

Treatment of Urolithiasis with medicinal plant *Phyllanthus niruri*

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ABSTRACT: *Phyllanthus niruri* is a globally distributed herb used to treat Urolithiasis. *Phyllanthus niruri* has been shown to affect several stages of stone formation, reducing crystals aggregation, modifying their structure and composition as well as altering the interaction of the crystals with tubular cells which lead to reduce subsequent endocytosis. The plant have some clinical beneficial affects like ureteral relaxation, elimination of calculi, decrease in the excretion of calcium and other substances that result in urine crystallization. During in-vivo/in-vitro or clinical studies, no toxic effects on kidneys, heart, brain or nervous system are found. Through these studies, it is clear that *Phyllanthus niruri* has preventive measures against stone formation or elimination but validation of longer term randomized clinical trials are very necessary for its medical benefit.. *Phyllanthus niruri* reduces hyperoxaluria and hyperuricosuria; also inhibit the crystallization of calcium oxalate. Without any side effects the efficacy of shock wave lithotripsy is increased due to reduction of crystallization. Theobromine has been shown to reduce uric acid crystallization in patients, making it an effective dietary supplement to treat these stones.

KEYWORDS: *Phyllanthus niruri*, Stone breaker, Urolithiasis, Ureterscopy, Prevalence

I. INTRODUCTION

Phyllanthus niruri a small herb commonly known as “STONE BREAKER” [1]. It belongs to the Euphorbiaceae family and it is found to be used in folk Brazilian medicine for the treatment of urolithiasis. *Phyllanthus niruri* was found to contain about 50 different chemicals, including triterpenes, alkaloids, flavanoids, and lignans. The triterpenes have been found to inhibit the cytotoxicity induced by calcium oxalate well as to reduce excretion of stone forming constituents in the kidney [2]. The plant mainly grows in rainy season. And because the herb grows in land (bhumi) it is also known as “Bhui Amla”. The herb is called Bhumyamalaki in South India and used to treat constipation, gonorrhoea and syphilis. The herb contains

pharmacological activities including anti-viral, anti-bacterial, anti-inflammatory, antiplasmodial, anti-malarial, anti-diabetic, diuretic, hypolipidemic, antioxidant, hepatoprotective, nephroprotective and anticancer properties. *Phyllanthus niruri* L. has also shown to act as immunomodulator against Covid-19 [3]. The different names of this herbal plant in different languages are Bahupatra (Sanskrit), Bhui amla, Jangli amla (Hindi), Bhanya amla (Gujrati), Chanca piedra (Spanish), Quebra-pedra (Portuguese), Keezha nelli (Tamil), Keezhar nelli (Malayalam), Turi hutan and Meniran hijau (Indonesian) [4]. In Ayurveda and Unani system of medicine the plant has its important activities [5]. Urolithiasis or kidney stones are a commonly occurring worldwide disease. The symptoms are characterized by back pain, abdominal pain, hematuria, nausea, and vomiting. It can cause serious urinary tract infection, acute renal function declines, urinary tract obstruction, and other adverse consequences [6].

HISTORICAL BACKGROUND

During sixteenth to eighteenth centuries the widespread of Urolithiasis disease was found to be increased in all ages and social groups due to change in nutritional habits as well as consumption of alcohol [7]. In El Amrah, Egypt a mummy of 4500-5000 years old was found to have bladder stone by an English archeologist E. Smith in 1901[8][9]. Over the past few decades it is seen that urolithiasis is more common in children because of rapid variations in habits and increasing affluence [10]. The pain of urolithiasis is one of the painful disease that affects a human physically and mentally [11].

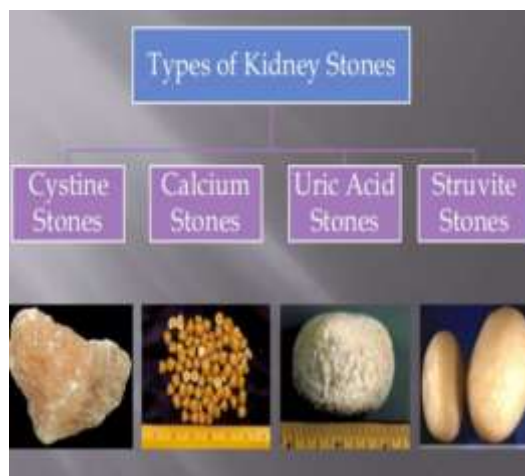
TYPES OF STONES

Calcium stone (70-80%): Calcium stones consists of Calcium oxalate stone and Calcium phosphate stone are the most common kidney stone. Calcium oxalate stones consists of Calcium oxalate monohydrate (COM), and Calcium oxalate dehydrate (COD) [12].

