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"Research And Development Of Therapeutic Herbal Tablets From *Kalanchoe Pinnata* (*Oken*) Extract: Formulation, Optimisation, And Evaluation."

" ***Shrot title:*** *"Formulation, Optimisation, and Evaluation of Herbal Tablets Incorporating Kalanchoe pinnata (Oken) Extract."*

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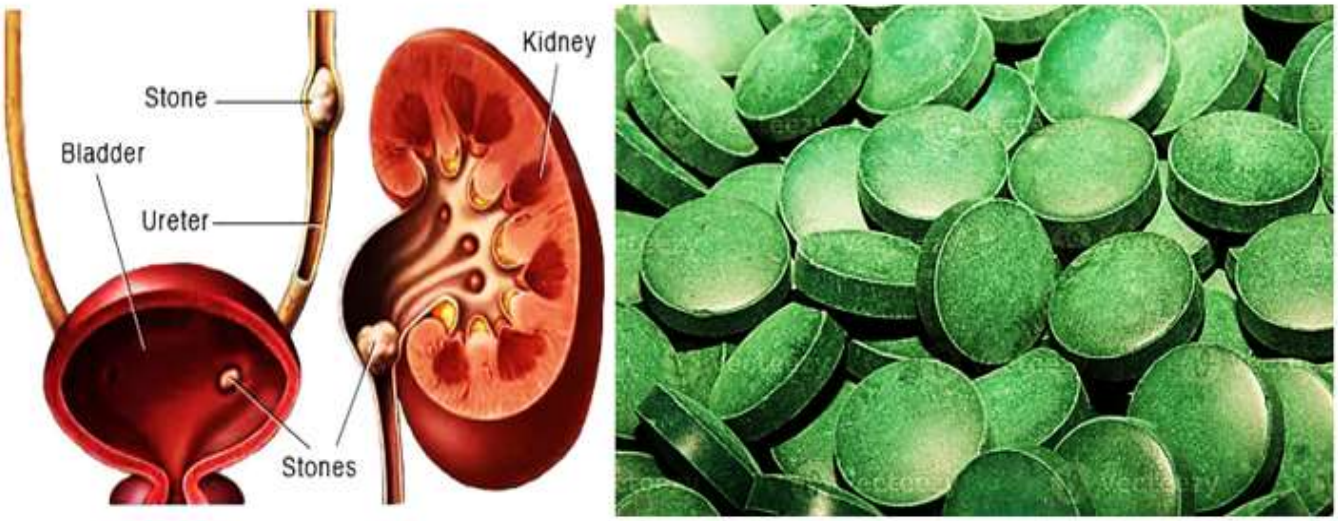
Abstract:

This research works aims to study and develop herbal tablets using Kalanchoe pinnata extract, exploring its potential as a natural remedy for various health conditions. Kalanchoe pinnata, commonly known as cathedral bells or life plant, is a succulent herb with ethnomedical applications, including its purported anticancer properties, along with its potential application in treating urinary stone along with Butea monosperma as an active ingredients. The study will involve the formulation of tablets using different concentrations of Kalanchoe pinnata extract and excipients, followed by optimisation of the formulation for enhanced efficacy and stability. The tablets will be evaluated for various pharmaceutical parameters such as: hardness, friability, disintegration time, and dissolution profile. Additionally, the bioactive components present in the tablets will be analysed using appropriate analytical techniques. The research findings will provide valuable insights into the development of optimised herbal tablets from Kalanchoe pinnata extract for potential therapeutic applications.



Graphical abstract: The creation of tablet-based medication for kidney stone treatment aims to enhance patient adherence to therapy while effectively addressing the condition's therapeutic needs.

The development of tablets as a form of medication for kidney stones aims to enhance patient compliance and improve treatment efficacy. These tablets are designed with therapeutic objectives in mind, aiming to alleviate symptoms, facilitate stone dissolution or passage, and prevent recurrence. By providing a convenient and easily administered dosage form, tablet medications offer patients a practical and accessible means of managing their condition. Additionally, tablet formulations may incorporate various

pharmacological agents targeted at addressing specific aspects of kidney stone formation and progression. This approach seeks to optimise treatment outcomes while prioritising patient convenience and adherence to prescribed therapies.
IndexTerms - bioactive components, evaluation, tablet formulation, herbal tablets, *Kalanchoe pinnata*, Optimisation, renal therapeutics.

Background:

The popularity of herbal medicines is on the rise due to their recognised pharmacological effectiveness and economic significance, which offer substantial benefits to individuals. Nevertheless, there is a pressing need for extensive research aimed at establishing standardised and validated protocols for Ayurvedic medicines, ensuring their potency, safety, and efficacy.

Kidney stones, also known as renal calculi or nephrolithiasis, are solid deposits formed from minerals and salts inside the kidneys. Various factors contribute to their formation, including dietary habits, excess body weight, medical conditions, and certain medications or supplements. These stones can affect any part of the urinary tract, leading to discomfort and potential complications. Symptoms of kidney stones typically manifest when the stone moves within the kidney or travels through the ureters, causing blockages and spasms. Severe, sharp pain in the side and back, along with radiating pain to the lower abdomen and groin, are common symptoms. Other signs may include discolored or foul-smelling urine, increased frequency of urination, nausea, vomiting, fever, and chills. Seeking medical attention is crucial if symptoms are severe or accompanied by complications such as: fever, difficulty passing urine, or blood in the urine. Prompt treatment is essential to prevent permanent damage. The formation of kidney stones occurs when urine becomes concentrated, allowing minerals to crystallise and adhere together. Different types of kidney stones exist, including: calcium stones (the most common), struvite stones, uric acid stones, and cystine stones. Understanding the type of stone is essential for determining its cause and devising preventive measures. Various risk factors contribute to the development of kidney stones, including family or personal history, dehydration, certain dietary habits (such as: high protein, sodium, or sugar intake), obesity, digestive diseases or surgeries, and specific medical conditions (like: renal tubular acidosis or cystinuria). Additionally, certain supplements and medications, such as: vitamin C, laxatives, calcium-based antacids, and certain migraine or depression medications, may increase the risk of kidney stone formation. Preventive measures may include lifestyle modifications, dietary changes, adequate hydration, and medical interventions tailored to individual risk factors. Regular monitoring and consultation with a healthcare professional are essential for managing kidney stone risk effectively. Kidney stones, medically known as renal calculi or nephrolithiasis, are solid mineral and salt deposits that form within the kidneys or urinary tract. These stones can vary in size, ranging from as small as a grain of sand to as large as a golf ball.

Causes:

Imbalance in urine composition: Factors such as: high levels of calcium, oxalate, uric acid, or cystine in the urine can lead to the formation of kidney stones.

Dehydration: Insufficient fluid intake can result in concentrated urine, increasing the risk of stone formation.

Diet: Consuming foods high in oxalate, sodium, or protein can contribute to stone development.

Medical conditions: Certain medical conditions, such as: hyperparathyroidism, gout, urinary tract infections, and inflammatory bowel disease, can increase the likelihood of kidney stones.

Family history: Individuals with a family history of kidney stones are at higher risk of developing them.

Symptoms:

Severe pain in the back, side, abdomen, or groin
Painful or frequent urination
Blood in the urine
Nausea and vomiting
Fever and chills (if an infection is present)
Cloudy or foul-smelling urine

Treatment:

Pain management: Over-the-counter or prescription pain medications may be used to alleviate discomfort associated with kidney stones.

Fluid intake: Drinking plenty of water helps flush out the stones and prevent further formation.

Medications: Depending on the type of stone, medications may be prescribed to help dissolve or prevent the formation of kidney stones.

Medical procedures: In cases where stones are too large to pass on their own or are causing complications, procedures such as: shock wave lithotripsy, ureteroscopy, or surgery may be necessary to remove the stones.

Prevention:

Stay hydrated by drinking an adequate amount of water throughout the day.
Maintain a healthy diet low in sodium and oxalate-rich foods.

Limit consumption of foods high in animal protein.
Monitor calcium intake and avoid excessive calcium supplementation.
Manage underlying medical conditions that increase the risk of kidney stones.
Regular medical check-ups and consultations with a healthcare professional are essential for individuals at risk of kidney stones or those who have previously experienced them. Early detection and intervention can help prevent complications and improve treatment outcomes. [124]

Kidney stones are crystalline formations that develop in the kidneys, potentially obstructing the urinary tract. Their appearance varies based on composition, size, and colour.

This article will explore kidney stones, their causes, symptoms, treatments, and preventive measures.

Kidney stones form due to elevated levels of substances like calcium in the urine, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). They can range in size and texture, typically appearing brown or yellow.

There are four primary types of kidney stones:

Calcium stones, comprising calcium oxalate or calcium phosphate.

Uric acid stones, accounting for a percentage of kidney stones.

Struvite stones, larger in size compared to others.

Cystine stones, resulting from cystinuria, a hereditary condition.

Symptoms of kidney stones include back, side, and lower stomach pain, bloody urine, frequent urination, cloudy urine, nausea, vomiting, fever, and chills.

The formation of kidney stones can occur when the kidneys fail to adequately filter waste substances like calcium and phosphate, leading to crystal formation. These crystals may aggregate into stones, which can either remain in the kidney or travel through the urinary tract, causing pain and potential blockages.

Treatment options range from medical management to surgical intervention, depending on the size and location of the stones. Shock wave lithotripsy, cystoscopy and ureteroscopy, and percutaneous nephrolithotomy are common surgical procedures for kidney stone removal.

Preventive measures include staying hydrated, dietary modifications, medication, and lifestyle changes. For instance, drinking sufficient water, consuming citrus drinks, and following specific dietary guidelines based on the type of kidney stones can reduce the risk of recurrence.

Several risk factors contribute to the formation of kidney stones, including inadequate hydration, certain medical conditions, medications, and lifestyle factors. Regular medical check-ups and prompt treatment are crucial to avoid complications associated with kidney stones.

In summary, kidney stones manifest in various forms and require tailored treatment approaches. Understanding their causes, symptoms, and preventive measures is essential for effective management and prevention.

Introduction:
"Bryophyllum pinnatum" is a scientific name referring to a plant species commonly known as "air plant," "cathedral bells," "life plant," or "miracle leaf." It belongs to the family *Crassulaceae*. The plant is native to Madagascar but is widely distributed in tropical and subtropical regions worldwide. In traditional medicine, various parts of *Bryophyllum pinnatum* are used for their medicinal properties, including treating respiratory conditions, skin ailments, and digestive issues.
Globally, medicinal plants play a significant role in treating various ailments due to their accessibility, affordability, and relatively fewer side effects compared to synthetic drugs. The term "*Bryophyllum*"

originates from Greek, meaning "sprout leaf," indicating the plant's ability to grow from leaf cuttings. "Pinnatum," derived from Latin, refers to the leaf's quill-like appearance. *Bryophyllum pinnatum* is a perennial herb reaching heights of 3 to 5 metres, characterised by smooth, divergent leaves.

Throughout the world, *Bryophyllum pinnatum* is utilised for a wide range of health conditions, including: conjunctivitis, oedema, cholera, cuts, eczema, piles, chest colds, epilepsy, constipation, asthma, chickenpox, menstrual disorders, and fever. It is commonly employed in the treatment and management of: blisters, burns, coughs, rheumatoid arthritis, psychiatric disorders, insect bites, and abdominal discomfort. Additionally, it serves as a tocolytic agent to prevent premature labour.

Kalanchoe pinnata is a perennial shrub characterised by its succulent, glabrous, and glaucous appearance, growing between 0.3 to 2 meters tall. Its stems are cylindrical, upright, and sparsely branched, often forming clusters at the base. The leaves are arranged opposite each other in a decussate pattern, with adult plants typically bearing only upper leaves. These upper leaves are often divided into 3 or 5 leaflets, while the lower leaves are usually simple. Leaf blades are elliptical, measuring between 5 to 25 centimeters in length and 2 to 7 centimeters in width, with a rounded or slightly truncated apex and a finely serrated edge. Young plants frequently sprout from notches along the leaf margins, particularly after leaf detachment. Inflorescence leaves resemble foliage leaves but are smaller and simpler, typically located lower on the plant and on the ultimate branches. The inflorescence is panicle-shaped, with slender pedicels ranging from 1 to 2.5 centimeters in length. Pendulous flowers have papery, inflated calyxes measuring between 25 to 40 millimeters in length. The corolla, yellowish-green with pink or reddish tinges, can reach up to 7 centimeters in length, about twice the length of the calyx. Fruits consist of four thin, papery tubes enclosed within the base of the corolla tube, containing ellipsoid-oblong seeds measuring approximately 0.5 millimeters in length, with faint longitudinal stripes and a brown colouration. [89]

Distribution:

Figure 1. Distribution of the plant *Kalanchoe pinnata.* [89]

Kalanchoe pinnata, commonly referred to by various names including: cathedral bells, air plant, life plant, miracle leaf, Goethe plant, and love bush, is a succulent indigenous to Madagascar. It's a favoured indoor plant in regions with tropical or subtropical climates, renowned for its distinct sweet and tangy fragrance. It's not only cherished for its ornamental value, but it's also utilised as a herb. The leaves boast high levels of ascorbic acid (vitamin C), along with riboflavin, thiamine, niacin, magnesium, calcium, potassium, phosphorus, sodium, and trace minerals like: iron and zinc. [1] [2]

In addition to being adaptable, Palash flower extract is used to cure kidney stones; it is frequently used with a mixture of honey, lemon, and ginger extract. It is customary to combine it with *Kalanchoe pinnata*, as it is thought to augment medicinal effects and yield comparable advantages. Renowned in homes for its therapeutic qualities, *Kalanchoe pinnata* is trusted to relieve kidney stones. Online resources and records confirm *Kalanchoe pinnata's* similar therapeutic efficacy in addition to conventional treatments. But care should be taken while determining the dosage, with an emphasis on moderation in use. [1]

Kalanchoe pinnata, commonly known as cathedral bells, originates from Madagascar and is a popular choice for indoor cultivation as well as thriving in tropical and subtropical climates; this plant offers a range of health benefits as a nutritional supplement, known for its ability to bolster immune function, alleviate inflammation, and improve digestion. It's also reputed for its potential to lower cholesterol, enhance blood circulation, and reduce the risk of certain cancers. Moreover, it's valued for its stress-relieving properties, promoting better sleep, and reducing the likelihood of heart disease. [1] [3]

With a rich history in traditional medicine, *Kalanchoe pinnatum*, or *Bryophyllum pinnatum*, is regarded as a dietary supplement with purported anti-inflammatory, antioxidant, and anti-cancer properties. This succulent plant, native to Madagascar, is utilised in addressing various health issues, including digestive problems, skin conditions, and inflammation. Its antioxidant and anti-inflammatory attributes are particularly highlighted.

Traditional herbal medicine represents the most ancient healthcare system, embraced by diverse societies across the ages. It remains widely embraced today as a complementary and alternative treatment option, esteemed for its minimal side effects, reduced toxicity, economic accessibility, cost-effectiveness, efficacy, patient adherence, and widespread availability.

