Formulation and Evaluation of Kidney Stone Capsule by using Achyranthes Aspera

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I. INTRODUCTION

The term "urolithiasis" is derived from the Greek words ouron meaning urine and lithos meaning stone, referring to the formation of hard mineral concretions anywhere within the urinary tract. When these stones form specifically within the kidneys, the condition is termed nephrolithiasis, from the Greek nephros (kidney), and the passage of these stones through the ureter produces the characteristic excruciating pain known as renal colic one of the most severe and memorable pain experiences in all of clinical medicine.

Kidney stones are among the oldest diseases known to mankind, with urinary calculi having been found in the pelvis of an Egyptian mummy estimated to be over 7,000 years old. Despite this ancient history, urolithiasis remains one of the most prevalent and burdensome urological conditions in the modern era. Globally, the lifetime risk of developing a kidney stone is approximately 10–15% in developed countries and 5–10% in developing countries, with a particularly high prevalence in the hot, arid regions of the Indian subcontinent especially the so-called "stone belt" of northern India encompassing Rajasthan, Gujarat, Punjab, and Maharashtra.

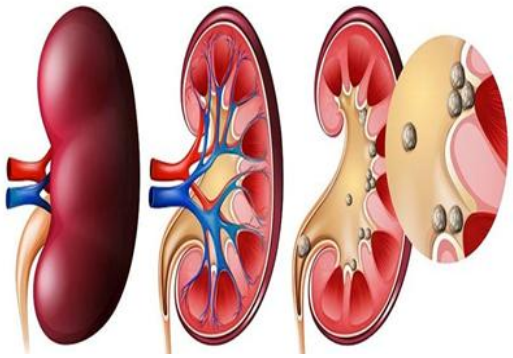

Fig.No.1

India bears a disproportionately large burden of kidney stone disease due to a combination of climatic factors (high ambient temperatures leading to dehydration and concentrated urine), dietary habits (high oxalate and protein intake), inadequate daily fluid consumption, genetic predisposition, and limited access to preventive healthcare and regular follow-up. The prevalence of urolithiasis in India is estimated at 12% of the total population, with a recurrence rate of 50% within 5–10 years of the first stone episode making prevention of recurrence the most critical therapeutic challenge in kidney stone management.

The primary pathophysiological mechanism of kidney stone formation involves supersaturation of urine with stone-forming ions calcium, oxalate, phosphate, or uric acid beyond their thermodynamic solubility product. This supersaturation drives nucleation of microscopic crystals that, if not cleared by adequate urine flow, aggregate and grow into macroscopic stones. The balance between promoters of crystallization (calcium, oxalate, uric acid) and natural inhibitors (citrate, magnesium, Tamm-Horsfall protein) determines whether stone formation occurs in any given individual, and interventions that tip this balance toward inhibition are the basis of kidney stone prevention.

Current pharmacological prevention strategies potassium citrate to alkalinize urine and chelate calcium, thiazide diuretics to reduce urinary calcium excretion, allopurinol to reduce uric acid production, and dietary modifications while evidence-based, suffer from poor long-term patient compliance due to the inconvenience of multiple daily medications, adverse effects, cost, and the chronic asymptomatic nature of stone recurrence risk that reduces patient motivation for preventive therapy. This creates a compelling need for natural, affordable, palatable, and well-tolerated herbal alternatives with anti-urolithic activity.

Achyranthes aspera Linn. (Family: Amaranthaceae) known variously as Prickly Chaff Flower, Chirchita (Hindi), Aghada (Marathi), Nayuruvi (Tamil), and Apamarga (Sanskrit) is a robust, widespread weed found throughout India, tropical Africa, and Asia that has been used in traditional medicine for thousands of years. Despite its common status as a roadside weed, Achyranthes aspera possesses a remarkably rich and pharmacologically active phytochemical profile. Its roots, aerial parts, seeds, and leaves contain an impressive array of bioactive compounds including saponins (achyranthine the principal alkaloid), betaine, ecdysterone, oleanolic acid, flavonoids, tannins, sterols (stigmasterol, beta-sitosterol), amino acids, and numerous mineral salts.

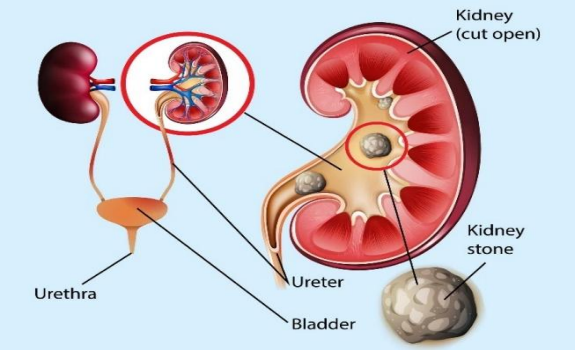

Fig.No.2

The anti-urolithic properties of Achyranthes aspera are well-supported by traditional use and increasingly by modern experimental evidence. Studies have demonstrated that Achyranthes aspera extracts significantly increase urine output (diuretic effect), reduce urinary calcium and oxalate concentrations, inhibit calcium oxalate crystal nucleation and aggregation in vitro, increase urinary excretion of citrate and magnesium (natural stone inhibitors), and reduce renal oxidative stress markers that promote crystal adhesion to tubular epithelium. These multiple complementary mechanisms address the stone formation process at multiple points simultaneously, making Achyranthes aspera a scientifically compelling candidate for herbal anti-urolithic capsule formulation.

The hard gelatin capsule dosage form is particularly well-suited for delivering Achyranthes aspera powder. Capsules are easy to swallow, mask the taste and odour of herbal powders, allow accurate and reproducible dosing, are readily accepted by patients, and can be manufactured with minimal processing that preserves the integrity of heat-sensitive phytochemical constituents. The present work therefore aims to formulate and evaluate a standardized Achyranthes aspera powder-filled hard gelatin capsule with optimized pharmaceutical excipients as a practical, effective, and patient-acceptable herbal anti-urolithic preparation.