Uric acid stone (5-10%): Uric acid stones are round, smooth and red- orange in colour and are radiolucent. These stone can be detected by Ultrasonography or CT . Uric acid stone are formed due to low urinary uric acid levels, low urine pH, and low urinary volume [13].

Struvite stone: Struvite stones are composed of magnesium ammonium phosphate. They are formed when bacteria like Proteus or Klebsiella converts the urea into ammonia which increases the urine pH [14].

Cystine stone (1%): Cystine stones are extremely hard stone. They are formed in acidic urine. Cystinuria is a genetic disorder in which Cystine starts to leak from blood to urine and its lead to form stones in the kidney [15]. Cystine stones are rare and hereditary [16].



SIZES OF KIDNEY STONES

The average size of a kidney stone is approximately 5 mm. Stone less than 4mm can pass through the urine easily without any medication.

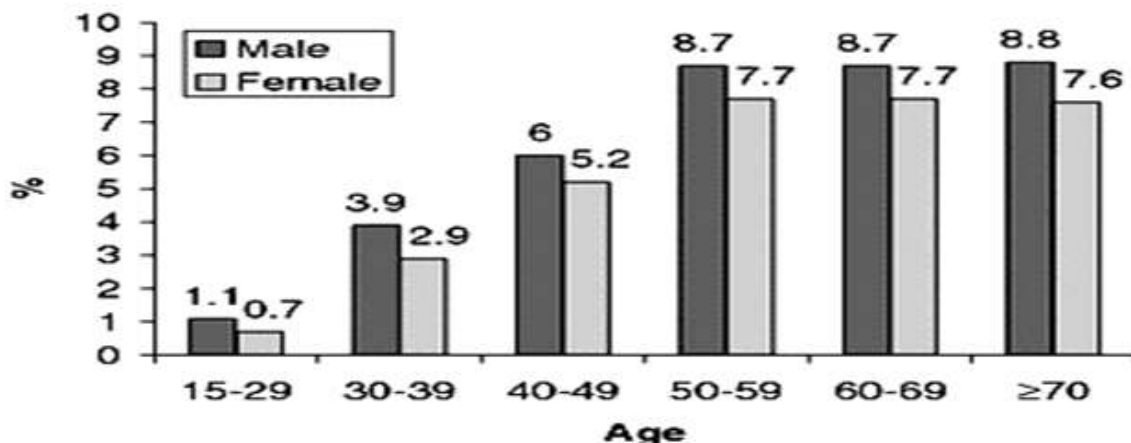
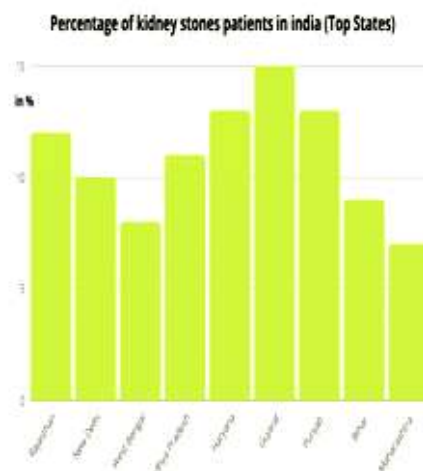
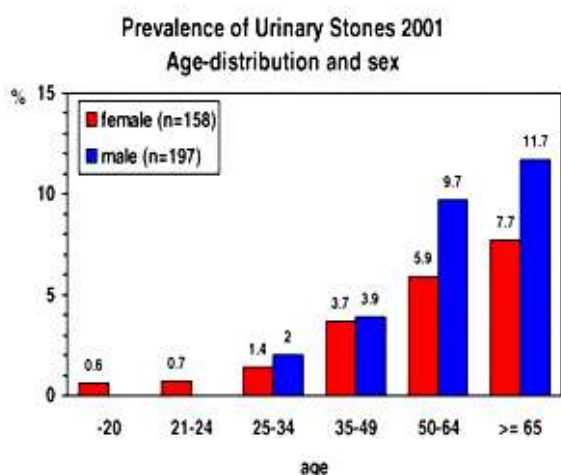
SIZE OF KIDNEY STONES	CHANCES OF PASSING NATURALLY	TIME REQUIRED TO PASS NATURALLY
Less than 2mm	About 80%	8 days (average)
2-4 mm	About 80%	12 days (average)
4mm	About 80%	31 days (average)
4-7mm	About 60%	45 days (average)
Larger than 7mm	About 20%	12 months (average)
1-2cm	Cannot pass	—
Larger than 2cm	Cannot pass	—

