are also found in *Varuna root* & *Erand* which has diuretic properties. The absorption of calcium mostly occurs in the duodenum by an energy dependent active process. *Nagradi Ghanvati* & *Swadanstradi Kashay* play very effective role in Ashmari because of rich properties like *Mutrasankramana*, *Bastishoola*, *Agnimandya*, *Mutral*, *Ashmaribhedana*, *Deepna*, *Pachana*, *Aampachaka*, *Agnideepka*, *Kapghna*. And because of *Tikta*, *Kashaya Rasa*, *Ushana Veerya*, *Katu Vipaka* and *Kapha-Vata shamaka*. Due to all above property both medicine is play important role in management of Renal calculus.

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