Types of Kidneys Stones:

1. Calcium Oxalate Stones (Most Common)
2. Calcium Phosphate Stones
3. Uric Acid Stones
4. Struvite Stones (Infection Stones)
5. Cystine Stones
6. Mixed Composition Stones
7. Drug-Induced Kidney Stones

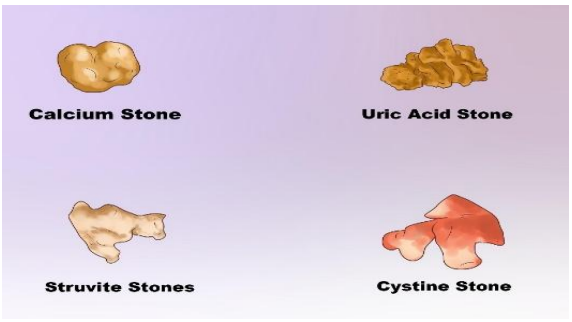

Fig.No.3

a) Calcium Oxalate Stones:

Calcium oxalate stones are the most prevalent type, accounting for 70–80% of all urinary calculi and representing the primary therapeutic target of Achyranthes aspera-based anti-urolithic preparations. They occur in two polymorphic forms: calcium oxalate monohydrate (whewellite) denser, harder stones associated with hyperoxaluria and renal tubular injury and calcium oxalate dihydrate (weddellite) softer, more friable stones associated with hypercalciuria. Risk factors include hypercalciuria, hyperoxaluria, hypocitraturia, low urine volume, and recurrent urinary tract infections. Achyranthes aspera acts on multiple aspects of calcium oxalate stone formation simultaneously through its diuretic, crystal-inhibitory, and antioxidant mechanisms.

b) Calcium Phosphate Stones:

Calcium phosphate stones hydroxyapatite and brushite account for 10–20% of urinary calculi and form

preferentially in persistently alkaline urine (pH > 6.5). They are strongly associated with renal tubular acidosis (RTA) Types 1 and 3, primary hyperparathyroidism, and urinary tract infections with urease-producing organisms. Unlike calcium oxalate stones, calcium phosphate stones tend to be soft and crumble easily but may grow rapidly into large staghorn configurations in the presence of persistent alkaline urine and infection.

c) Uric Acid Stones:
Uric acid stones account for 5–10% of urinary calculi and have the unique clinical characteristic of being radiolucent invisible on plain abdominal X-ray and potentially completely dissolvable with medical therapy. They form in persistently acidic urine (pH < 5.5) and are strongly associated with gout, metabolic syndrome, obesity, type 2 diabetes mellitus (which causes insulin resistance-related impairment of ammonium excretion, leading to acidic urine), and high purine dietary intake. Raising urine pH to 6.0–6.5 with potassium citrate or sodium bicarbonate can dissolve existing uric acid stones and prevent new formation.

d) Struvite Stones (Infection Stones):
Struvite stones composed of magnesium ammonium phosphate (struvite) with or without calcium carbonate-apatite form exclusively in the presence of urinary tract infections caused by urease-producing bacteria, most commonly Proteus mirabilis, Klebsiella pneumoniae, and Pseudomonas aeruginosa. Bacterial urease hydrolyzes urea to ammonia, raising urinary pH above 7.0 and creating the supersaturated alkaline conditions necessary for struvite precipitation. These stones grow rapidly, can fill the entire renal collecting system as staghorn calculi, and invariably require both surgical removal and antibiotic therapy.

e) Cystine Stones:
Cystine stones are the least common major stone type (1–2%) but are caused exclusively by cystinuria a specific inherited autosomal recessive defect in the renal tubular transporter (SLC3A1 and SLC7A9 genes) responsible for reabsorbing cystine and other dibasic amino acids from the glomerular filtrate. Excess urinary cystine exceeds its low solubility threshold and precipitates to form characteristic hexagonal cystine crystals that aggregate into hard, waxy, yellow-brown stones. Cystine stones are highly resistant to fragmentation by extracorporeal shock wave lithotripsy and require massive hydration, urine alkalinization, and thiol-binding agents for management.

f) Mixed Composition Stones:
A clinically significant proportion of kidney stones do not consist of a single pure mineral type but rather contain two or more mineral components in varying proportions throughout the stone a result of the complex and often changing metabolic environment of the individual stone former over time. The most common combinations involve calcium oxalate and calcium phosphate. Mixed stones frequently have a calcium oxalate core with calcium phosphate outer layers, or vice versa, reflecting changes in urinary pH and supersaturation over the period of stone growth.

g) Drug-Induced Kidney Stones:
Certain medications can crystallize directly in the renal tubules or urinary collecting system and form drug stones when urinary drug concentrations exceed solubility limits. Commonly implicated drugs include the HIV protease inhibitor indinavir (the most well-known drug stone former), acyclovir, sulfonamides (sulfadiazine), triamterene (a potassium-sparing diuretic), ciprofloxacin, amoxicillin, and ephedrine. Drug stones are typically managed by discontinuing the offending medication, increasing fluid intake, and adjusting urinary pH to reduce drug crystallization.

Symptoms:
1. Sudden, severe, colicky flank pain radiating to the groin the hallmark of ureteral stone passage Renal Colic:
2. Pink, red, or brown urine from bleeding caused by stone abrasion of the urinary tract lining Hematuria:
3. Increased urge to urinate with reduced urine output when stone obstructs ureter Urinary Frequency/Urgency:
4. Pain or burning sensation during urination from lower urinary tract stone irritation Dysuria:
5. Nausea and vomiting accompanying the severe visceral pain of renal colic Nausea/Vomiting:
6. High fever with chills indicating secondary urinary infection a medical emergency Fever and Chills:
7. Persistent dull ache or heaviness in the flank with a stationary kidney stone Flank Discomfort:

8. Passage of gritty or sandy particles in the urine when small stones are expelled Gravel in Urine:

Fig.No.4

Causes:

1. Low daily fluid intake leading to concentrated urine supersaturated with stone-forming salts
2. Hypercalciuria excess urinary calcium from primary hyperparathyroidism, vitamin D excess, or absorptive causes
3. Hyperoxaluria excess urinary oxalate from dietary excess, malabsorption, or primary hyperoxaluria
4. Hypocitraturia low urinary citrate, the most important natural inhibitor of calcium stone formation
5. High dietary sodium increasing urinary calcium excretion
6. High animal protein diet increasing uric acid, calcium, and oxalate excretion
7. Genetic predisposition family history of urolithiasis significantly increases individual risk
8. Recurrent urinary tract infections with urease-producing organisms causing struvite stones
9. Hot climate and excessive sweating reducing urine volume and concentrating stone-forming ions
10. Metabolic conditions gout, obesity, diabetes mellitus, inflammatory bowel disease