Table: sizes of kidney stones. [17]

EPIDEMIOLOGY

About 12% of the world population is affected by the disease Urolithiasis. It has been seen that men between the ages of 20-49 are more likely than women to be affected by Kidney stones. According to recent studies, Urolithiasis has been increasing due to lack of food and lifestyle changes [18]. The prevalence of urolithiasis was 5.7% in Iran in 2005, 8.8% in North America between 2007-2010, 5%-10% in Europe, and 7.54% in

Mainland China between 1990 -2016. [19]. Calcium Oxalate is the major component for causing Urolithiasis. It has been demonstrated that Obesity and Metabolic Syndrome are the risk factors of Urolithiasis. It has been found that, occurrence of Urolithiasis increases with ages. In males around 80 years of old had the highest occurrence 19.7 %, 18.8% in male 60-79 years of age, 11.5% in male 40-59 years of age, and 5.1% in male adults 20-39 years of age [20].



CLINICAL MANAGEMENT

In 1980s the treatment known as Shockwave lithotripsy (SWL) was introduced. And due to low costs and recurrence the treatment Ureteroscopy is increasing for removal of smaller stones [21]. Clinical management of Urolithiasis involves Medical expulsion therapy (MET), Dietary management and Disease specific treatment [22]. MET- It is usually means an unsurgical attempt to help to pass the kidney stone

with the help of prescription medication. In this therapy alpha blocker medication is prescribe to take up to 4-6 weeks which results in relaxation of ureter muscle to pass the stone easily. Intake of plenty of fluids is highly recommended [23]. Dietary management- The initial stage for the treatment of Urolithiasis is intake of high amount of fluids to produce at least 2.5L urine per day [24]. According to studies it is found that Urolithiasis are unaffected by Vitamin B (riboflavin, thiamine, niacin, B12, and

B6). People consuming fish liver oils, Vitamin D or other calcium-containing mineral supplement are found to discover kidney stones [25]. Minimized the daily sodium (salt) consumption to not more than 2300 mg (teaspoon) because sodium increases the amount of calcium in urine [26]. Fruits and vegetable contain citrate which help to reduce the formation of kidney stone [27].

CHINESE HERBAL MEDICINE(CHM) IN THE TREATMENT OF UROLITHIASIS

After giving 2gms of *P. niruri* extract daily to the patient in the treatment condition and control group for 3 months, it was found to have no Kidney Stones. This indicates that self – administration of

P. niruri on a regular basis may arise the rate of stone- free patients, particularly those with lower calical location. Oxygen heterocycles, amino acids, carboxyl, and hydroxyl group are the active component of CHM which have the inhibiting characteristics that prevent Hypercalcemia and reduce urine saturation. These components adhere to the crystal's development location to prevent Urolithiasis from accumulating further. In Clinical study, the anti-urolithiasis effectiveness of *P. niruri* Linn was found in 150 patients with extracorporeal shock wave lithotripsy and calcium oxalate kidney stones. For the treatment and prevention of Urolithiasis CHM has been used in US, Brazil, India and many other nations for many years.