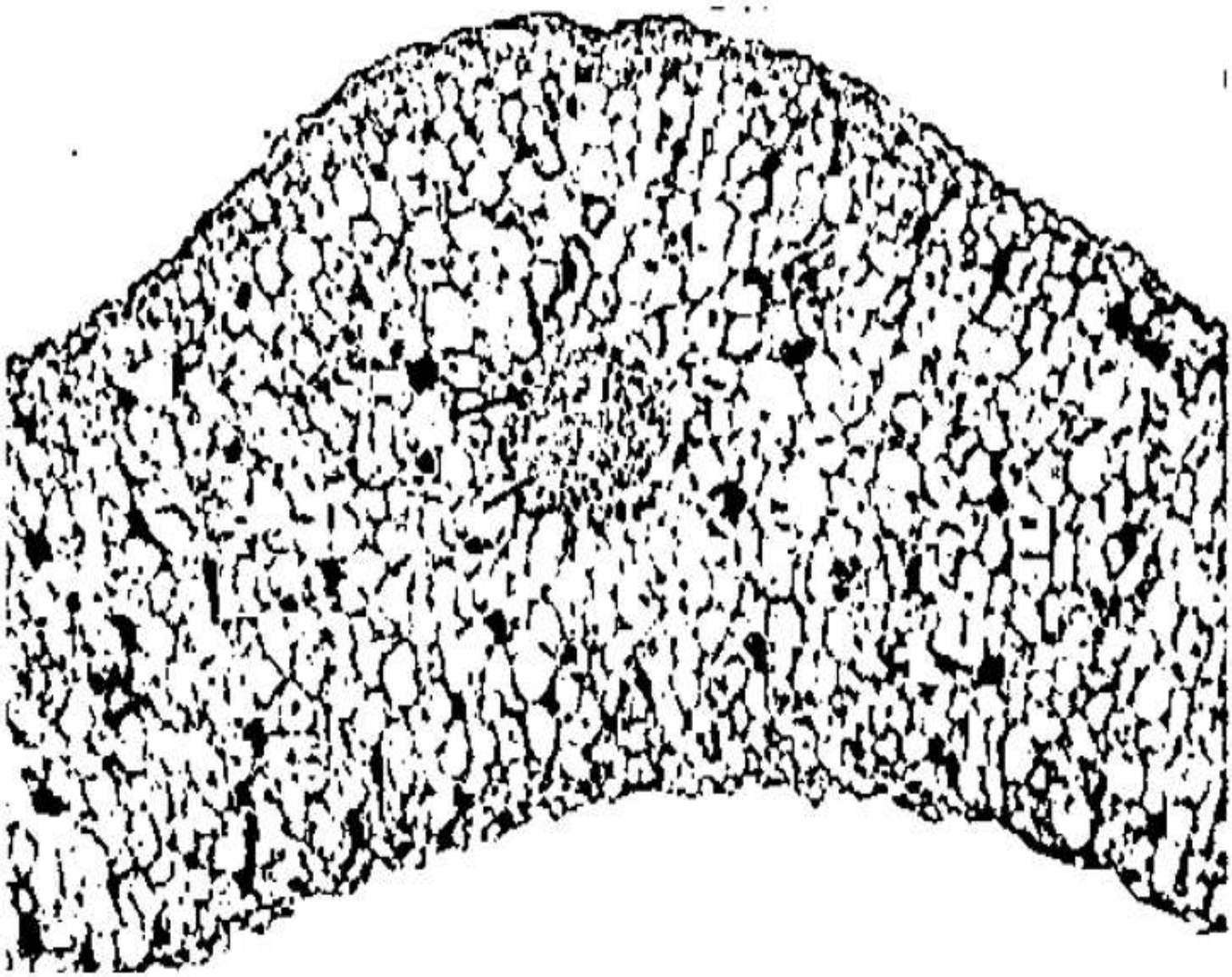
Although not subject to international regulations as a dietary supplement, individual countries may have their own regulations in place. In the United States, for example, the Food and Drug Administration (FDA) oversees the regulation of dietary. [1]

In folk medicine, *Kalanchoe pinnata* is esteemed for its therapeutic potential. Its leaves are often utilised in various applications, such as applying the pulp directly to the skin to create poultices, which are believed to aid in treating skin lesions, sores, inflammation, and stopping bleeding. Additionally, the leaves can be processed into lotions to address conditions like smallpox, while a paste made from the leaves is sometimes applied to the chest for cough relief or to the temples to alleviate headaches. [4]

Chemical analyses of extracts from various parts of *K. laciniata* and *B. pinnatum* have revealed the presence of several compounds, with flavonoids being the predominant ones. These plants have a long history of traditional use in treating a range of conditions, including inflammation, microbial infections, pain, respiratory ailments, gastritis, ulcers, diabetes, and cancer. In laboratory studies, non-clinical tests have primarily focused on assessing their antimicrobial and antioxidant properties, while *in vivo* experiments have explored their effectiveness against leishmaniasis, inflammation, and immune system modulation. However, there's limited information available regarding the toxicity of these species. The findings presented here could help emphasis the importance of *K. laciniata* and *B. pinnatum* and guide future research endeavours. [5]

Figure 2. a. The foliage and flower clusters of *Kalanchoe laciniata (L.)*.

Figure 2. b. The foliage and flower clusters of *Kalanchoe pinnata (Lam.)* cathedral bells.

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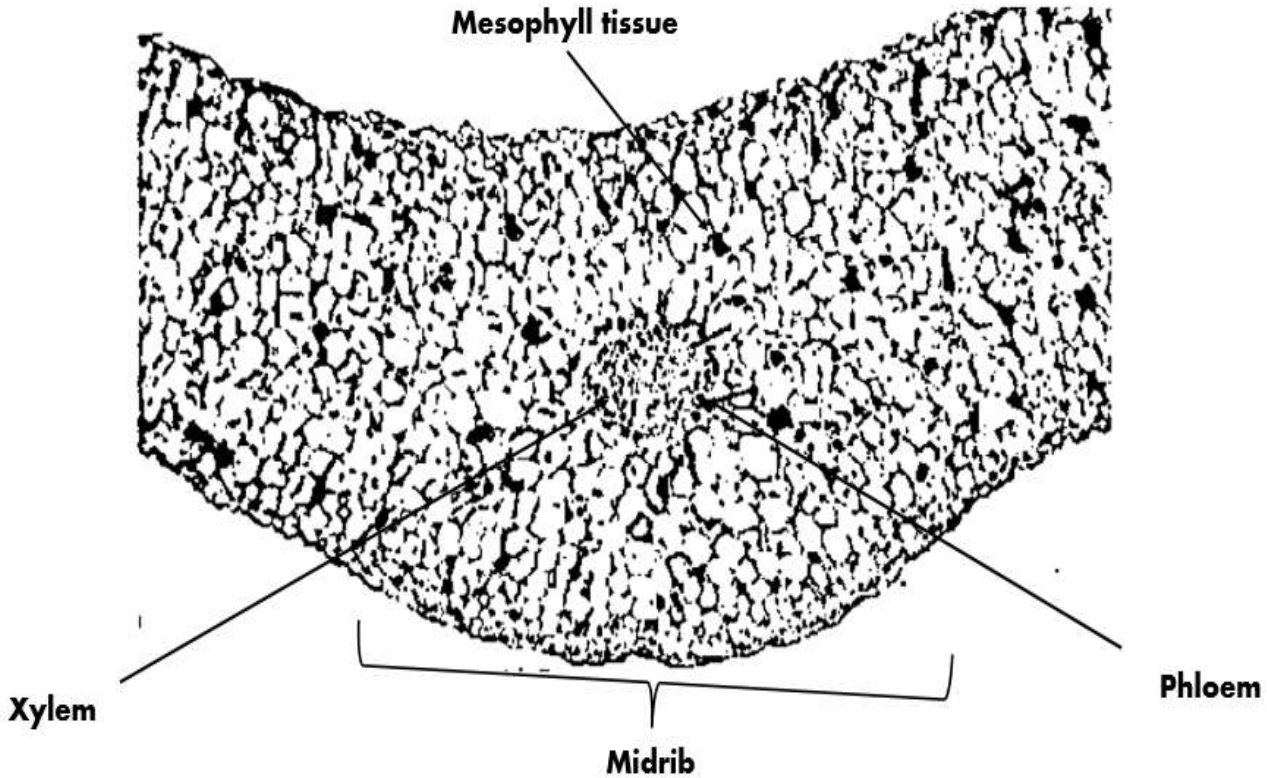
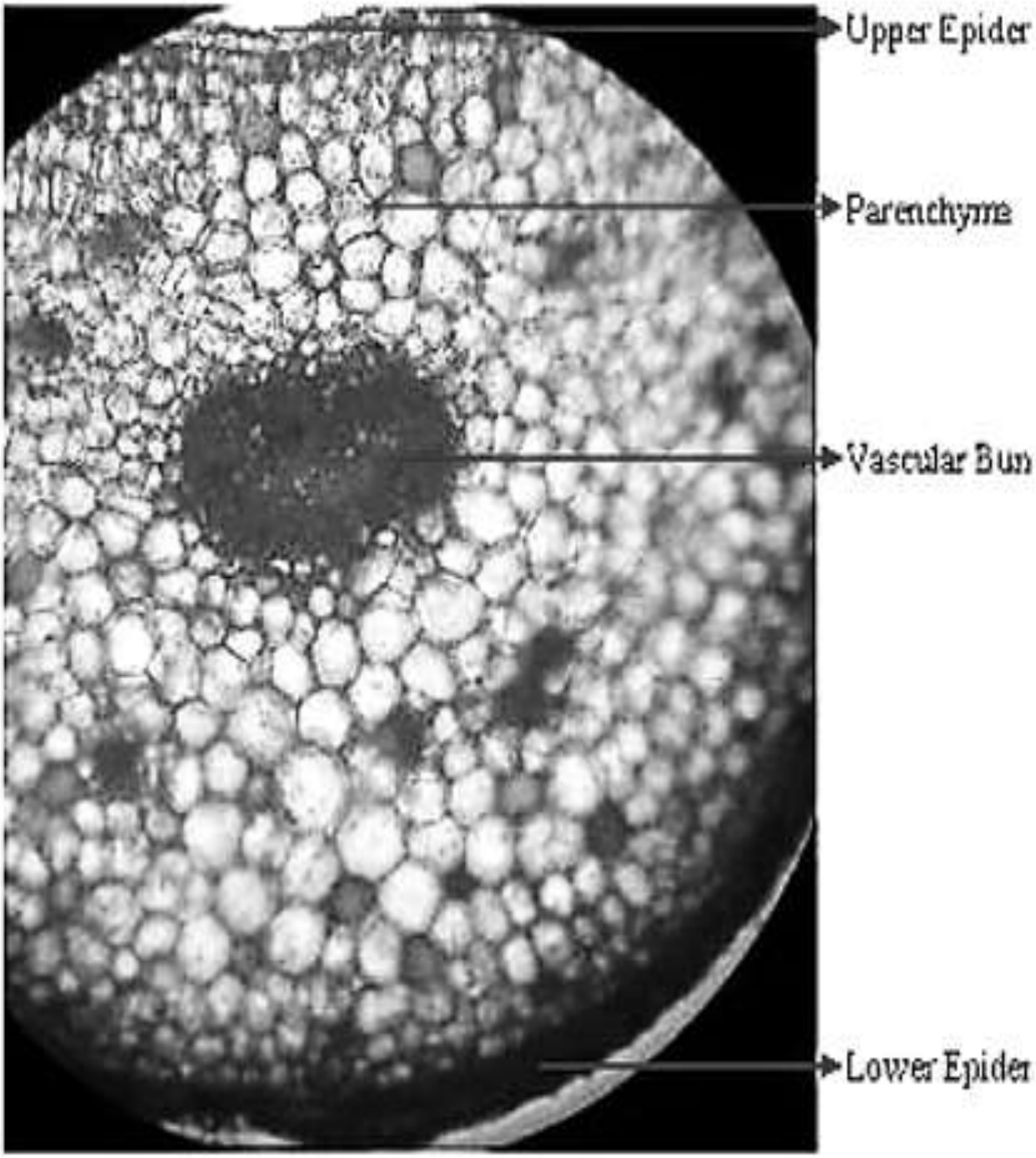

Mesophyll tissue
Xylem
Phloem
Midrib



T.S. of stem.

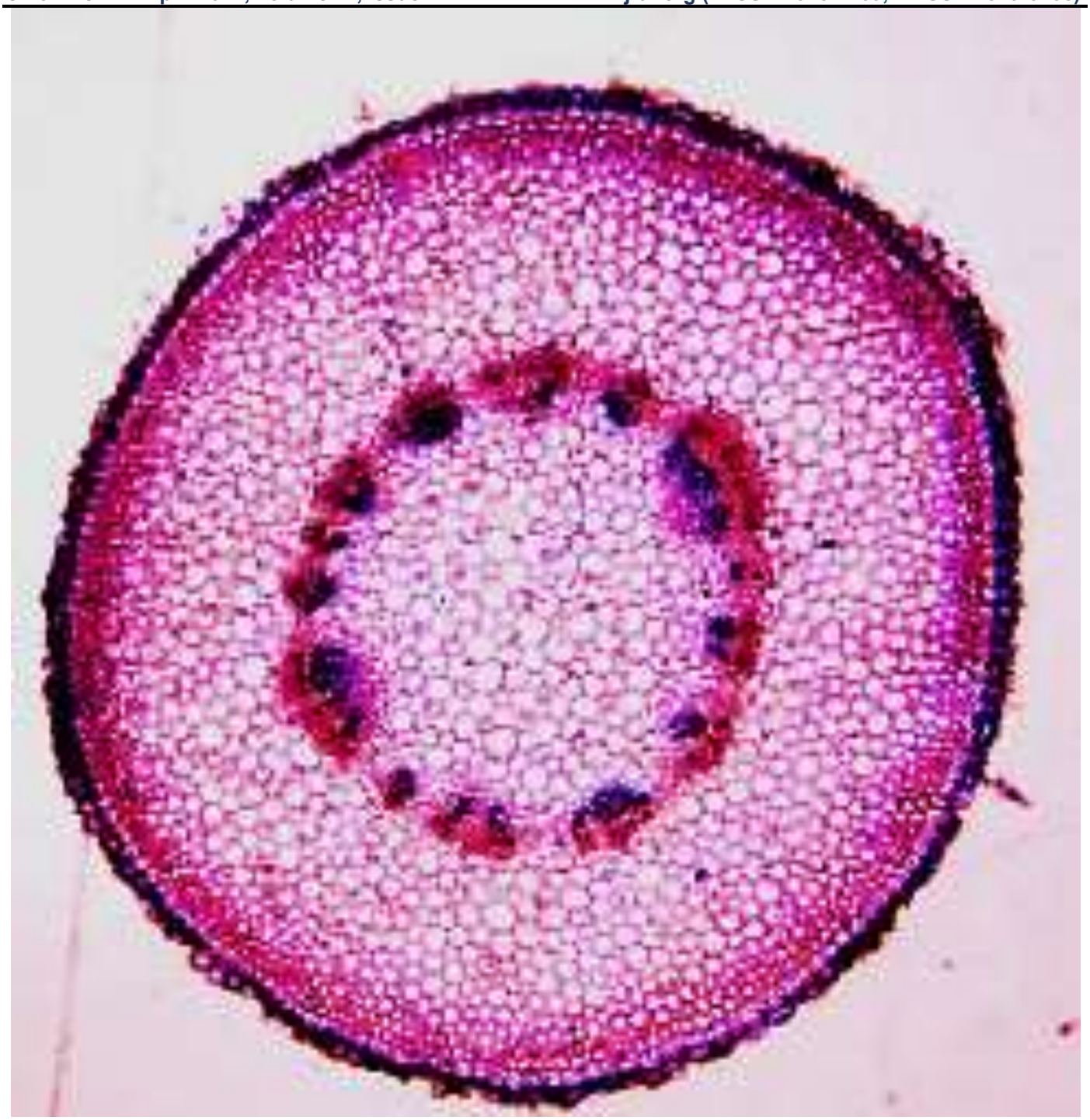


Figure 2. c. T.S. of leaf midrib and stem.