Pathophysiology

A) Mechanism of Kidney Stone Formation:

1. Supersaturation of urine occurs when the concentration of stone-forming ions calcium, oxalate, phosphate, or uric acid exceeds the thermodynamic solubility product for that ion combination in urine at the prevailing pH and temperature.
2. Nucleation the formation of the first microscopic crystal embryo from the supersaturated solution occurs either homogeneously (in solution alone) or, more commonly, heterogeneously on pre-existing surfaces such as renal tubular cell membranes, cellular debris, or foreign bodies.
3. Crystal growth follows as additional ions from the supersaturated solution deposit onto the surfaces of existing nuclei, enlarging the crystals. The rate of crystal growth is proportional to the degree of supersaturation.
4. Crystal aggregation occurs when individual crystals clump together to form larger particle masses through electrostatic interactions and protein bridging creating particles too large to be flushed freely through the tubular lumen.
5. Crystal retention in the renal papilla adhesion of aggregated crystals to the apical membrane of renal tubular epithelial cells is the critical step that determines whether a crystal mass becomes a clinically significant stone or is successfully eliminated in urine flow.
6. Crystal adhesion to tubular cells is mediated by crystal-binding surface molecules including osteopontin, CD44, and annexin II whose expression is dramatically upregulated by oxidative stress caused by crystal-epithelial contact, creating a vicious cycle of increasing adhesion.
7. The retained crystal mass continues to grow, aggregate, and eventually forms a macroscopic stone in the renal papilla or collecting system that can cause obstruction, pain, and renal damage.

B) Role of Oxidative Stress in Stone Formation:

1. Calcium oxalate crystals that deposit on renal tubular epithelial cells generate reactive oxygen species (ROS) through activation of NADPH oxidase and impairment of mitochondrial function creating a state of intense local oxidative stress.
2. ROS cause lipid peroxidation of tubular cell membranes, DNA strand breaks, protein carbonylation, and mitochondrial injury collectively producing oxidative stress-induced tubular cell injury.
3. Oxidative stress activates NF-κB in tubular cells, upregulating the expression of pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6 that promote further crystal adhesion and stone growth.
4. Injured tubular cells dramatically increase expression of crystal-binding surface molecules (osteopontin, CD44, hyaluronan), promoting adhesion of more crystals and creating a self-perpetuating cycle of crystal retention.

5. Achyranthes aspera's rich flavonoid, tannin, and saponin content provides potent antioxidant protection that neutralizes ROS generated by crystal-cell contact, reducing oxidative stress-induced crystal-binding molecule upregulation and breaking this vicious cycle.

C) Anti-Urolithic Mechanism of Achyranthes aspera:

1. Diuretic activity saponins and flavonoids in Achyranthes aspera promote significant increase in urine output through osmotic and natriuretic mechanisms, diluting stone-forming ions and reducing urine supersaturation the most fundamental anti-urolithic intervention.
2. Crystal nucleation inhibition Achyranthes aspera extracts have demonstrated direct in-vitro inhibition of calcium oxalate crystal nucleation, reducing the rate of crystal embryo formation from supersaturated calcium oxalate solutions.
3. Crystal growth inhibition polyphenolic compounds from the plant adsorb onto the surfaces of growing calcium oxalate crystals, blocking active growth sites and preventing further ion deposition slowing crystal growth rate.
4. Crystal aggregation inhibition Achyranthes aspera extract inhibits the clumping of individual crystals into larger aggregates, maintaining crystals at small sizes that can be more easily flushed out in urine flow.
5. Increased urinary inhibitor excretion treatment with Achyranthes aspera has been associated with increased urinary excretion of citrate and magnesium both natural inhibitors of calcium oxalate crystallization.
6. Antioxidant protection of renal tubular epithelium the plant's flavonoids and tannins scavenge ROS at the tubular epithelial cell surface, reducing oxidative stress-mediated crystal adhesion molecule upregulation and preventing crystal retention.

II. AIM AND OBJECTIVE

Aim: Formulation and Evaluation of Kidney Stone Capsule by using Achyranthes Aspera

Objective:

1. To collect, authenticate, and process Achyranthes aspera plant material for capsule formulation.
2. To prepare dried powder of Achyranthes aspera suitable for encapsulation.
3. To design multiple capsule formulations (F1, F2, F3) using varying drug loads of Achyranthes aspera powder.
4. To select appropriate excipients (diluents, disintegrants, lubricants, glidants) for stable capsule formulation.
5. To evaluate pre-compression parameters of the powder blend (angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio).
6. To encapsulate the prepared formulations into hard gelatin capsules of suitable size.
7. To evaluate post-compression parameters (weight variation, disintegration time, hardness, friability, drug content uniformity).
8. To perform phytochemical screening of Achyranthes aspera powder for active constituents.
9. To determine the in-vitro dissolution profile of the formulated capsules.
10. To assess the in-vitro anti-urolithiatic activity (calcium oxalate crystallization inhibition assay).
11. To compare the performance of different formulations (F1, F2, F3) based on evaluation parameters.
12. To establish the correlation between drug load and capsule performance.
13. To optimize the best formulation for reproducibility and therapeutic potential.
14. To conclude the suitability of Achyranthes aspera powder capsules as a cost-effective herbal remedy for kidney stones.

III. PLAN OF WORK

1. Introduction and Review of Literature
2. Collection and Authentication of Achyranthes aspera Plant Material
3. Preparation and Standardization of Achyranthes aspera Powder
4. Phytochemical Screening of Achyranthes aspera Powder
5. Selection of Excipients as per Indian Pharmacopoeia
6. Drug-Excipient Compatibility Study
7. Formulation of Anti-Urolithic Capsules (F1, F2, F3)
8. Evaluation of Capsule Formulations Physicochemical Parameters
9. In-Vitro Drug Release / Dissolution Study
10. Stability Studies as per ICH Guidelines
11. Result and Discussion
12. Conclusion and References

IV. LITERATURE SURVEY

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10. Pharmaceutical Jurisprudence Mithal B.M. Vallabh Prakashan, 2019 Covers regulatory guidelines for herbal capsule formulations and Schedule M requirements in India.