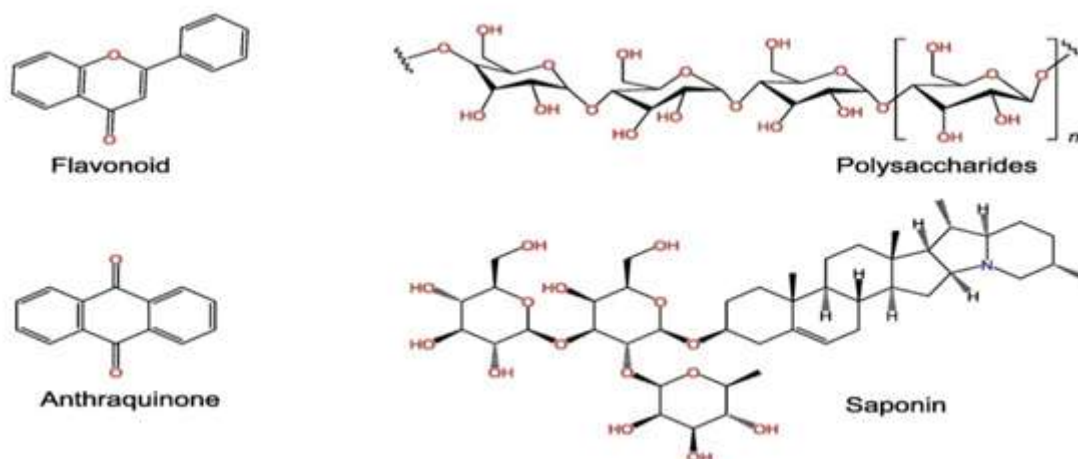


Fig: Active ingredient of CHMs in the treatment of Kidney stones

CHMs	Chinese names	Parts used	Dosage used
<i>Lysimachia christinae</i> Hance	Jinqiancao	Whole plant	A daily dose of 150 to 200 g for over six months
<i>Alisma orientale</i> (Sam.) Juzep.	Zexie	Roots	5 to 10 g
<i>Tribulus terrestris</i> L.	Jili	Fruits	6 to 10 g
<i>Lygodium japonicum</i> (Thunb.) Sw.	Haijinsha	Seeds	6 to 12 g
<i>Salvia miltiorrhiza</i> Bge.	Danshen	Roots	5 to 15 g
<i>Boerhavia diffusa</i> L.	Laolaiqing/ Huangxixin	Roots	3 to 9 g
<i>Aquilaria sinensis</i> (Lour.) Gilg.	Chenxiang	Wood	1 to 5 g, Decocted later
<i>Crocus sativus</i> L.	Fanhonghua	Flowers	1.5 to 3 g
<i>Carthamus tinctorius</i> L.	Honghua	Flowers	3 to 10 g
<i>Paeonia lactiflora</i> Pall.	Baishao	Roots	6 to 12 g, An overdose or long-term use may damage liver function

<i>P. petiolosa</i>	Shiwei	Leaves	6 to 12 g, decocted later
Wuling San (<i>Polyporus umbellatus</i> (Pers.) Fries, <i>Poria cocos</i> (Schw.) Wolf, <i>Atractylodes macrocephala</i> Koidz, <i>Alisma orientale</i> (Sam.) Juzep., <i>Cinnamomum cassia</i> Presl)	Wuling San	Chinese herbal compound	200 mL twice a day
Zhuling Tang (<i>Polyporus umbellatus</i> (Pers.) Fries, <i>Poria cocos</i> (Schw.) Wolf, <i>Alisma orientale</i> (Sam.) Juzep., <i>Equus asinus</i> L., <i>Talcum</i>)	Zhuling Tang	Chinese herbal compound	200 mL twice a day

Table: Chinese Herbal Medicine to prevent kidney stone [28]

UROLITHIASIS SIGNS AND SYMPTOMS

- Renal colic (intense cramping pain)
- Hematuria (bloody urine)
- Flank pain (pain in the back side)
- Obstructive uropathy (urinary tract disease)
- Blockage of urine flow
- Hydronephrosis (dilation of the kidney)
- Nausea
- Vomiting [29]

II. CONCLUSION

Urolithiasis or kidney stones are a commonly occurring worldwide disease. It has been shown that *Phyllanthus niruri* aids in the elimination of stones. Kidney stone prevention and management requires both nutritional and clinical interventions. Dehydration is the major risk of kidney stone. Herbal remedies are also more readily available, less likely to have adverse effects, eco-friendly, affordable, and have a high safety margin. Therefore *Phyllanthus niruri* plays a great role in herbal medicine, particularly for the treatment of urinary stones,

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