Kalanchoe laciniata is a semi-woody, perennial vegetable reaching heights of 30 to 100 cm. Its succulent leaves are oval or oblong, arranged oppositely, with short petioles and serrated edges. The flowers, appearing in abundance, are small and yellow-orange, forming dense clusters atop composite stems or branched inflorescences. They are hermaphroditic, with fused petals forming a corolla longer than the calyx, and possess scaly carpels that develop into multiple-seeded follicles. The fruit produced is a follicle measuring about 6 cm in length, containing brown, oblong seeds. [6] [7] [8] [9]

Cathedral bells classification: [59]

Kingdom:	*Plantae* - Plants
Subkingdom:	*Tracheobionta* - Vascular plants
Superdivision:	*Spermatophyta* - Seed plants
Division:	*Magnoliophyta* - Flowering plants
Class:	*Magnoliopsida* - Dicotyledons
Subclass:	*Rosidae*
Order:	*Rosales*
Family:	*Crassulaceae J. St.-Hil.* - Stonecrop familyP
Genus:	*Kalanchoe Adans.* - widow's-thrillP
Species:	*Kalanchoe pinnata (Lam.)* Pers. - cathedral bells

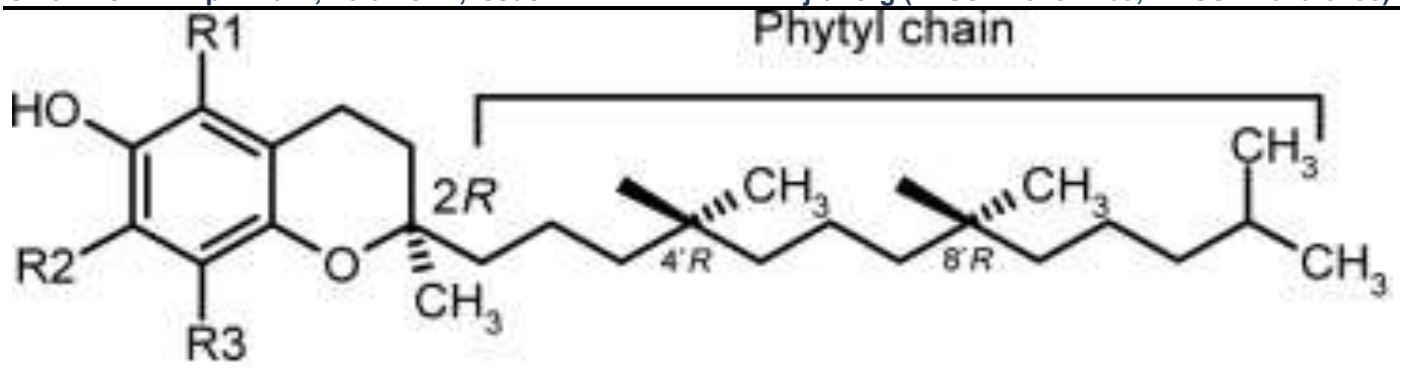
Bryophyllum pinnatum (Lam.) Oken, a plant native to certain regions and introduced in others, has been extensively utilised by traditional healers for addressing a range of health issues such as: renal calculi, hypertension, asthma, colds, abscesses, and bleeding disorders. Over time, numerous studies have been conducted to explore its pharmacological activities, including its potential as: a urolithic agent, diuretic, anti-diabetic agent, and wound healer. Further, phytochemical investigations have revealed the presence of various compounds such as: alkaloids, cardiac glycosides, and flavonoids within *Bryophyllum pinnatum*.

Patharchatta, [(पत्थरचट्टा), पासनफोड , फत्तरफोड, काचूफोड, मुतखडाफोड, पर्णबीजा.] also referred to as *Kalanchoe Pinnata*, is renowned for its medicinal attributes, encompassing the reduction of acidity, heartburn, and facilitation of digestion. This plant, recognised for its therapeutic properties, serves as an aesthetically pleasing indoor foliage with numerous advantages for health and well-being. According to the research conducted by Prof. Dr. Saurabh Dilip Bhandare and Prof. Dr. Sarika Shivaji Malode, there is a clear indication of the synergistic health benefits derived from the infusion of *Butea monosperma* and *Crocus sativus*. This infusion, along with the extract of *Bryophyllum pinnatum*, is used as a remedy for urinary stones (Renal calculus, commonly known as a kidney stone, refers to a hard, crystalline mineral deposit that forms in the kidneys or urinary tract. These stones are typically composed of various substances, such as: calcium oxalate, calcium phosphate, uric acid, and others. Renal calculi can vary in size, from tiny particles to large stones that can cause significant pain and discomfort. They may be asymptomatic and pass out of the body through urine, or they can cause symptoms such as: severe pain in the abdomen, groin, (*Amr*. Groyne), or back, along with nausea, vomiting, and blood in the urine. Treatment for renal calculi depends on the size and composition of the stone and may include pain management, hydration, medications to help pass the stone, or procedures such as: lithotripsy or surgical removal.). It is widely consumed by the population either by ingesting the raw leaves or by preparing juice from them, which is then consumed with plain water or coconut water. [1] A common traditional remedy for kidney stones involves the use of extracts from *Butea monosperma*, *Crocus sativus*, *Bryophyllum pinnatum*, and *Tribulus terrestris*, often combined into a syrup or dark molasses-like preparation made with sugar or jaggery. This mixture is typically diluted in coconut water before being consumed by patients. Additionally, coriander water and barley water are frequently used as traditional drinks in various cultures.

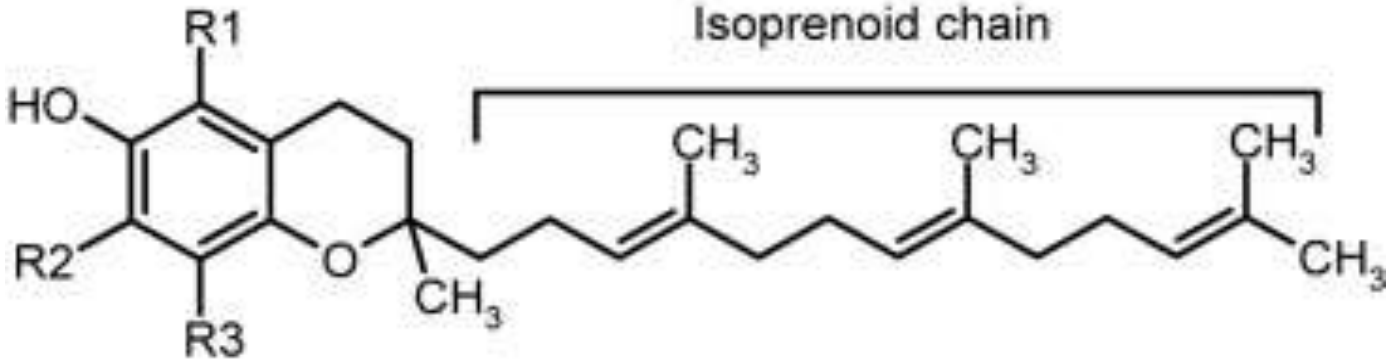
Barley water is made by boiling barley grains in water, then straining the mixture and optionally adding sugar or other ingredients. Barley water contains compounds called tocols, which are known to lower LDL cholesterol levels and promote cardiovascular health. It also contains antioxidants that help reduce the risk of heart diseases by combating oxidative stress on the heart.

Barley water is considered highly beneficial for urinary tract infections, acting as a diuretic to enhance urine production and eliminate toxins from the body. It is particularly effective for managing kidney stones and cysts. Barley water is often recommended for both children and adults to be consumed daily until the urinary infection resolves. [102]

Vitamin E encompasses a group of eight lipid-soluble substances derived from plants, collectively known as tocols, which include four tocopherols and four tocotrienols. Its molecular structure comprises a chromanol ring with a side chain positioned at the C-2 position. Tocopherols are characterised by a saturated phytyl side chain, whereas tocotrienols have an unsaturated isoprenoid side chain. The specific number and arrangement of methyl groups surrounding the chromanol ring differ among the various tocopherols and tocotrienols, leading to their classification as alpha-, beta-, gamma-, or delta-forms. Natural alpha-tocopherol is exclusively found in the RRR-configuration (formerly referred to as d-alpha-tocopherol). Conversely, synthetic alpha-tocopherol comprises an equal racemic mixture of eight stereoisomers (RRR, RSR, RRS, RSS, SRR, SSR, SRS, and SSS), resulting from the three chiral centres of the molecule at positions C2, C4', and C8', and is termed as all-rac-alpha-tocopherol (or dl-alpha-tocopherol). [103] Tocopherols (α, β, δ, γ) and tocotrienols, members of the vitamin E family, are vital bioactive components found in vegetable oils, renowned for their antioxidative properties. Comprising a chroman ring and a lengthy saturated phytyl chain, tocopherols are thick oils at room temperature and undergo gradual oxidation when exposed to atmospheric oxygen. The biosynthesis of tocopherols primarily occurs in plant chloroplasts, with the aromatic amino acid tyrosine serving as their fundamental precursor. Susceptible to degradation by light, heat, alkali, and metals, tocopherols are prone to oxidation, leading to the formation of tocoquinones, which lack antioxidant capabilities. α-Tocopherol, insoluble in water, exhibits solubility in oils, fats, and fat solvents. [104] [105]



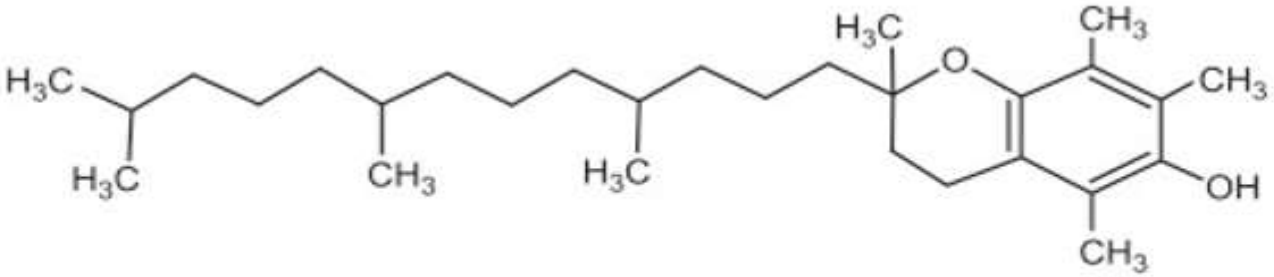
Tocopherol



Tocotrienol

The four isoforms of tocopherols and tocotrienols:

α-:	$R_1 = CH_3$	$R_2 = CH_3$	$R_3 = CH_3$
β-:	$R_1 = CH_3$	$R_2 = H$	$R_3 = CH_3$
γ-:	$R_1 = H$	$R_2 = CH_3$	$R_3 = CH_3$
δ-:	$R_1 = H$	$R_2 = H$	$R_3 = CH_3$



α-tocopherol, $C_{29}H_{50}O_2$.

Figure 3. Structure of tocols.

The traditional medicinal applications of *K. laciniata* and *B. pinnatum* primarily involve the use of their leaves, with the juice being the preferred mode of preparation. Both species share common properties that are utilised in treating various conditions, including skin issues, respiratory ailments, pain, inflammation, and

gastrointestinal disorders. Among these, inflammatory conditions and gastric problems such as: ulcers and gastritis are most frequently addressed. Additionally, both *K. laciniata* and *B. pinnatum* are applied externally in the form of poultices or plasters to manage dermatological issues and burns. Additionally, the leaves of both plants have been noted for their antivenom effects against snake and scorpion bites in traditional practices. [5]

The leaves and stems of *Kalanchoe laciniata* and *Bryophyllum pinnatum* are utilised in traditional medicine for treating various ailments, such as: otitis and skin diseases. They are particularly valued for their healing properties, often applied in the form of juice, syrup, or poultice to address conditions like: bronchitis, flu, and soreness. Additionally, the leaves are employed in managing ovarian and uterine inflammations, either in their pure juice form or combined with other plants to create syrup preparations.

Moreover, these plants are used to alleviate ulcers and gastritis, with their juice being a common remedy. They are also relied upon for addressing coughing, diabetes, and general pains, and are believed to have anxiolytic effects. The leaves are applied in various forms, including as teas, syrups, and plasters, to tackle respiratory disorders, aid in healing, and relieve flu and cough symptoms. Additionally, the leaves and roots are employed for their depurative and blood-thinning properties, as well as for treating uterine inflammation, cough, influenza, and general pains. They are administered through decoctions, tinctures, soaking, or poultices. The aerial parts of the plants are used in macerations to alleviate fever, fractures, and ear pain, while the leaves are applied as a paste to treat snakebites. Additionally, various parts of the plants are utilised to combat microbial diseases through decoctions, sap application, maceration, or heating in ash. Additionally, the leaves are significantly employed to facilitate delivery, manage bleeding during pregnancy, and relieve postpartum abdominal pain, often through decoctions or macerations. Lastly, they are used in paste form to treat snakebites, demonstrating the wide-ranging medicinal applications of *Kalanchoe laciniata* and *Bryophyllum pinnatum* in traditional practices. [10] [11] [12] [13] [14] [15] [16] [17] [18] [19] [20] [21] [22] [23] [24] [25] [26] [27] [28]

Utilised in alleviating migraines, headaches, and inflammations, *Kalanchoe pinnata* leaves are employed topically for boils, sores, and both skin and gastric ulcers. When crushed, the leaves possess a mildly sour and bland taste and are utilised to alleviate symptoms of asthma. The freshly extracted juice from the leaves serves as a remedy for bronchitis, various upper respiratory infections, and whooping coughs. [60]