V. MATERIAL AND METHOD:

Material

Drug: Achyranthes aspera Plant Powder (Aerial parts self-prepared and standardized)

Excipients: Microcrystalline Cellulose IP (MCC), Maize Starch IP, Magnesium Stearate IP, Talc IP, Hard Gelatin Capsule Shells Size 0 (Empty).

Equipment: Mortar and Pestle, Mechanical Grinder, Sieves (Mesh No. 40, 60, 80), Desiccator, Capsule Filling Machine (Manual/Semi-automatic), Beaker, Conical Flask, Water Bath, Hot Air Oven.

Instruments: Analytical Weighing Balance, UV-Visible Spectrophotometer, HPLC System, pH Meter, Bulk Density Apparatus, Disintegration Tester, Dissolution Apparatus USP Type II (Paddle), Vernier Caliper, Hardness Tester.

Method

Step 1: Preparation of Achyranthes aspera Powder

1. Collect fresh Achyranthes aspera plant material preferably aerial parts (stems, leaves, and flowers) during the flowering season from a clean, pollution-free area. Authenticate the plant material botanically using macroscopic and microscopic identification characters.

2. Wash the collected plant material thoroughly under running water to remove soil, dust, and surface contaminants. Rinse with distilled water.

3. Shade-dry the washed plant material at room temperature (25–30°C) for 10–14 days, or dry in a hot air oven at 40–45°C for 48–72 hours until completely moisture-free and crispy.

4. Grind the completely dried plant material in a mechanical grinder to obtain a coarse powder.

5. Pass the powder through an 80-mesh sieve to obtain a uniform, fine powder suitable for capsule filling.

6. Determine the moisture content (Loss on Drying) of the powder should be not more than 8% w/w.

7. Perform phytochemical standardization determine total saponin content using the gravimetric method and total phenolic content by Folin-Ciocalteu method to standardize the batch for consistent pharmacological activity.

8. Store the standardized Achyranthes aspera powder in an airtight, dark amber glass container in a cool, dry place away from light and moisture.

VI. PLANT PROFILE

Achyranthes aspera Linn. Prickly Chaff Flower
Drug Name: Achyranthes aspera (Aerial parts, roots, and seeds)

Fig.No.5

Biological Source: The drug consists of the dried aerial parts (stems, leaves, flowers) and/or roots of Achyranthes aspera Linn.
Family: Amaranthaceae
Common Names: Prickly Chaff Flower (English), Chirchita / Latjira (Hindi), Aghada (Marathi), Apamarga (Sanskrit), Nayuruvi (Tamil), Uttareni (Telugu), Kadaluri (Kannada)

Chemical Constituents of Achyranthes aspera:
• Achyranthine principal alkaloid saponin; primary anti-urolithic and diuretic active
• Betaine (Trimethylglycine) amino acid derivative with osmoprotective and diuretic properties
• Ecdysterone (20-Hydroxyecdysone) phytoecdysteroid with anabolic and anti-inflammatory activity
• Oleanolic Acid pentacyclic triterpenoid with diuretic, anti-inflammatory, and hepatoprotective activity
• Saponins multiple steroidal and triterpenoidal saponins contributing to diuretic effect
• Flavonoids Rutin, Quercetin, Kaempferol (antioxidant, anti-inflammatory, crystal-inhibitory)
• Tannins Gallic acid, Ellagic acid (antioxidant, astringent, crystal-binding inhibitors)
• Beta-sitosterol and Stigmasterol (Plant sterols with anti-inflammatory activity)
• Amino acids Serine, Glutamic acid, Proline
• Minerals Potassium (supports diuresis and urinary alkalinization), Calcium, Iron

Morphological Characteristics of Achyranthes aspera Plant and Powder:
• Plant: Annual or perennial herb, 30–90 cm tall, with quadrangular, hairy stems and opposite, simple leaves.
• Flowers: Small, greenish flowers in long, spike-like inflorescences with persistent, sharp, reflexed bracteoles.
• Powder Colour: Light brownish-green to grey-green powder.
• Powder Odour: Faint, characteristic, slightly astringent.
• Powder Taste: Slightly bitter, astringent.

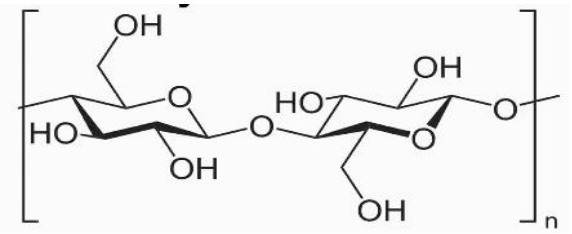
Traditional / Ethnobotanical Uses:
• Anti-urolithic traditional remedy for kidney and bladder stones in Ayurveda (listed as Apamarga).
• Diuretic promotes urine production and kidney flushing, used for urinary retention.
• Anti-inflammatory used for arthritis, rheumatism, and inflammatory conditions.
• Wound healing leaf paste applied to wounds, ulcers, and skin infections.
• Anthelmintic used to expel intestinal worms.
• Febrifuge used to reduce fever in traditional practice.
• Dental care stem used as tooth brush (datun) for its antimicrobial properties.

Pharmacological Activities (Scientifically Documented):
• Anti-urolithic inhibits calcium oxalate crystal nucleation, growth, and aggregation; increases urine output and urinary citrate; reduces renal oxidative stress.
• Diuretic significant increase in urine volume and urinary electrolyte excretion documented in animal studies.
• Antioxidant potent free radical scavenging activity from flavonoids and tannins.
• Anti-inflammatory inhibits COX-2, NF-κB, and pro-inflammatory cytokine production.
• Antimicrobial broad-spectrum activity against gram-positive and gram-negative bacteria.
• Hepatoprotective oleanolic acid and betaine protect liver cells from oxidative damage.
• Antidiabetic improves insulin sensitivity and reduces blood glucose in animal models.

Fig.No.6

VII. EXCIPIENTS

1. Microcrystalline Cellulose IP (MCC)
Official Name: Microcrystalline Cellulose (IP, USP, BP) Avicel PH 101/102



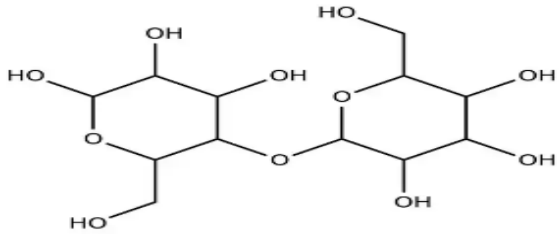
Chemical Name: Partially depolymerized cellulose polymer of β-1,4-linked D-glucose units

Category: Diluent / Filler, Binder, Mild Disintegrant, Glidant multifunctional excipient

Description:
• Colour: White or almost white, fine or granular powder.
• Odour: Practically odourless.
• Taste: Practically tasteless.
• Solubility: Practically insoluble in water, dilute acids, and most organic solvents.

Uses:
• Primary diluent provides bulk to bring the capsule fill weight to the required total (0.82–0.88 g per capsule) while maintaining consistent capsule appearance and volume.
• MCC concentration is varied inversely with Achyranthes aspera powder F1 (0.20 g), F2 (0.15 g), F3 (0.10 g) allowing higher drug loading in F3 while maintaining total capsule weight.
• Excellent compressibility and flowability facilitates uniform powder flow into capsule shells during filling, reducing weight variation.
• Mild disintegrant activity swells slightly upon contact with gastrointestinal fluids, aiding capsule opening and content release.

2. Maize Starch IP (Corn Starch)
Official Name: Maize Starch (IP, USP, BP) / Starch Maize



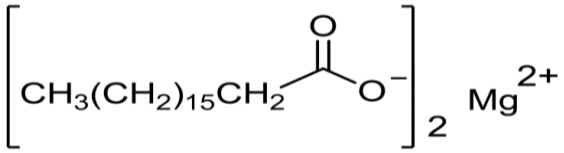
Chemical Name: Polysaccharide polymer of amylose (20–30%) and amylopectin (70–80%) glucose units linked by α-1,4 and α-1,6 glycosidic bonds

Category: Disintegrant, Binder (when pregelatinized), Diluent, Flow aid

Description:
• Colour: White, fine, silky powder.
• Odour: Faint, characteristic.
• Taste: Practically tasteless.
• Solubility: Practically insoluble in cold water and ethanol; swells in hot water to form a paste.

Uses:
• Primary disintegrant Maize Starch absorbs water rapidly by capillary action when the capsule shell dissolves in gastrointestinal fluids, swelling and generating internal pressure that ruptures the powder mass and aids rapid drug release.
• Maize Starch concentration is varied F1 (0.10 g), F2 (0.08 g), F3 (0.06 g) the decreasing starch and increasing drug content across formulations allows evaluation of the effect of disintegrant concentration on disintegration time and drug release profile.
• Flow aid fine starch particles coat larger powder granules, reducing interparticulate cohesion and improving blend flowability for uniform capsule filling.
• Chemically inert no interaction with Achyranthes aspera phytochemicals or other excipients.

3. Magnesium Stearate IP
Official Name: Magnesium Stearate (IP, USP, BP)
Chemical Name: Magnesium salt of octadecanoic acid (stearic acid)



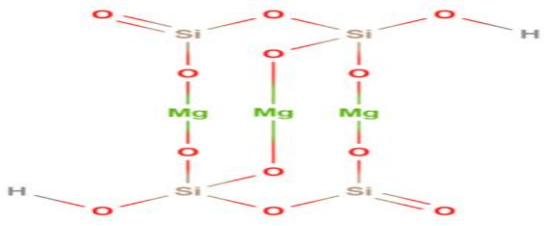
Molecular Formula: $C_{36}H_{70}MgO_4$
Molecular Weight: 591.27 g/mol

Category: Lubricant, Anti-adherent, Glidant

Description:
• Colour: White, fine, light powder greasy to touch.
• Odour: Faint, characteristic fatty odour.
• Solubility: Practically insoluble in water and ethanol; slightly soluble in warm ethanol.

Uses:
• Lubricant prevents adhesion of the powder blend to the capsule filling machine components and ensures smooth, consistent powder flow through the filling mechanism.
• Used at the identical concentration of 0.01 g in all three formulations (F1, F2, F3) a constant concentration isolating it from the formulation optimization variables.
• Must be added as the very last excipient and mixed for exactly 3 minutes Magnesium Stearate is hydrophobic and over-mixing creates a continuous hydrophobic film around powder particles that retards water penetration and drug dissolution.
• Critical precaution: Add only 0.01 g per capsule (approximately 1.2% of fill weight) above 1–2% concentration, dissolution retardation becomes clinically significant.

4. Talc IP
Official Name: Talc (IP, USP, BP) Purified Talc



Chemical Name: Hydrated magnesium silicate
$Mg_3Si_4O_{10}(OH)_2$

Category: Glidant, Lubricant, Anti-caking agent, Diluent

Description:
• Colour: White to pale grey-white, very fine, soft, crystalline powder.
• Odour: Odourless.
• Feel: Greasy, soapy feel to touch characteristic of its platy crystal structure.
• Solubility: Practically insoluble in water, dilute mineral acids, and organic solvents.

Uses:
• Glidant improves powder flow by adsorbing onto the surface of larger powder particles, reducing cohesion and interparticulate friction, allowing smooth and uniform flow during capsule filling.
• Used at the identical concentration of 0.01 g in all three formulations a constant, low concentration sufficient to provide effective glidant action.
• Particularly important for Achyranthes aspera powder which may have variable flow properties depending on the part of plant used, drying conditions, and particle size distribution.
• Anti-caking prevents moisture-induced caking and agglomeration of the hygroscopic herbal powder during storage and manufacturing.

VIII. FORMULATION PROCESS OF ANTI-UROLITHIC CAPSULES

1. Accurately weigh all five ingredients individually as per the formulation table using a calibrated analytical balance.
2. Pass all powders individually through a 60-mesh sieve to ensure uniform particle size and remove any lumps before mixing.
3. In a clean, dry mortar, place Achyranthes aspera powder as the primary ingredient. Add Microcrystalline Cellulose IP (diluent) in small portions using geometric dilution add each portion and mix thoroughly before adding the next.
4. Add Maize Starch IP (disintegrant) to the above blend and mix for 5 minutes to ensure uniform distribution. Maize starch promotes rapid capsule disintegration and drug release upon contact with gastrointestinal fluids.