The *Zygophyllaceae* family includes the genus *Tribulus*, which consists of approximately 20 species globally. Among these species, three, namely *Tribulus cistoides*, *Tribulus terrestris*, and *Tribulus alatus*, are commonly found in India. [113] *Tribulus terrestris*, commonly known as puncture vine, is an herb native to the Mediterranean region with a rich history of use in Indian, Chinese, and European traditional medicine. TT, which is often referred to by its Sanskrit name "Gokshur," is a commonly recognised botanical ingredient. In Ayurvedic practices, it's renowned as a sexual stimulant, while in European folk medicine, it's prized for its purported ability to enhance sexual potency. The fruit, leaves, or roots of the plant are utilised for medicinal purposes. *Tribulus* is sought after for a variety of potential health benefits, including improving athletic performance, aiding in bodybuilding, addressing heart and circulatory conditions, managing sexual issues, alleviating chest pain and dizziness, treating skin and eye disorders, and assisting in the expulsion of kidney stones. It contains protodioscin, a steroidal saponin, as well as β-carboline compounds like harman and norharman. While it contains chemicals that may influence hormone levels, *Tribulus* doesn't seem to significantly elevate testosterone levels in humans. [106] The plant contains a diverse array of chemical compounds with medicinal significance, including flavonoids, flavonol glycosides, steroidal saponins, and alkaloids. Its wide-ranging pharmacological properties encompass diuretic, aphrodisiac, antiurolithic, immunomodulatory, antidiabetic, absorption-enhancing, hypolipidemic, cardiotonic, central nervous system, hepatoprotective, anti-inflammatory, analgesic, antispasmodic, anticancer, antibacterial, anthelmintic, larvicidal, and anticariogenic activities. Over recent decades, considerable research has been dedicated to elucidating its biological activities and the pharmacological effects of its extracts. [107] The preliminary analysis of *Tribulus terrestris* TT revealed the presence of various phytochemicals, such as: saponins, flavonoids, glycosides, alkaloids, and tannins. Research indicates that the composition and content of saponins in TT vary across different geographic regions. Studies on the chemistry and bioactivity of TT saponins have identified several types, including: furostanol and spirostanol saponins like: tigogenin, neotigogenin, gitogenin, neogitogenin, hecogenin, neohecogenin, diosgenin, chlorogenin, ruscogenin, and sarsasapogenin. Additionally, sulfated saponins of tigogenin and diosgenin types have been isolated. Among the furostanol glycosides, protodioscin and protogracillin are predominant, with protodioscin being the most abundant, while spirostanol glycosides are present in smaller amounts. Flavonoid analysis has also been conducted, revealing compounds like: kaempferol, kaempferol-3-glucoside, kaempferol-3-rutinoside, and tribuloside, which were identified through spectroscopic analysis. Further studies using high-performance liquid chromatography (HPLC) detected various flavonoids, including: caffeoyl derivatives, quercetin glycosides like: rutin, and kaempferol glycosides, in TT leaf extracts. Extraction optimisation experiments have led to the isolation of

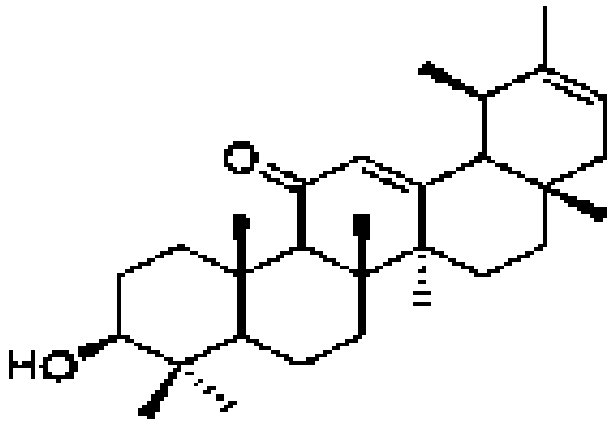
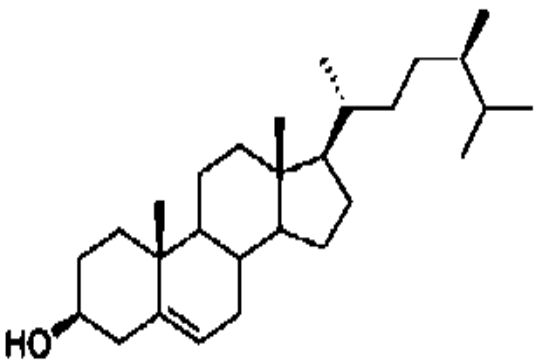
flavonoid glycosides such as: quercetin 3-O-glycoside, quercetin 3-O-rutinoside, and kaempferol 3-O-glycoside from different parts of *T. terrestris L. var. orientalis.* [108-112]

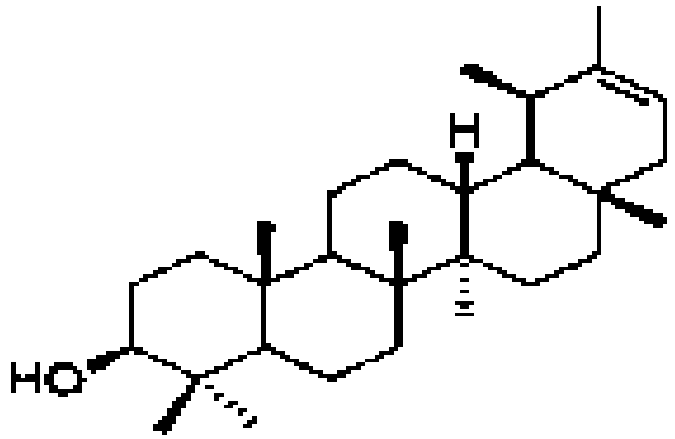
Phytochemical chemical constituents documented in *Bryophyllum pinnatum*:

A variety of chemical compounds have been identified in *Bryophyllum pinnatum*. The sap contains polysaccharides, minerals, and flavonoids, while the leaves contain alkanes, triterpenes, and steroids. Fresh leaves yield organic acids, steroids, hydrocarbons, phenolic compounds, and flavonoids in methanolic extracts. Shoots are rich in steroids, particularly identified in dichloromethane extracts. Bufadienolide orthoacetate is found in the chloroform fraction of the methanolic extract of the aqueous residue of the whole fresh plant. Leaves also exhibit a high content of palmitic acid, stearic acid, and traces of other acids in the acid fraction. Bufadienolides such as: bryophyllin A, bryophyllin C, and bersaldegenin-3-acetate are prevalent in methanolic extracts of leaves. Other compounds include: quercitrin in aqueous extracts of fresh leaves, 1-Octen-3-O-α-l-arabinopyranosyl-(1 → 6)-β glucopyranoside in ethanolic extracts of dried leaves, and rubisco (ribulose 1,5-bisphosphate carboxylase-/Oxigenase) in tampon TEGN of leaves. The plant's powdered form contains alkaloids, tannins, steroids, flavonoids, sugars, and organic acids in various extracts. Flavonoids like: quercetin 3-O-α-l-arabinopyranosyl (1 → 2) α-l-rhamnopyranoside and kaempferol 3-O-α-l-arabinopyranosyl (1 → 2) α-l-rhamnopyranoside are present in aqueous extracts of leaves. Phenolic acids and flavonoids such as: gallic acid, caffeic acid, and kaempferol-3-O-rutinoside are found in ethyl acetate and methanol extracts of leaves. Other compounds include: 1-Ethanamino-7-hex-1-yne-5'-one phenanthrene in ethanolic extracts of dried leaves, 5i Methyl 4i ,5,7-trihydroxyflavone and 4i ,3,5,7-Tetrahydroxy-5-methyl-5i-propenamine; anthocyanidines in ethanolic extracts of powdered plants, and kaempferitrin, afzelin, and α-rhamnoisorobin in methanolic extracts of leaves. Steroids like stigmasterol are present in petroleum ether extracts of shoots, while rutin, luteolin, and luteolin 7-O-β-glucoside are identified in methanolic extracts of leaves. Bufadienolides such as: bersaldegenin-1-acetate, bersaldegenin-3-acetate, bersaldegenin-1,3,5-orthoacetate, and bufalin are found in dichloromethane and ethanol extracts of leaves. Phenolic compounds like: KPB-100 and KPB-200 are also reported in acetone and methanol extracts of leaves. [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55] [56].

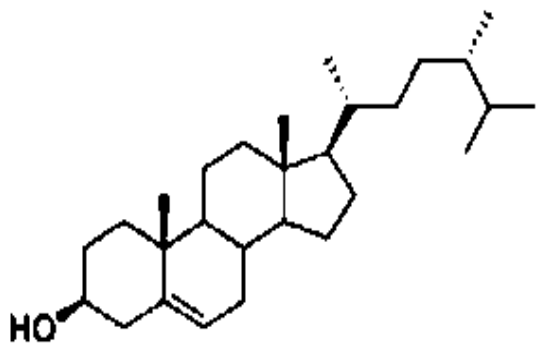
Research on the potential anticancer activity of *Kalanchoe pinnata* highlights its significance as a potential source of therapeutic compounds. While numerous plant components show promise as anticancer agents, clinical trials are necessary to validate their pharmacokinetic effects. The *Kalanchoe* genus, including *Kalanchoe pinnata*, is recognised for its diverse medicinal properties, ranging from treating gastric ulcers and urolithiasis to combating bacterial, viral, and parasitic infections, as well as addressing skin ailments, colds, and even enhancing memory and sleep quality during cancer treatment. Ethnobotanical evidence supports the evaluation of *Kalanchoe* species against various cancer cell lines, with studies focusing on the phytochemical composition of *Kalanchoe pinnata* revealing its potential anticancer properties. [57]

Table 1. *Kalanchoe pinnata* phytochemical constituents present in the plant.

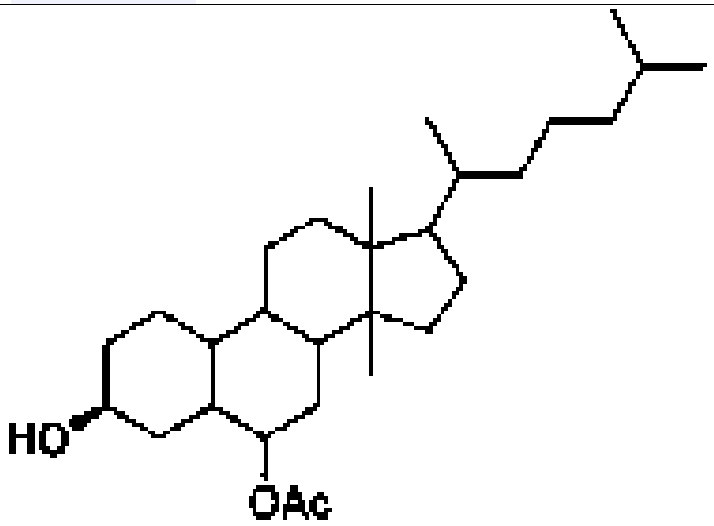
 **Bryophynol**	 **(24 *R*)-ergost-5-enol**



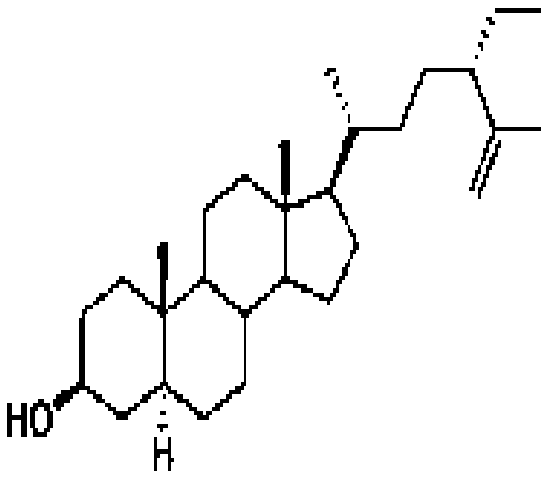
Ψ -taraxasterol



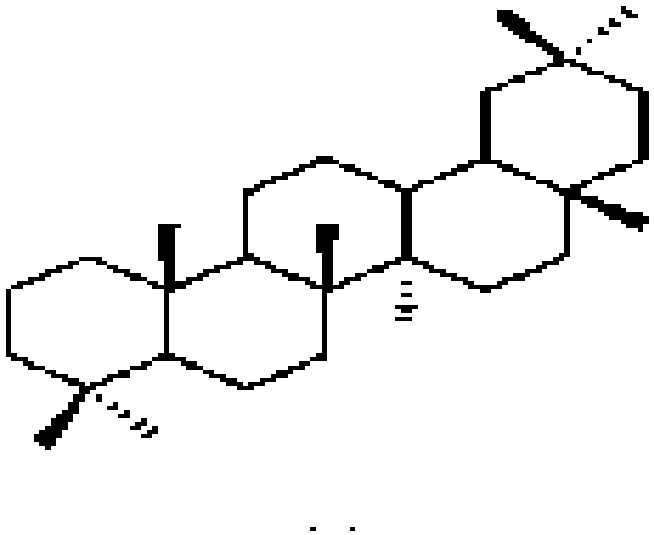
(24 S)-ergost-5-enol



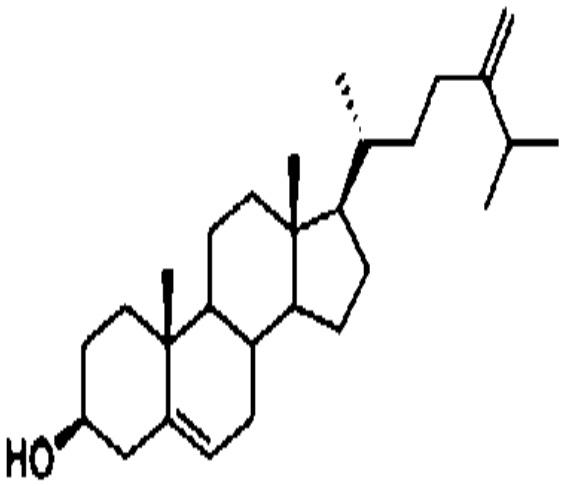
Bryophyllol



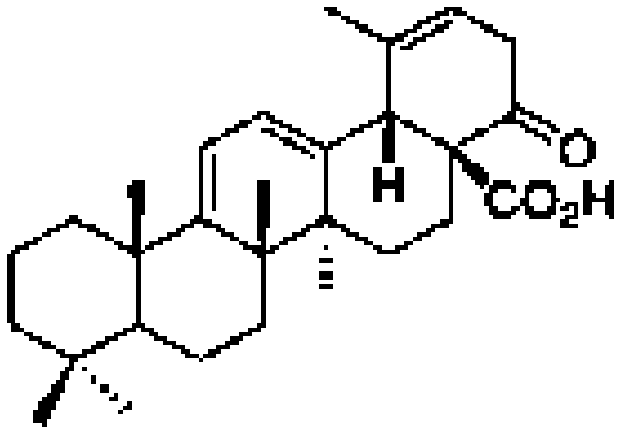
(24 *S*)-stigmast-25-enol.