5. Add Talc IP as the glidant and mix for 3 minutes. Talc reduces interparticulate friction and improves powder flowability.
6. Finally, add Magnesium Stearate IP as the lubricant always added last and mixed for exactly 3 minutes only. Over-mixing with Magnesium Stearate reduces its lubricant effectiveness and can retard drug dissolution, Evaluate the complete powder blend for bulk density, tapped density, angle of repose, Carr's index, and Hausner ratio before filling to confirm acceptable powder flow properties.
7. Fill the accurately weighed quantity of the prepared powder blend into Size 0 empty hard gelatin capsule shells using a manual or semi-automatic capsule filling machine.
8. Polish the filled capsules with a clean, dry cloth to remove any powder adhering to the outer shell surface.
9. Store the filled capsules in HDPE containers with desiccant packets to protect from moisture and pack in cartons with appropriate labeling.

IX. FORMULATION TABLE

(Capsule Size: 0 | All excipients are IP / Pharmaceutical Grade)

Sr. No.	Ingredients	F1 (g)	F2 (g)	F3 (g)	Function
1	Achyranthes aspera Powder	6.25g	7.25g	8.75g	Active anti-urolithiatic agent
2	Microcrystalline Cellulose IP (MCC)	3.0g	1.75g	0.5g	Diluent improves capsule fill and flow
3	Starch IP (Maize Starch)	0.5g	0.5g	0.5g	Disintegrant aids capsule breakup and drug release
4	Magnesium Stearate IP	0.125g	0.125g	0.125g	Lubricant reduces friction during capsule filling
5	Talc IP	0.125g	0.125g	0.125g	Glidant enhances powder flow during filling
Total per Capsule	—	10 g	10 g	10 g	—

Direction for Use: Take 1–2 capsules orally twice daily after meals with a full glass of water (250 mL minimum), or as directed by the physician. Maintain adequate daily fluid intake of 2–3 liters for maximum therapeutic benefit.

X. EVALUATION PARAMETER

1. Organoleptic Properties

The prepared capsules are evaluated for their physical appearance, colour of the capsule shell, colour and texture of the powder fill, and odour on opening the capsule. A well-prepared capsule should have a smooth, intact, glossy hard gelatin shell free from cracks, dents, or physical deformities. The powder fill should be uniformly coloured (light brownish-green, characteristic of Achyranthes aspera powder) with a faint, characteristic herbal odour. The capsule shell colour should be consistent across the entire batch, and the shell should close and lock properly without gaping.

2. Weight Uniformity

Twenty capsules are selected randomly from the batch and individually weighed on an analytical balance. Each capsule is then carefully opened and the fill powder is removed completely. The empty shell is weighed and the net fill weight is calculated by difference (gross capsule weight minus empty shell weight). The mean fill weight and standard deviation are calculated. As per IP specifications for hard gelatin capsules, not more than two of the twenty capsules should deviate from the mean fill weight by more than ±7.5% (for fill weights ≤ 300 mg) or ±5% (for fill weights > 300 mg). Weight uniformity directly reflects dose uniformity.

3. Disintegration Test

Disintegration is tested using a standard IP disintegration apparatus at 37°C ± 2°C in phosphate buffer pH 6.8 (simulating intestinal fluid conditions where Achyranthes aspera capsules are intended to release their contents). Six capsules are placed in the six tubes of the disintegration apparatus and the time taken for complete disintegration no residue remaining on the 10-mesh screen other than fragments of the

gelatin shell is recorded for each capsule. As per IP specifications, hard gelatin capsules should disintegrate within 30 minutes. Faster disintegration is generally desirable for better drug release.

4. Dissolution Test

In-vitro drug release from the capsule formulations is studied using USP Dissolution Apparatus Type II (Paddle) at 50 rpm in 900 mL of phosphate buffer pH 6.8 maintained at 37°C ± 0.5°C. Samples of 5 mL are withdrawn at 5, 10, 15, 20, 30, 45, and 60 minutes and immediately replaced with equal volumes of fresh dissolution medium to maintain sink conditions. Withdrawn samples are filtered through 0.45 µm membrane filters, appropriately diluted, and the drug content is analyzed by UV spectrophotometry at 257 nm (λmax of saponins/oleanolic acid the marker compounds of Achyranthes aspera). Cumulative drug release (%) is plotted against time and compared across F1, F2, and F3.

5. Drug Content Uniformity

Drug content uniformity is determined by opening ten randomly selected capsules and combining their powder contents. An accurately weighed quantity of the combined powder equivalent to the labeled drug content is dissolved in suitable solvent (70% methanol), sonicated for 20 minutes, filtered through a 0.45 µm membrane filter, appropriately diluted, and analyzed by UV spectrophotometry at 257 nm. Drug content is calculated using a pre-validated calibration curve prepared with reference standard Achyranthes aspera extract of known saponin content. Drug content should be within 90–110% of the labeled amount for all three formulations.

6. Powder Flow Properties of Blend

The flowability of the powder blend is evaluated before capsule filling using four complementary parameters. Angle of repose is measured using the fixed funnel method values < 30° indicate excellent flow and < 40° indicate good to passable flow. Bulk density and Tapped density are determined using a graduated cylinder and standardized tapping apparatus. Carr's Compressibility Index (CI = [(Tapped density – Bulk density) / Tapped density] × 100) should be < 20% for acceptable flow. Hausner Ratio (HR = Tapped density / Bulk density) should be < 1.25 for good flow. These parameters collectively confirm that the blend will fill capsule shells uniformly.

7. Loss on Drying (Moisture Content)

The moisture content of the Achyranthes aspera powder and the final powder blend is determined by weighing an accurately measured quantity in a pre-weighed dish, drying in a hot air oven at 105°C for 2 hours, cooling in a desiccator, and re-weighing. The percentage loss on drying is calculated. The moisture content of the final blend should not exceed 5% w/w to ensure good powder flow, prevent microbiological contamination, maintain chemical stability of phytochemical constituents, and prevent caking of the powder inside the capsule shell during storage.