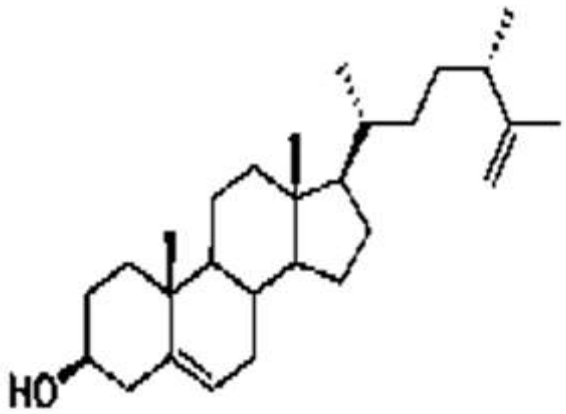
18α-oleanane



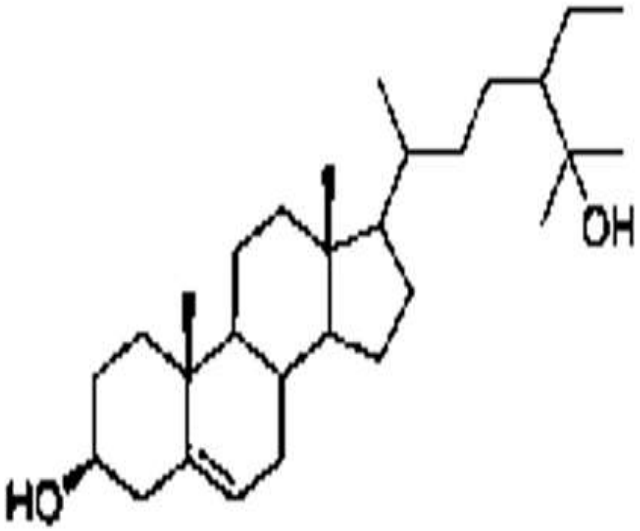
ergost-5,24(28)-dienol



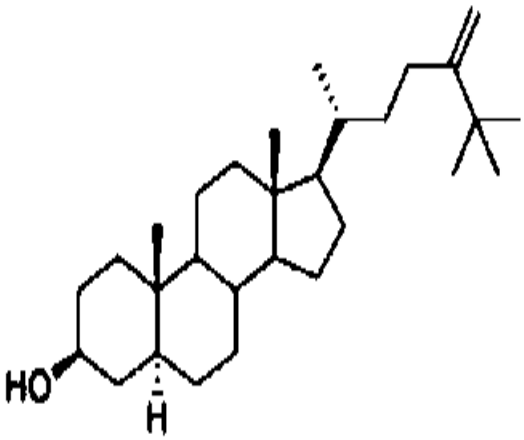
Bryophollone



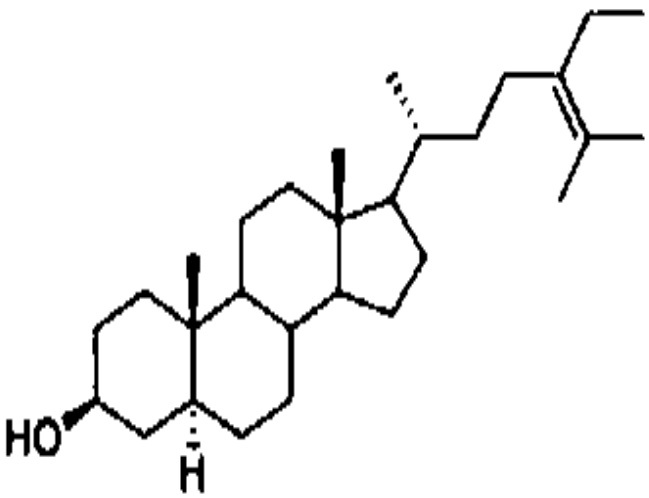
(24 S)-ergosta-5,25-dienol



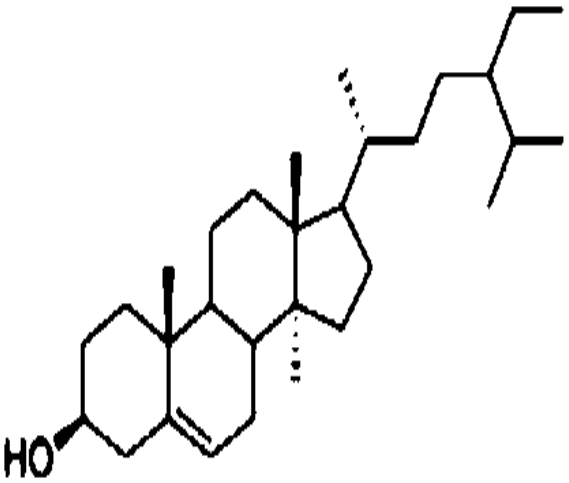
bryophollenone; 24-ethyl-25-hydroxycholesterol



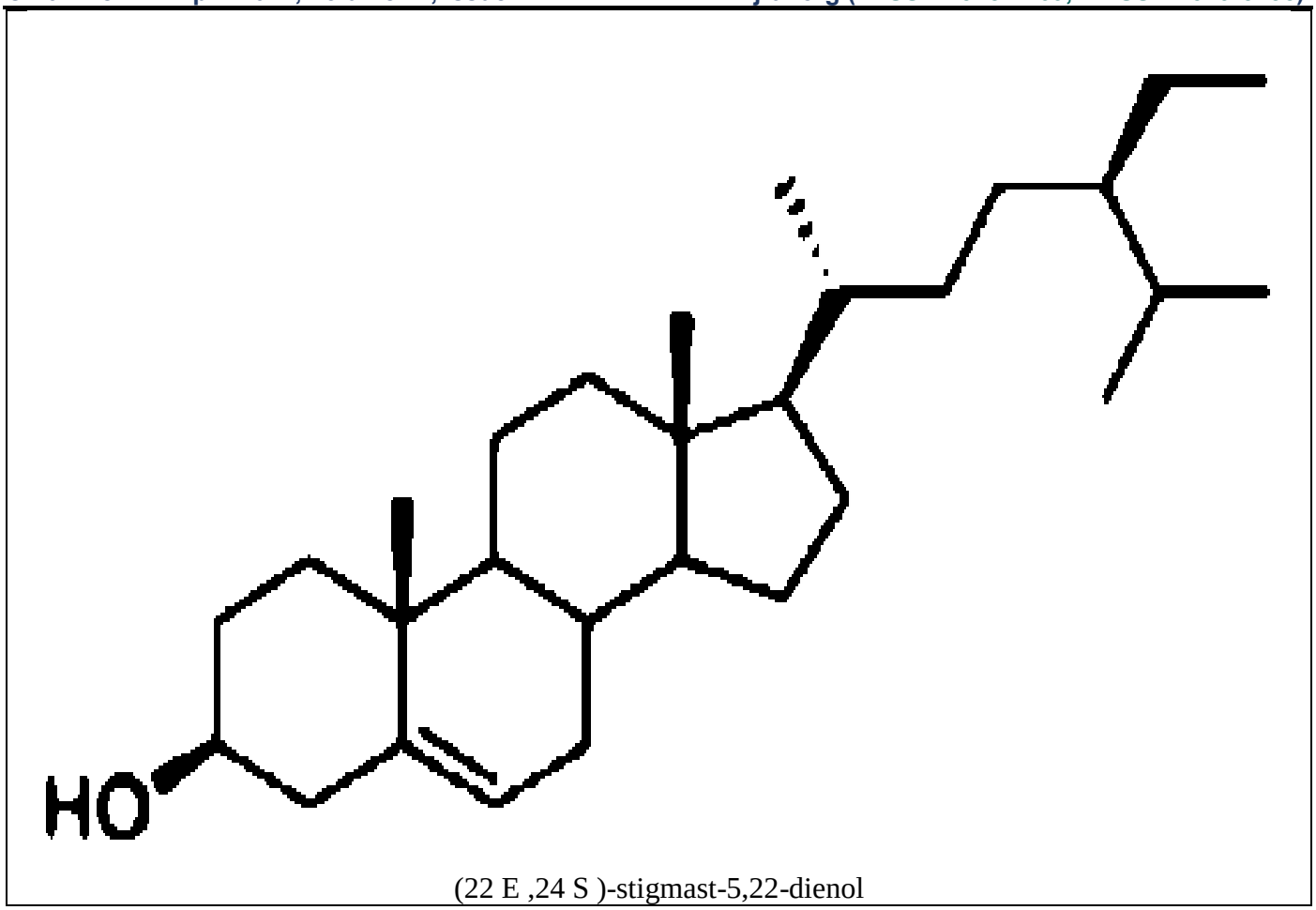
25-metylergost-24(28)-enol



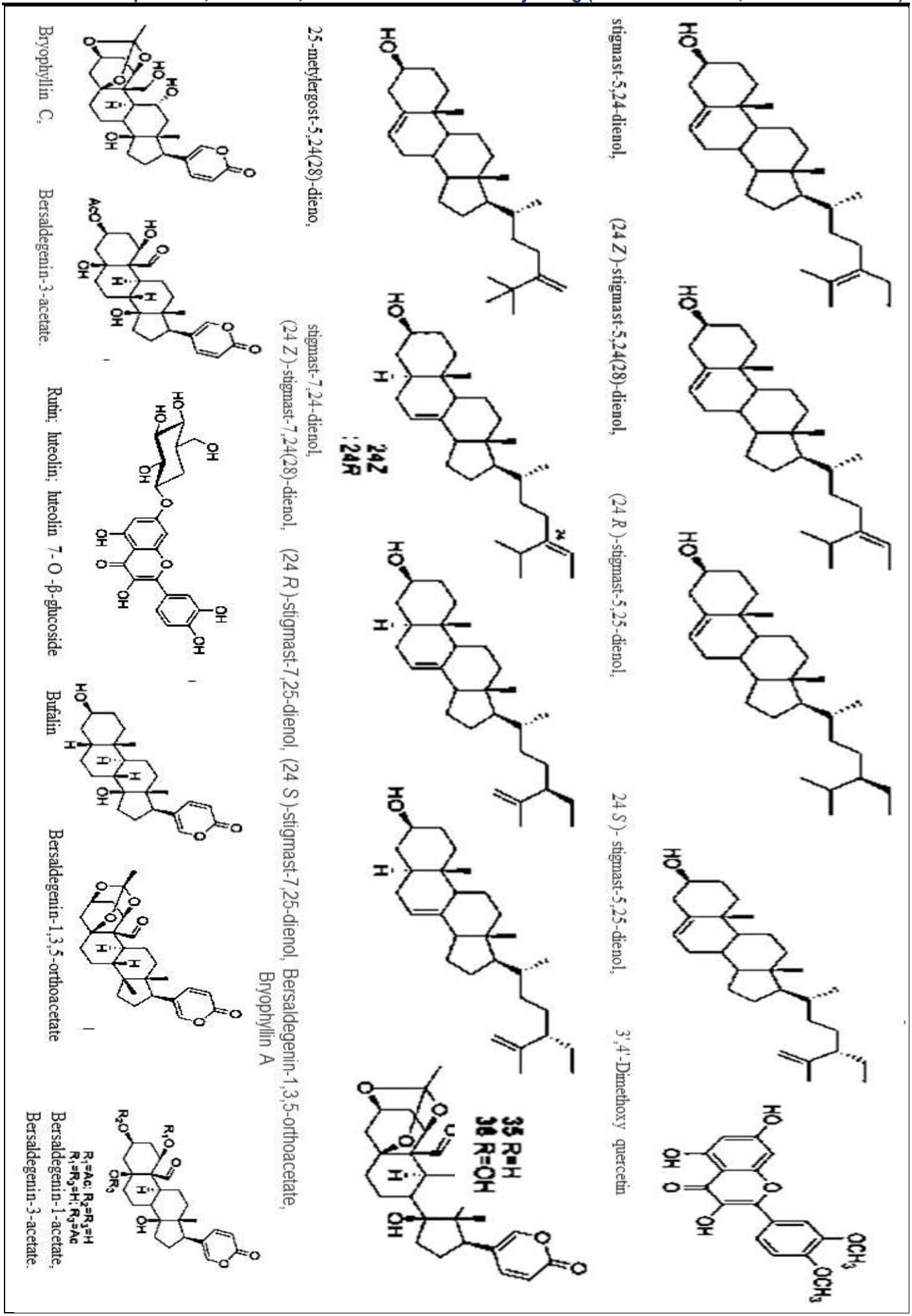
Stigmast-24-enol



(24 *R*)-stigmast-5-enol



(22 E ,24 S)-stigmast-5,22-dienol



Research examining the pharmacological properties of *K. laciniata* and *B. pinnatum* predominantly focuses on assessing the activities of their juices or extracts derived from the leaves and/or aerial parts. Most studies involving *K. laciniata* employ hydroethanolic extracts, whereas for *B. pinnatum*, ethanolic extracts are

commonly used for *in vitro* investigations, while aqueous extracts are favored for *in vivo* studies. However, there is a notable discrepancy in the quantity of studies conducted on each species, with *B. pinnatum* being the subject of a greater number of investigations. This aligns with the observed trends in both chemical analyses and ethnopharmacological research, as previously discussed in this article. Here is a summary of the principal pharmacological activities explored (both *in vitro* and *in vivo*) for both species, along with the respective number of studies conducted for each plant.

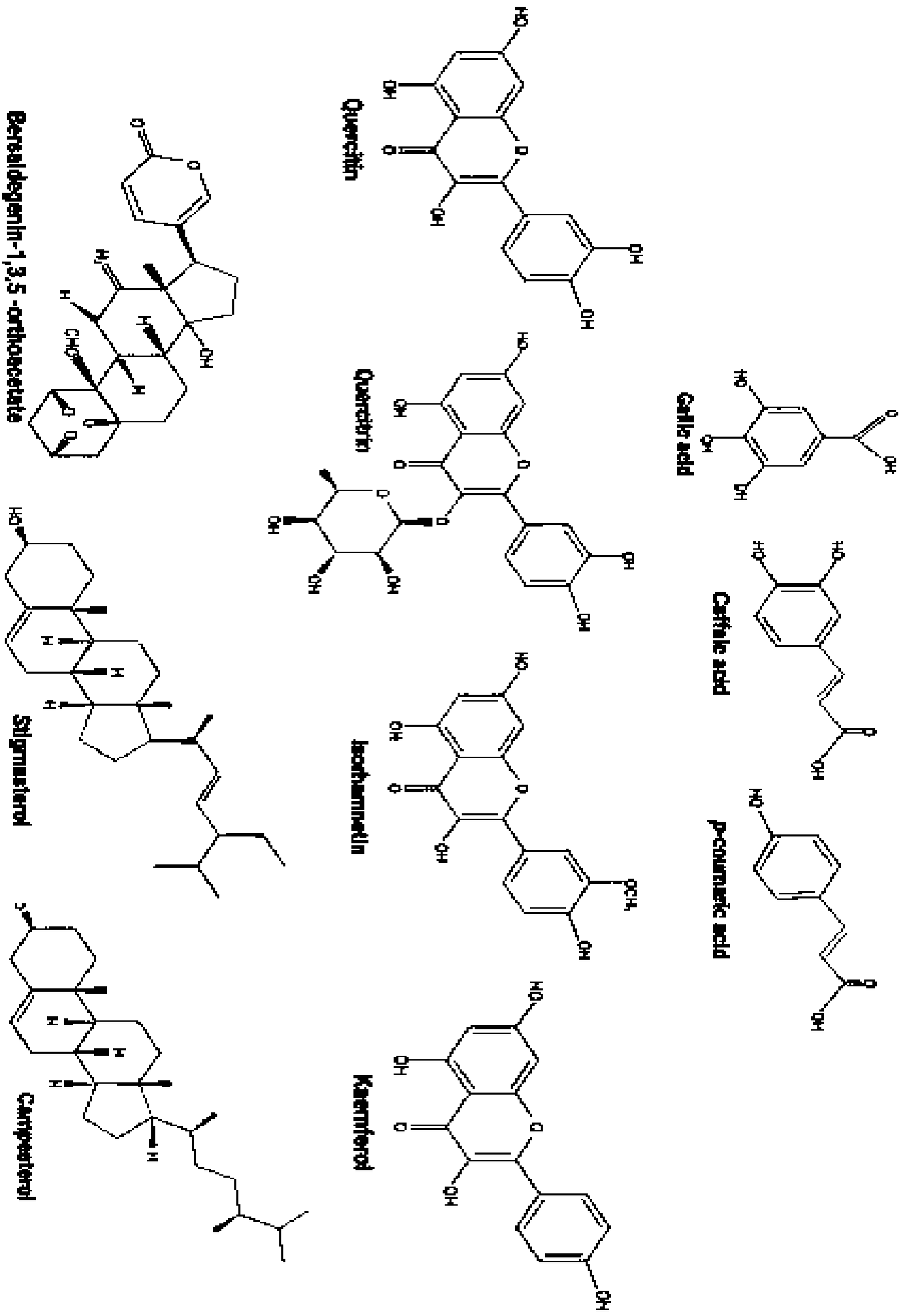
Bryophyllum pinnatum exhibits a range of pharmacological effects, including: modulation of the immune system, influence on the nervous system, impact on the urinary system, gastroprotective properties, anti-snake venom activity, cholesterol-lowering effects, antidiabetic effects, antioxidant activity, and antimicrobial action. [5]