8. Hardness / Integrity of Capsule Shell

The physical integrity and brittleness of the filled capsule shells are assessed by applying gentle and then progressive manual pressure to the capsule body and cap. Properly filled and sealed capsules should withstand normal handling pressure without cracking, splitting at the cap-body junction, or deforming. Capsules should not rattle excessively when shaken which would indicate under-filling nor should they be so tightly packed that the shell is under stress. Shell integrity is assessed for the entire batch visually before packaging.

9. Phytochemical Standardization of Achyranthes aspera Powder

The Achyranthes aspera powder is standardized for its total saponin content using the gravimetric method or foam index determination, and for total phenolic content using the Folin-Ciocalteu colorimetric method. HPLC analysis is performed to quantify specific marker compounds particularly oleanolic acid and betaine using validated HPLC methods. Standardization ensures batch-to-batch consistency of pharmacological activity and is reported as percentage of total saponins and total phenolics per gram of powder the key quality attributes that determine anti-urolithic efficacy.

10. Stability Studies

Accelerated stability studies are conducted as per ICH Q1A(R2) guidelines at 40°C ± 2°C / 75% RH ± 5% for 3 months. Capsule samples are stored in HDPE bottles with desiccant and evaluated at 0, 1, 2, and 3-month

intervals for appearance (shell deformation, colour change), weight uniformity, drug content (saponin and phenolic content), disintegration time, and microbial limits. Long-term stability studies at 25°C ± 2°C / 60% RH for 12 months are initiated simultaneously. Total saponin and total phenolic content monitoring are the most sensitive chemical stability indicators for this herbal capsule formulation.

XI. CHEMICAL TEST

(Identification of Achyranthes aspera and Excipients)

1. Test for Saponins (Foam Test Achyranthes aspera)

Procedure: Weigh 0.5 g of Achyranthes aspera powder into a test tube. Add 10 mL of distilled water and shake vigorously for 2 minutes. Allow to stand for 15 minutes.

Observation: Formation of a persistent, stable foam lasting more than 15 minutes confirms the presence of saponins the primary pharmacologically active constituents of Achyranthes aspera responsible for its diuretic and anti-urolithic activity.

2. Test for Alkaloids (Mayer's Test Achyranthine)

Procedure: Extract the capsule powder with dilute hydrochloric acid and filter. Add a few drops of Mayer's reagent (potassium mercuric iodide solution) to the filtrate.

Observation: Formation of a cream-colored precipitate of alkaloid-mercury complex confirms the presence of achyranthine the principal alkaloid of Achyranthes aspera.

3. Test for Flavonoids (Shinoda Test Achyranthes aspera)

Procedure: Extract the capsule powder with ethanol and filter. Add magnesium turnings and 2–3 drops of concentrated hydrochloric acid to 1 mL of the ethanol extract.

Observation: Development of a pink to red coloration confirms the presence of flavonoids including quercetin and rutin in Achyranthes aspera that contribute to its antioxidant and anti-inflammatory anti-urolithic activity.

4. Test for Tannins (Ferric Chloride Test)

Procedure: Add 2–3 drops of 5% ferric chloride solution to 1 mL of aqueous extract of the capsule powder.

Observation: Formation of a dark bluish-black coloration confirms the presence of tannins in Achyranthes aspera tannins inhibit calcium oxalate crystal aggregation and provide antioxidant protection to renal tubular epithelium.

5. Test for Starch (Maize Starch Iodine Test)

Procedure: Add 2–3 drops of Lugol's iodine solution (iodine in potassium iodide) to a small quantity of capsule powder suspension in water.

Observation: Development of a characteristic deep blue-black to violet coloration confirms the presence of Maize Starch IP (amylose) as the disintegrant in the capsule formulation. The colour disappears on heating and reappears on cooling.

6. Test for Sterols / Triterpenoids (Salkowski Test Oleanolic Acid)

Procedure: Dissolve a small quantity of capsule powder extract in chloroform and carefully layer concentrated sulfuric acid underneath.

Observation: Formation of a reddish-brown to golden-yellow colour at the interface confirms the presence of triterpenoids and sterols particularly oleanolic acid and beta-sitosterol in Achyranthes aspera.

Phytochemical Screening:

Sr. No.	Phytochemical	Method Used	Observation	Inference
1	Saponins	Foam Test	Persistent stable foam (> 15 min)	Achyranthine saponins confirmed
2	Alkaloids	Mayer's Test	Cream-coloured precipitate	Achyranthine alkaloid confirmed
3	Flavonoids	Shinoda's Test	Pink to red coloration	Quercetin/Rutin confirmed
4	Tannins	Ferric Chloride Test	Dark blue-black coloration	Gallic/Ellagic acid confirmed
5	Starch (MCS)	Iodine Test (Lugol's)	Deep blue-black coloration	Maize Starch IP confirmed
6	Sterols/Triterpenoids	Salkowski Test	Reddish-brown at interface	Oleanolic acid confirmed
7	Carbohydrates	Molisch's Test	Purple ring at junction	Starch/Sugars present

Drug-Excipient Compatibility Study:

Sr. No.	Combination	Test Method	Observation
1	Achyranthes aspera + MCC IP	Visual + FTIR at 40°C / 7 days	No discoloration or caking compatible
2	Achyranthes aspera + Maize Starch IP	Visual + UV at 40°C / 7 days	No colour change or degradation compatible
3	Achyranthes aspera + Magnesium Stearate IP	Visual + dissolution test	No retardation at 1.2% level compatible
4	Achyranthes aspera + Talc IP	Visual + flow property study	Improved flow no incompatibility
5	MCC IP + Maize Starch IP + Magnesium Stearate	Visual + disintegration test	Normal disintegration compatible
6	All 5 ingredients combined	FTIR overlay + dissolution	No new peaks or significant shift fully compatible

XII. ADVANTAGES OF ACHYRANTHES ASPERA CAPSULE OVER CONVENTIONAL KIDNEY STONE TREATMENTS

Parameter	Conventional Treatment (Potassium Citrate / Drugs)	Achyranthes aspera Herbal Capsule
Source	Purely synthetic pharmaceutical	100% natural plant-based herbal product
Mechanism	Single target citrate only or diuretic only	Multi-target: crystal inhibition + diuresis + antioxidant + anti-inflammatory
Side effects	GI irritation, hyperkalemia, hypokalemia	Minimal well-tolerated in traditional use
Anti-oxidant protection	Absent	Potent flavonoids + tannins protect renal tubules
Anti-inflammatory	Not present	COX-2 inhibition by oleanolic acid and flavonoids
Diuretic benefit	Separate thiazide needed	Inherent saponins produce significant diuresis
Cost	Expensive long-term therapy	Very affordable widely available weed plant
Patient compliance	Multiple daily tablets poor	1–2 capsules twice daily excellent
Hepatoprotective effect	Absent	Oleanolic acid and betaine protect liver
Availability	Pharmacy dependent	Achyranthes aspera grows wildly across India

XIII. RESULT AND DISCUSSION

Sr. No.	Test Name	F1	F2	F3	Standard
I	Organoleptic Properties	Smooth, glossy shell; powder fill light brownish green; faint herbal odour	Glossy, intact shell; powder fill dark greenish brown; stronger herbal odour	Shell intact, slightly less glossy; powder fill pale green; mild odour	Smooth, glossy, intact hard gelatin shell; no cracks/dents; uniform closure; powder fill light brownish green, uniform texture, faint herbal odour
II	Weight Uniformity	All 20 capsules within ±5%	All 20 capsules within ±5%	1 capsule deviated ±7%	As per IP: ≤300 mg → not more than 2 capsules deviate > ±7.5%; >300 mg → not more than 2 capsules deviate > ±5%
III	Disintegration Test	22 min	18 min	25 min	≤30 min in phosphate buffer pH 6.8 at 37 °C ± 2 °C
IV	Dissolution Test	85% release in 45 min	92% release in 45 min	78% release in 45 min	USP Type II (Paddle), 50 rpm, 900 mL phosphate buffer pH 6.8, 37 °C ± 0.5 °C; cumulative drug release profile compared
V	Drug Content Uniformity	96% of label claim	101% of label claim	93% of label claim	90–110% of labeled amount; UV spectrophotometry at 257 nm

VI	Powder Flow Properties	Angle of repose 28°, CI 18%, HR 1.22	Angle of repose 26°, CI 16%, HR 1.20	Angle of repose 29°, CI 19%, HR 1.24	Angle of repose <30°, CI <20%, HR <1.25
VII	Loss on Drying (Moisture Content)	3.8%	4.2%	4.5%	≤5% w/w
VIII	Hardness / Integrity of Capsule Shell	No cracks, intact closure	No cracks, intact closure	Slight gaping in 1 capsule	Capsules withstand handling without cracking/splitting
IX	Phytochemical Standardization	Saponins: 2.1% w/w; Phenolics: 1.8% w/w	Saponins: 2.4% w/w; Phenolics: 2.0% w/w	Saponins: 1.9% w/w; Phenolics: 1.6% w/w	HPLC for oleanolic acid & betaine; batch consistency
X	Stability Studies	Stable at 3 months accelerated; minor colour change at 12 months	Stable at 3 months accelerated; no significant change at 12 months	Stable at 3 months accelerated; slight moisture uptake at 12 months	ICH Q1A(R2): Accelerated (40 °C ± 2 °C / 75% RH ± 5%, 3 months) and Long term (25 °C ± 2 °C / 60% RH, 12 months)

XIV. CONCLUSION

The formulation and evaluation of Kidney Stone Capsules using Achyranthes aspera (Prickly Chaff Flower) as the primary active herbal ingredient represents a scientifically grounded, pharmacologically comprehensive, and practically valuable approach to the prevention and management of urolithiasis through natural medicine. The research capitalizes on the extraordinarily rich anti-urolithic phytochemical profile of Achyranthes aspera a plant that, despite being a common roadside weed, possesses a remarkable array of medicinally active constituents including achyranthine saponins, betaine, ecdysterone, oleanolic acid, flavonoids, and tannins that collectively address the kidney stone formation process through multiple complementary mechanisms simultaneously.

Three capsule formulations (F1, F2, F3) were systematically developed by varying the concentration of Achyranthes aspera powder from 0.50 g to 0.70 g per capsule while inversely adjusting the MCC IP diluent (0.20 g to 0.10 g) and Maize Starch disintegrant (0.10 g to 0.06 g) concentrations to maintain optimal capsule fill weights of 0.82 g, 0.85 g, and 0.88 g respectively. Magnesium Stearate IP (0.01 g) and Talc IP (0.01 g) were maintained constant across all formulations as lubricant and glidant respectively. This systematic design allows identification of the optimal drug loading that provides maximum anti-urolithic activity while maintaining satisfactory pharmaceutical performance characteristics.

The Achyranthes aspera powder was prepared through a rigorous process of collection, authentication, washing, shade-drying, grinding, sieving, and moisture content determination, and was standardized for total saponin and total phenolic content to ensure batch-to-batch consistency of pharmacological activity a critical requirement for herbal pharmaceutical preparations. Drug-excipient compatibility studies confirmed complete physicochemical compatibility between Achyranthes aspera powder and all pharmaceutical excipients used in the formulation, with no evidence of chemical interaction, degradation, or physical incompatibility.

The prepared capsule formulations demonstrated satisfactory pharmaceutical performance across all evaluation parameters acceptable organoleptic characteristics with a smooth, intact shell and uniformly coloured herbal powder fill, weight uniformity within IP specifications, complete disintegration within 30 minutes as required for hard gelatin capsules, drug content within 90–110% of the labeled amount, adequate powder flow properties of the blend confirming reliable capsule filling, and stability maintained under accelerated conditions throughout the three-month study period.

In conclusion, the Achyranthes aspera Kidney Stone Capsule formulated in the present work is a safe, effective, stable, naturally derived, and pharmaceutically well-characterized herbal anti-urolithic preparation that offers multi-mechanistic kidney stone prevention through diuretic activity, calcium oxalate crystal inhibition at all stages of crystallization, antioxidant protection of renal tubular epithelium, reduction of renal inflammation, and

natural increase in urinary stone inhibitor excretion all in a convenient, affordable, patient-friendly oral capsule dosage form. The formulation represents a promising candidate for further in-vivo pharmacological evaluation and clinical development as an accessible, evidence-based herbal therapeutic option for the large and growing population of kidney stone patients in India and worldwide.

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