The botanical, chemical, ethnopharmacological, pharmacological, and toxicological properties of *Bryophyllum pinnatum* have been extensively studied, but *Kalanchoe laciniata* has been the subject of much less studies. There are not enough toxicological investigations for either species. *K. laciniata* has a wide range of traditional uses, so assessing its pharmacological qualities requires immediate scientific attention. Clinical research is still scarce despite the known traditional usage and non-clinical pharmacological studies of both species. To pinpoint the precise substances in charge of their purported pharmacological effects, more investigation is necessary. Overall, the information presented in this review emphasises the importance of *K. laciniata* and *B. pinnatum* as priceless botanical resources for complementary therapy modalities for a range of illnesses. [5]

Overall, a study suggests that *Kalanchoe pinnata* has promising anticancer properties mediated through multiple mechanisms, making it a valuable candidate for further research and potential integration into cancer treatment regimens. [57]

The main scientific findings of the study on *Kalanchoe pinnata's* anticancer potential are as follows:

I. **Identification of bioactive ingredients:** The herb contains various bioactive compounds such as: bersaldegenin, bryophollone, bryophyllin A, bryophyllin C, bryophyllol, bryophynol, caffeic acid, campesterol, coumaric acid, gallic acid, isorhamnetin, kaempferol, quercetin, quercitrin, stigmasterol.



II.

Figure 3. Chemical constituents. [58]

III. **Anticancer mechanisms:** These phytochemicals play a role in regulating key processes involved in cancer progression, including: proliferation, apoptosis, cell migration, angiogenesis, metastasis, oxidative stress, and autophagy.

IV. **Epigenetic modulation:** The bioactive compounds have the potential to act as epigenetic drugs by reversing acquired epigenetic changes associated with tumour resistance to therapy. This includes inhibiting promoter methylation of suppressor genes, inhibiting the activity of DNMT1 and DNMT3b enzymes, and regulating histone deacetylase (HDAC) activity.

V. **Pathway regulation:** The phytochemicals regulate various signaling pathways implicated in cancer development and progression, including the: PI3K/Akt/mTOR, Nrf2/Keap1, MEK/ERK, and Wnt/β-catenin pathways.

VI. **Adjuvant role in cancer treatment:** Based on the data, *Kalanchoe pinnata* shows potential as an adjuvant therapy in cancer treatment, particularly when used in combination with conventional therapies such as: chemotherapy or radiotherapy.

VII. *Kalanchoe pinnata*, also known as: *Bryophyllum pinnatum*, is a succulent plant from the *Kalanchoe* genus, typically found as a herb or shrub in gardens. It boasts opposite, simple, and compound leaves with a distinctive red to dark purple crenate margin. This plant reproduces through seeds and vegetatively via leaves, showcasing clusters of reddish-purple pendulous flowers. With a history deeply rooted in traditional medicine, *Kalanchoe pinnata* is utilised to address various ailments, including cancer. [57] [61] [62] [63] [64] [65] [66] [67] [68] [69] [70] [71] [72]

VIII. Studies by Mora-Pérez and Hernández-Medel have revealed the diverse phytochemical composition of *Kalanchoe pinnata*. Methanolic root extracts contain alkaloids and sterols, while stem extracts boast terpenes, sterols, flavonoids, chlorides, nitrates, and potassium. The leaves of *Kalanchoe pinnata* are particularly rich in phenols like gallic acid, and flavonoids such as: quercetin, lycopenes, and β-carotenes, along with tannins and alkaloids. Moreover, analyses have identified phenolic acids (gallic, caffeic, and coumaric acids), flavanol glycosides (quercetin, isorhamnetin, and kaempferol), and other compounds like: quercitrin and bufadienolides (bersaldegenin acetate, bryophyllin a, bryophyllin c, and bersaldegenin-1,3,5-orthoacetate). [57] [61] [62] [63] [64] [65] [66] [67] [68] [69] [70] [71] [72]

IX. Phenanthrene derivatives including Ψ-taraxasterol and 18-α-oleanane, as well as sterols like stigmasterol and campesterol, have also been identified. Notably, the leaves of *Kalanchoe pinnata* are abundant in ascorbic acid (vitamin C) and various essential nutrients such as: riboflavin, thiamine, niacin, magnesium, calcium, potassium, phosphorus, sodium, iron, and zinc. Additionally, the flowers of *Kalanchoe pinnata* exhibit a higher concentration of glycosides, akin to other species within the *Kalanchoe* genus. [57] [61] [62] [63] [64] [65] [66] [67] [68] [69] [70] [71] [72]

The *Kalanchoe* genus exhibits diverse anticancer properties across various studies: *Kalanchoe daigremontiana Raym*.-Hamet and H. Perrier demonstrated antiproliferative, cytotoxic, and antioxidant activity against ovarian, cervical, breast cancer, and melanoma cell lines (SCOV-3, HaCaT, HeLa, MCF-7, A375), inducing cell cycle arrest and caspase-independent cell death *in vitro*. *Kalanchoe integra var. crenata* (Andr.) exhibited cardio-protection against doxorubicin-induced cardiotoxicity and induced apoptosis in colorectal adenocarcinoma, lung cancer, mesothelioma, hepatocarcinoma, and breast cancer cell lines (DLD-1, A549, SPC212, HepG2, MCF-7) both *in vivo* (rats) and *in vitro*. *Kalanchoe tubiflora* (Harvey) induced autophagy, cell cycle arrest, senescence, and apoptosis in lung cancer, lung adenocarcinoma, oral adenosquamous carcinoma, melanoma, and leukemia cell lines (CL1-5, A549, Cal-27, A2058, HL-60) *in vitro* and *in vivo* (mice). *Kalanchoe gastonis-bonnieri Raym*.-Hamet exhibited antiproliferative activity and apoptosis induction in benign prostatic hyperplasia and prostate cancer cell lines (stromal cells, LAPC-4, LNCaP, PC-3, DU145) *in vitro*. *Kalanchoe flammea* induced apoptosis and cell cycle arrest in prostate cancer cell lines (PC-3, LNCaP, PrEC) *in vitro*. *Kalanchoe laetivirens* reverted etoposide resistance in lung cancer cell lines (A549, A549RT-eto) *in vitro*. *Kalanchoe gracilis* (L.) DC displayed antiproliferative, antioxidant, and anti-inflammatory activity in murine macrophage and human hepatocarcinoma cell lines (RAW264.7, HepG2) *in vitro*. *Kalanchoe beharensis* induced apoptosis and inhibited NF-κB in acute myeloid leukemia cell lines (HL-60, HL60R) *in vitro*. *Kalanchoe brasiliensis* exhibited cytotoxic activity against kidney carcinoma cell lines (3T3, 786-0) *in vitro*. *Kalanchoe laciniata* demonstrated cytotoxic activity against a baby hamster kidney cell line (BHK-21) both *in vitro* and *in vivo* (mice). [57] [73- 88]

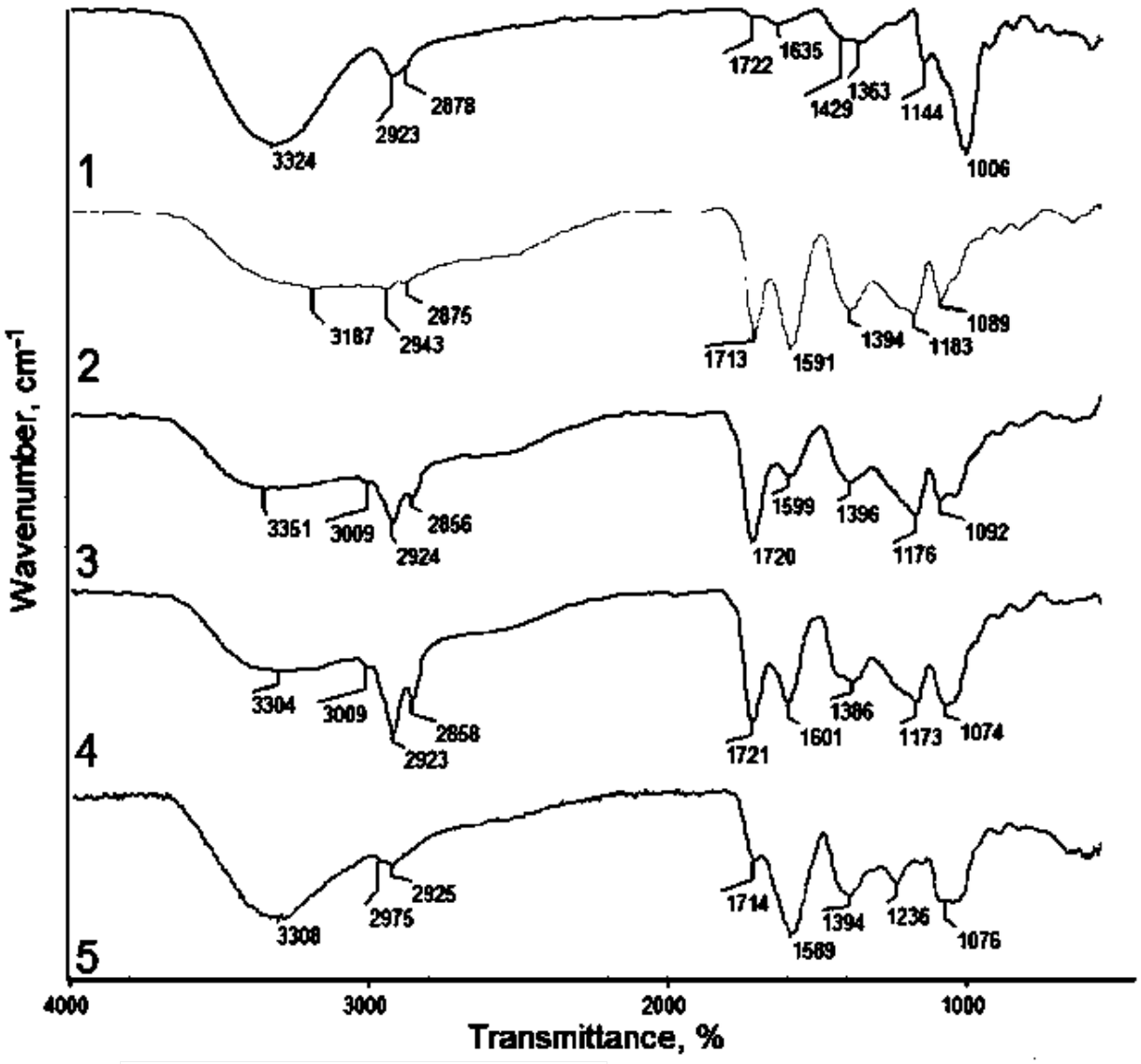


Figure 4. FTIR spectra of *Kalanchoe pinnata* leaf.

The **FTIR**[90] spectra were obtained for various samples including *Kalanchoe pinnata* leaf, a commercially available extract, and plant extracts prepared using different ethanol solutions. These solutions included those made with 50% ethanol, 95% ethanol, and 95% ethanol with ultrasonic treatment.

Snippet:

In a study focusing on lupus nephritis, the aqueous extract derived from *Kalanchoe pinnata* leaves exhibited immunosuppressive effects. However, when combined with methylprednisolone, there was a risk of interaction observed. Rats were divided into two groups: one group received methylprednisolone (MP) at a dosage of 0.72 mg/kgBW, while the other group received a combination of MP (at a dosage of 0.36 mg/kg BW) and the *K. pinnata* extract (at a dosage of 140 mg/kg BW). These treatments were administered daily for a duration of 4 weeks. The concentration of methylprednisolone in the rats' serum was assessed using HPLC, employing an extraction method based on the Lawson method (1985). The analysis utilised an Inertsil C-18 column with a mobile phase consisting of KH_2PO_4: methanol (15:85) buffer, a flow rate of 0.6 mL/minute, UV detection at $\lambda = 230$ nm, and a pressure of 1319 psi. The findings revealed an interaction between the two substances. Specifically, the combination of methylprednisolone and the aqueous extract of *K. pinnata* leaves led to an interaction, resulting in methylprednisolone levels comparable to those observed in the MP-only group. It was found that the aqueous extract of *Kalanchoe Folium* may raise the concentration of methylprednisolone in plasma, as evidenced by the mean drop in serum methylprednisolone levels of 0.285 ppm. Therefore, careful adjustment of the dosage should be considered when administering this combination therapy. [91]

Kalanchoe crenata Andr. is a succulent herbaceous plant utilised in African traditional medicine to alleviate various ailments including: otitis, headaches, inflammations, convulsions, and general debility. This study investigated the analgesic and anticonvulsant properties of different extracts and fractions obtained from the plant. The methylene chloride/methanol (CH_2Cl_2/CH_3OH) extract and its hexane, methylene chloride (CH_2Cl_2), ethyl acetate, n-butanol fractions, and aqueous residue were evaluated using various pain models such as: acetic acid, formalin, and pressure tests. Additionally, the anticonvulsant effects of the CH_2Cl_2/CH_3OH extract were assessed against seizures induced by different convulsant agents.

Oral administration of the CH_2Cl_2/CH_3OH extract and its fractions at doses of 150 and 300 mg/kg demonstrated a protective effect of at least 30% against acetic acid-induced pain, with the CH_2Cl_2 fraction exhibiting a maximal effect of 78.49% at 300 mg/kg. The extract and its CH_2Cl_2 fraction significantly reduced the first phase of formalin-induced pain, while completely inhibiting the second phase. Moreover, the CH_2Cl_2 fraction showed over 45% reduction in sensitivity to pressure-induced pain. The CH_2Cl_2/CH_3OH extract also prolonged the latency period in seizures induced by pentylenetetrazol (PTZ) and reduced the duration of seizures induced by PTZ, strychnine sulphate (STN), and thiosemicarbazide (TSC). Additionally, 20% of the mice were shielded from mortality in seizures brought on by TSC and STN by the extract. These results point to the possibility of anticonvulsant properties and both peripheral and cerebral analgesic effects from *Kalanchoe crenata* leaves. [92]

In traditional medicine, both *Kalanchoe brasiliensis* and *Kalanchoe pinnata* are commonly used for treating peptic ulcers and inflammatory conditions. This study aims to characterise the chemical constituents and assess the gastroprotective activity of the leaf juices from these two species using acute gastric lesion models. Chemical characterisation was conducted through thin layer chromatography (TLC) and ultra-high-performance High Performance Liquid Chromatography coupled to Mass Spectrometer (UHPLC-MS). Pre-treatment with leaf juices (at doses of 125, 250, and 500 mg/kg) or ranitidine (at 50 mg/kg) was administered orally to Wistar rats. Analysis of the chromatogram of *K. brasiliensis* revealed peaks with mass spectra resembling flavonoid glycosides derived from patuletin and eupafolin. *K. pinnata* similarly showed mass spectra similar to those of substances produced from kaempferol, patuletin, quercetin, and eupafolin. In the ethanol induction paradigm, administration of *K. brasiliensis* at all doses and *K. pinnata* at 250 mg/kg and 500 mg/kg dramatically decreased lesions. At dosages of 250 and 500 mg/kg, both species demonstrated noteworthy outcomes in the indomethacin induction model.

Further, pre-treatment with leaf juices increased the levels of the antioxidant defence system, glutathione (GSH), while decreasing the levels of malondialdehyde (MDA), myeloperoxidase (MPO), interleukin-1β (IL-1β), and tumour necrosis factor-α (TNF-α). Treatment with leaf juices also upregulated the expression of zone occludens-1 (ZO-1) and downregulated the expression of inducible nitric oxide synthase (iNOS) and nuclear factor-κB transcription (NF-κB-p65), indicating a cytoprotective effect and maintenance of mucus production. These results demonstrate the gastroprotective effects of the leaf juices from both *Kalanchoe* species against ethanol and gastric indomethacin-induced injury. This protective effect is attributed to the suppression of gastric inflammation, antioxidant activity, and the preservation of cytoprotective defenses and mucosal structure. [93]

The leaves of *Kalanchoe pinnata* are widely used for wound healing, and its effectiveness against leishmaniasis has been proven in animal studies, with active flavonoid components identified. This study aimed to standardise the *K. pinnata* leaf extract by assessing the impact of harvest season, sunlight exposure, and extraction method on flavonoid content with antileishmanial properties. HPLC-DAD-MS was employed to identify and quantify active flavonoids in various extracts, while statistical analyses included ANOVA followed by the Tukey test for multiple comparisons. Antileishmanial potential was evaluated by measuring nitric oxide production by murine macrophages using the Griess method. Results showed that active flavonoids were notably more abundant when leaves were harvested in the summer, and aqueous extraction at 50°C yielded the highest flavonoid content. Sunlight exposure proved beneficial, as plants grown under direct sunlight exhibited a 7-fold increase in the yield of the most active flavonoid, quercitrin, compared to those grown in shade. All aqueous extracts tested enhanced macrophage nitric oxide production, with hot aqueous extracts from summer-harvested leaves demonstrating the highest activity, consistent with HPLC-DAD-MS findings. Further, *in vitro* monoclonal KP specimens were developed to minimise individual chemical variations and optimise the production of the active extract. These monoclonal specimens produced anti-leishmanial flavonoids and were quickly adapted to field circumstances. Overall, this study highlights optimal cultivation, harvest, and extraction conditions for obtaining a *K. pinnata* extract with the highest antileishmanial activity, providing valuable insights for future research and therapeutic applications. [94]

Through bioassay-guided fractionation of a methanol extract from *Kalanchoe pinnata* leaves, two potent insecticidal bufadienolides were isolated. One of these compounds, identified as bryophyllin A (also known as bryotoxin C), was already known. The second compound, designated as bryophyllin C, was structurally elucidated using spectroscopic methods and by chemically transforming compound 1. Both compounds exhibited significant insecticidal activity against third instar larvae of the silkworm (*Bombyx mori*), with LD_{50} values of 3 and 5 microg/g of diet for compounds 1 and 2, respectively. [95]

This research investigates the potential morphological and anatomical responses of *Kalanchoe pinnata* to high levels of UV-B radiation. *K. pinnata*, known for its CAM leaf-succulent nature and flavonoid-rich composition, is often found in hot and arid regions. The study aims to determine if *K. pinnata* employs strategies to counter the effects of elevated UV-B exposure. Plants of the same age were subjected to either

white light (control) or white light supplemented with UV-B radiation for 5 hours daily. Both groups received identical environmental conditions, including photoperiod, temperature, and watering regimen. Upon examination, it was noted that additional exposure to UV-B radiation resulted in the curling of leaves and the appearance of brown patches, which subsequently transformed into a protective tissue primarily on the upper surface of the leaf, particularly in areas directly exposed to radiation. Anatomically, this protective tissue resembled a wound-periderm, characterised by cell walls containing suberin and lignin. This study marks the first documentation of wound-periderm formation in leaves as a response to UV-B radiation. The presence of this protective tissue suggests its significance in enabling *K. pinnata* to survive in desert regions subjected to high UV-B stress. [96]

Kalanchoe pinnata (Lam.) Pers., also known as *Bryophyllum pinnatum* and belonging to the *Crassulaceae* family, holds a significant place in traditional medicine across various temperate regions, notably in South America, where it is utilised for its anti-inflammatory and antiseptic properties in treating ailments like: coughs, ulcers, and sores. This study aimed to devise a method for pinpointing and characterising molecules possessing antimicrobial attributes, potentially serving as substitutes for chemical preservatives in cosmetic formulations. The leaves underwent extraction utilising pressurised liquid extraction (PLE), employing various solvents. Subsequently, antimicrobial activity and cytotoxicity assessments were conducted to identify the most promising extract. The chosen crude extract underwent fractionation via centrifugal partition chromatography (CPC), followed by assessing the antimicrobial activity and cytotoxicity of each fraction. Finally, LC-MS/MS analysis was employed to identify the primary compounds within the most active fraction. [97]

The species *Kalanchoe brasiliensis* and *Kalanchoe pinnata*, commonly known as "Saião," are frequently utilised interchangeably in traditional medicine due to their reputed antiophidic properties. This work intends to clarify the chemical composition and assess the inhibitory effects of hydroethanolic leaf extracts from *K. brasiliensis* and *K. pinnata* against the local effects generated by the venom of *Bothrops jararaca* snake, despite the paucity of research on their anti-venom characteristics. Chemical characterisation utilising Thin Layer Chromatography (TLC) and High Performance Liquid Chromatography coupled with Diode Array Detection and Electrospray Mass Spectrometry (HPLC-DAD-MS/MS) revealed distinct chemical profiles for each species. Significantly, *K. brasiliensis* showcased predominant peaks resembling flavonoid glycosides linked to patuletin and eupafolin, whereas *K. pinnata* displayed UV spectra reminiscent of flavonoid glycosides associated with quercetin and kaempferol. Both extracts demonstrated a significant reduction in the hemorrhagic activity induced by *B. jararaca* venom, particularly in pre-treatment protocols, with around 40% inhibition observed. Additionally, *K. pinnata* displayed activity in post-treatment protocols, achieving approximately 30% inhibition. Moreover, *K. pinnata* demonstrated significant antiedematogenic effects, with inhibition rates of approximately 66% and 30% observed in pre-treatment and post-treatment protocols, respectively. Both extracts also showed inhibition of phospholipase activity, with *K. pinnata* exhibiting higher potency. These findings emphasise the potential antiophidic activity of *Kalanchoe* species against the local effects induced by *B. jararaca* snake venom. [98]

A study aimed to investigate the impact of an aqueous leaf extract of *Kalanchoe pinnata* on blood pressure in both normotensive rats (NTR) and salt hypertensive rats (SHR), alongside its antioxidant properties. Hypertension was induced in rats by orally administering 18% NaCl for a duration of 4 weeks. For the preventive aspect of the study, rats were divided into groups receiving 18% NaCl solution along with plant extract at doses of 25 mg/kg/day, 50 mg/kg/day, or 100 mg/kg/day through gavage. Two positive control groups were gavaged with an 18% NaCl solution and given either spironolactone (0.71 mg/kg/day) or eupressyl (0.86 mg/kg/day) for the same duration of time. Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and heart rate (HR) were measured using invasive methods at the end of the experimental period. Additionally, various oxidative stress biomarkers such as: reduced glutathione (GSH), superoxide dismutase (SOD), and nitric monoxide (NO) were evaluated in the heart, aorta, liver, and kidney, with nitrite concentration serving as an indirect measure of NO levels. The findings demonstrated that *Kalanchoe pinnata* extract effectively mitigated the increase in systolic and diastolic arterial pressures in salt-loaded rats (SHR). Simultaneous treatment of 25 mg/kg/day, 50 mg/kg/day, and 100 mg/kg/day of *Kalanchoe pinnata* in SHR considerably reduced the rise in blood pressure by 32%, 24%, and 47% (for SAP); and 35%, 33%, and 56% (for DAP); respectively. No discernible changes in heart rate were seen. Moreover, the plant extract exhibited an enhancement in antioxidant status across various organs, particularly in the aorta. Because of this, *Kalanchoe pinnata's* antioxidative and vasculature-modifying properties may significantly add to its total antihypertensive effectiveness. This study emphasis the preventive potential of concurrent administration of high salt and aqueous extract of *Kalanchoe pinnata* against salt-induced hypertension in rats. [99]

Okra mucilage, derived from the fresh fruits of the *Abelmoschus esculentus* plant, is a pharmaceutical excipient also known as: *Abelmoschus* Gum or okra gum. Its composition comprises galactose, galacturonic acid, and rhamnose, along with smaller proportions of glucose, mannose, arabinose, and xylose.

Extraction process: To obtain okra (*Abelmoschus esculentus*) mucilage, the pods are first washed carefully and then dried in the shade for 24 hours. Subsequently, they are further dried at 30–40°C until a constant weight is achieved, and their size is reduced using a grinder. The resulting powder is passed through a sieve with a mesh size #22 to obtain a fine powder, which is then stored in an airtight container for future use.

The extraction of mucilage involves the following steps:

Step 1: The powdered fruits are soaked in 500 ml of distilled water and heated at 60°C with continuous stirring for approximately 4 hours. The concentrated solution is then filtered through a muslin cloth and cooled to a temperature between 4°C and 6°C.

Step 2: The mucilage is further isolated from the cooled filtrate using acetone, while simultaneously filtering it through the muslin cloth. The mucilage obtained is dried until a constant weight is achieved at a temperature ranging from 35°C to 45°C in a hot air oven. Any hardened mucilage cake is ground and sieved through a sieve with mesh size #22 and stored in a desiccator for subsequent use. [100]

Other type of binder and disintegrant that can be incorporated in the tablets includes as follows:

Watermelon rind powder holds promise for various applications beyond consumption. Its potential health benefits make it a viable ingredient for dietary supplements and herbal tablets, offering convenience for users. Rich in antioxidants and vitamins, it becomes a valuable addition to skincare products, including: face packs, masks, and exfoliating scrubs, to invigorate the skin and combat signs of aging. Additionally, its anti-inflammatory properties can provide relief for irritated skin.

In cosmetic formulations, watermelon rind powder serves as a cleansing agent, effectively removing impurities and unclogging pores in facial cleansers, toners, and masks. Its gentle exfoliating qualities ensure a refreshed complexion by eliminating dead skin cells. Moreover, it finds utility in haircare products like: shampoos, conditioners, and hair masks, contributing to scalp hydration, follicle strengthening, and overall hair health.

The pleasant aroma of watermelon rind powder lends itself well to aromatherapy products, such as: candles, essential oil blends, and room sprays, offering a refreshing and mood-lifting ambiance. It's imperative to ensure proper processing of the powder to maintain purity and safety when incorporating it into non-consumable items like: skincare or cosmetics. Additionally, patch testing on the skin is advisable to preempt any potential allergic reactions before extensive usage of such products. Such polymers can also be extracted from musk melons (*Cucumis melo*) and other such families for its application as binder or disintegrant in tablet.

Figure 5. Natural polymer isolation. [Saurabh D. Bhandare. *Citrullus lanatus* polymer and tablet binders or as an excipient. *YouTube*. Published online April 6, 2024. https://www.youtube.com/watch?v=7hoaZdx4_MQ]

In summary, the formulation and development of tablets involve careful selection of ingredients, optimisation of the manufacturing process, and rigorous quality control measures to produce safe, effective, and stable dosage forms for patient use.

A tablet is a pharmaceutical dosage form that is typically solid and flat, often round or oval in shape. It is made by compressing powdered or granulated ingredients into a coherent, compact mass. Tablets can vary in size, shape, colour, and composition depending on the specific medication and its intended use.

Tablets are distinguished from capsules primarily by their formulation and appearance. While tablets are compressed powders, capsules are made of two separate gelatin shells that contain powder, granules, or liquid medication. Tablets are generally easier to manufacture in large quantities and are more stable than capsules. Additionally, tablets can be designed with special coatings or layers to control the release of medication over time, which can be advantageous for certain drugs.

The formulation and development of tablets involve several key steps:

i. **Formulation Development**: This step involves selecting the active pharmaceutical ingredient (API) and determining the appropriate excipients, which are inactive substances used as carriers or binders in the tablet formulation. Excipients can include fillers, binders, disintegrants, lubricants, and glidants. The formulation must be carefully optimized to ensure the tablet's stability, bioavailability, and efficacy.

ii. **Preformulation studies**: Before formulating the tablet, preformulation studies are conducted to assess the physical and chemical properties of the API and its compatibility with various excipients. These studies help identify any potential challenges or limitations in formulation development.

iii. **Granulation**: Granulation is the process of forming granules from the powdered ingredients of the tablet formulation. Granulation can be achieved through dry granulation, wet granulation, or direct compression methods. This step improves the flow properties of the powder mixture and facilitates uniform tablet compression.

iv. **Tablet compression**: Once the granules are prepared, they are compressed into tablets using a tablet press machine. During compression, the granules are forced together under high pressure to form solid tablets of the desired size and shape.

v. **Coating (if necessary)**: Some tablets may require coating to improve stability, mask taste, or control drug release. Coating materials can include polymers, sugars, or waxes, which are applied as a thin layer onto the tablet surface using coating equipment.

vi. **Quality control and testing**: Throughout the formulation and development process, quality control tests are performed to ensure the tablets meet specifications for identity, potency, purity, and dissolution. These tests help confirm the tablet's safety, efficacy, and consistency.

vii. **Packaging**: Once the tablets are manufactured and tested, they are packaged into containers suitable for distribution and dispensing to patients. Proper packaging helps protect the tablets from environmental factors such as light, moisture, and air, which could affect their stability.

Objectives:

i. To formulate herbal tablets using *Kalanchoe pinnata* extract.
ii. To optimise the tablet formulation for improved efficacy and stability.
iii. To evaluate the pharmaceutical properties of the developed tablets, including hardness, friability, disintegration time, and dissolution profile.
iv. To analyse the bioactive components present in the tablets using appropriate analytical techniques.

Research methodology:

1. **Extraction of *Kalanchoe pinnata*:** The leaves of *Kalanchoe pinnata* will be collected and subjected to extraction using suitable solvents to obtain the plant extract. Soxhlet extraction combines elements of both percolation and maceration methods. It involves using a specialised apparatus called the Soxhlet apparatus, which was invented by Franz von Soxhlet in 1879. [101]

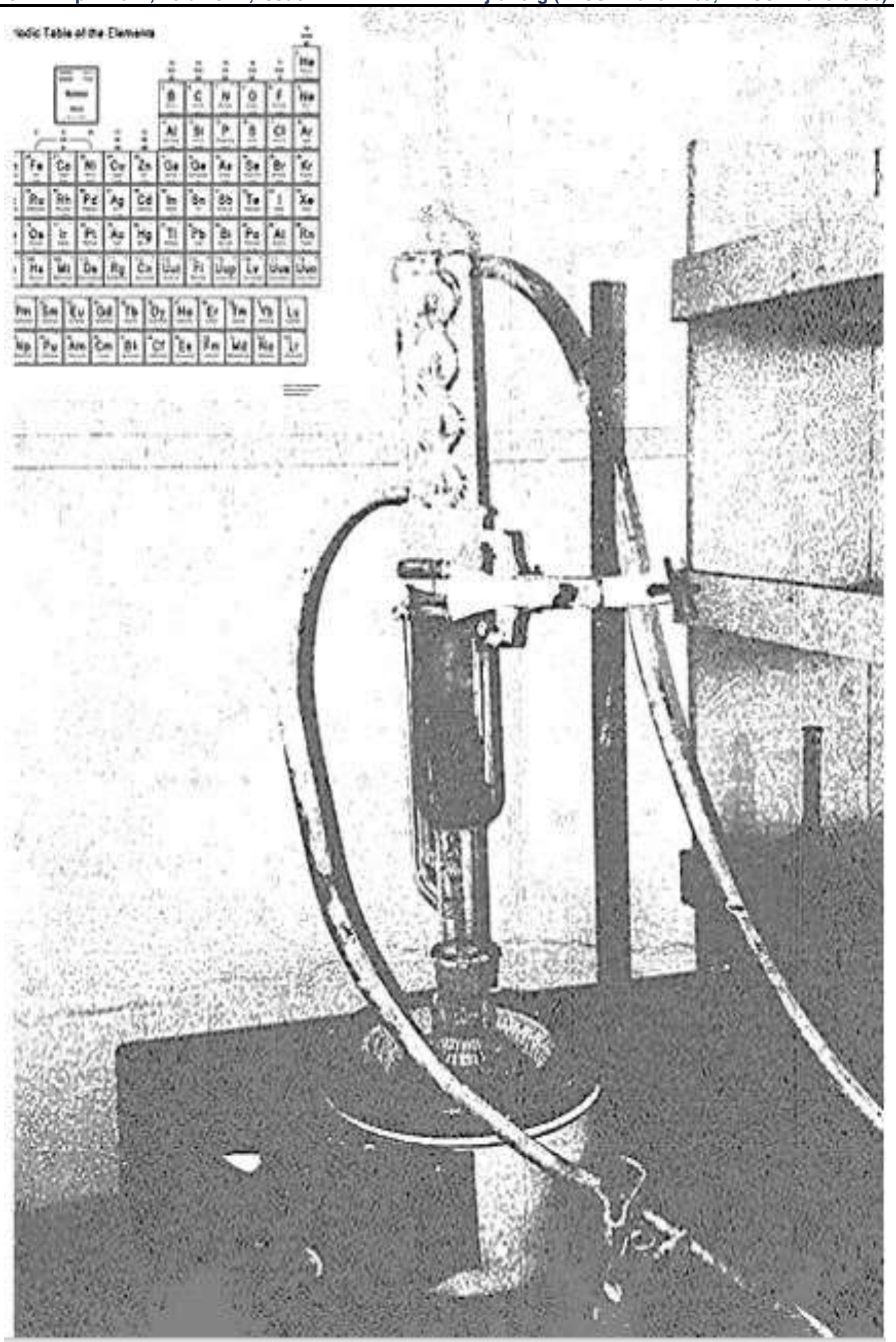


Figure 6. Soxhlet extraction.

2. **Formulation of herbal tablets:** Different concentrations of *Kalanchoe pinnata* extract will be incorporated into tablet formulations along with excipients such as: binders, disintegrants, and lubricants.

3. **Optimisation of tablet formulations:** The tablet formulations will be optimised based on various parameters such as: tablet hardness, friability, disintegration time, and dissolution profile using a factorial design approach.
4. **Evaluation of tablet properties:** The developed tablets will be evaluated for their physical characteristics, including: appearance, dimensions, hardness, friability, disintegration time, and dissolution profile, according to pharmacopoeial standards.

5. **Analysis of bioactive components:** The presence of bioactive compounds in the tablets will be analysed using techniques such as: high-performance liquid chromatography (HPLC) or gas chromatography-mass spectrometry (GC-MS). As its future scope.

Expected results: The research is expected to yield herbal tablets containing *Kalanchoe pinnata* extract with optimised formulation and desirable pharmaceutical properties. The tablets are anticipated to exhibit improved stability and efficacy, making them suitable for further preclinical and clinical studies for potential therapeutic applications.

Table 1. Batch optimisation of tablets:

Run	CMC. (%)	Lactose (%)	Okra Mucilage (%)	Mg St (%)	*Ficus racemose* Powder (%)	Disintegration Time (min)	Hardness (kp)
1	7.5	7.5	28.7	2.8	3.8	26.7 ± 1.3	6.7 ± 0.2
2	0.1	15.1	27.2	2	6.1	24.1 ± 1.6	6 ± 0.4
3	8.9	6.6	26.9	2.7	5.5	24.7 ± 1.3	5.9 ± 0.5
4	15.1	13	15.7	4.1	2.5	21.3 ± 1.0	5.2 ± 0.5
5	7.5	7.5	28.7	2.8	3.8	26.7 ± 1.9	6.6 ± 0.8
6	0.2	3.2	37.1	4.2	6.2	36.2 ± 2.3	6.6 ± 0.4
7	0.3	15.3	28.7	4.3	2.9	30.3 ± 2.1	7.1 ± 0.8
8	13.6	15.2	17.5	2.9	1.8	20.8 ± 1.3	5.8 ± 0.6
9	15.5	0.5	32.3	2.1	2.1	38 ± 2.8	8 ± 1.1
10	7.5	7.5	28.7	2.8	3.8	26.9 ± 1.8	6.5 ± 0.6
11	7.4	15.2	18	4.2	6.2	16.8 ± 1.2	4.2 ± 0.5
12	11.9	2.3	29.5	1.7	5.6	29.6 ± 1	6.4 ± 0.3
13	14.9	14.9	15.0	1.5	3.6	18.2 ± 0.9	5.0 ± 0.0
14	0.0	0.0	44.3	4.0	1.7	46.4 ± 2.6	8.3 ± 0.4
15	5.7	11.1	30.5	1.6	1.6	25.3 ± 1.3	7.7 ± 0.3
16	8.5	12.8	21.5	1.6	6.1	16.9 ± 1.5	5.2 ± 0.6
17	0.0	11.4	35.8	1.6	1.6	33.9 ± 1.8	8.4 ± 0.8
18	7	2.8	33.9	2.9	3.9	34.5 ± 2.6	7.1 ± 0.7
19	15.1	11.00	15.5	2.8	6.1	17.7 ± 0.8	4.2 ± 0.2
20	15.0	1.1	24.0	4.0	6.0	28.4 ± 1.4	5.0 ± 0.2
21	0.0	0.0	42.8	1.6	5.9	40.3 ± 2.01	7.5 ± 0.5

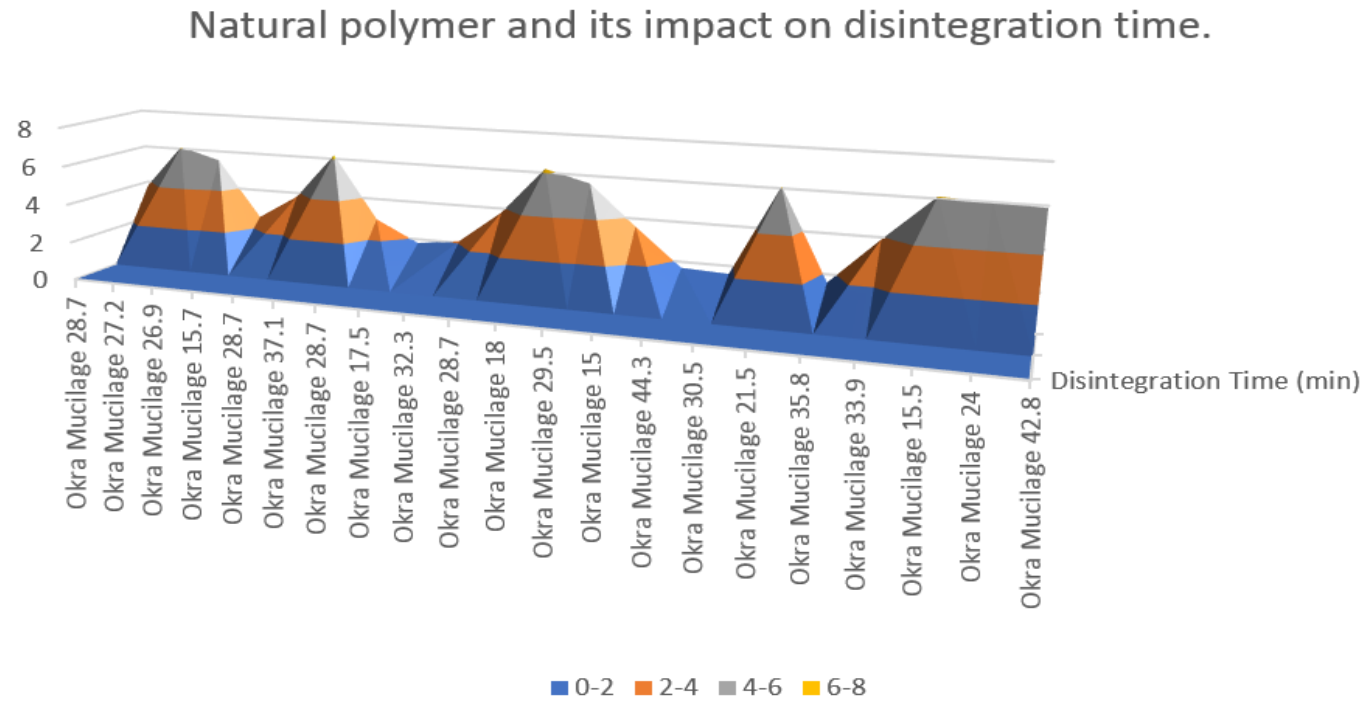


Figure 7. Disintegration time test.

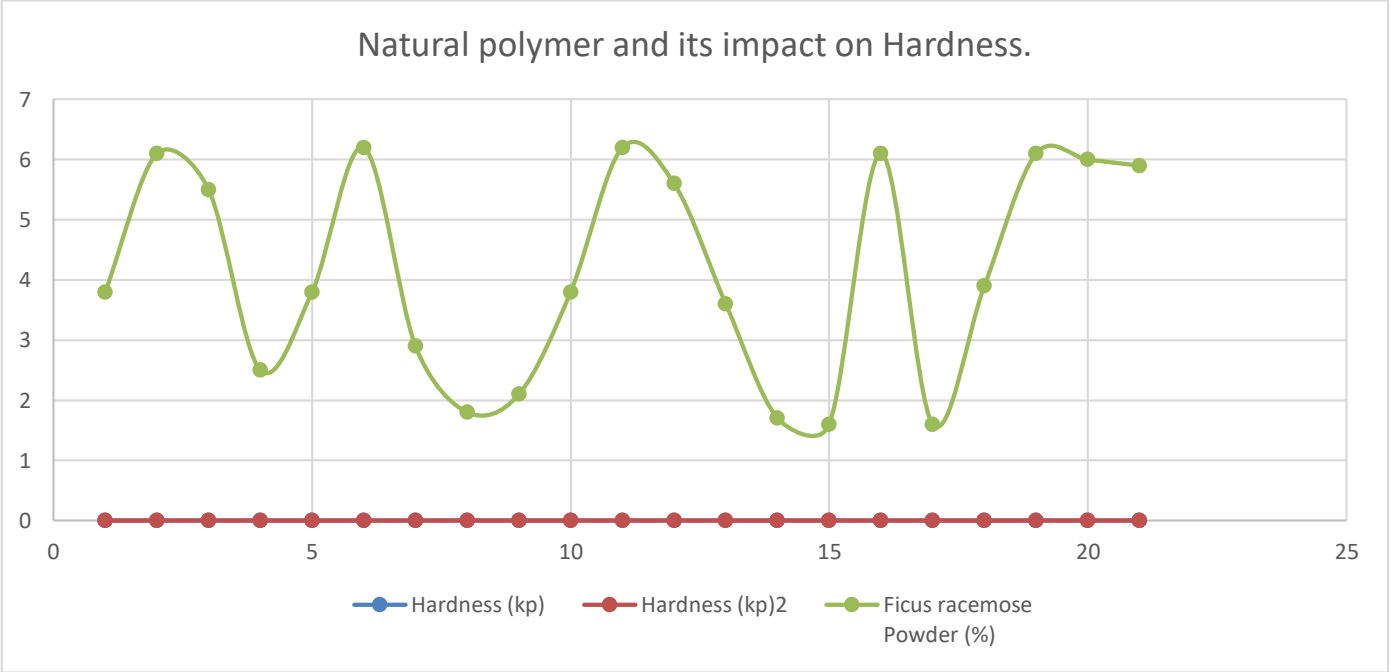


Figure 8. Hardness test.

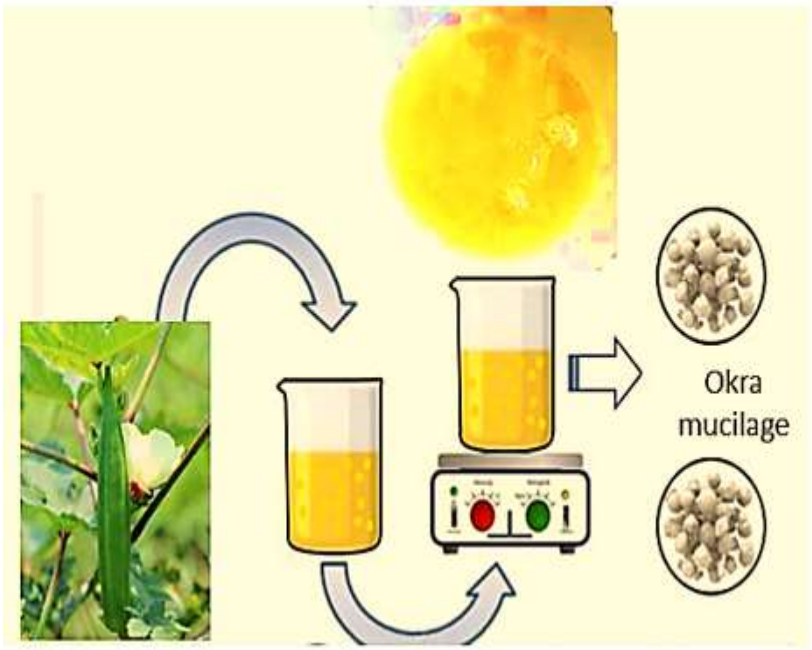
Table 2. Formula batches taken for re-evaluation:

Run	CMC. (%)	Lactose (%)	Okra Mucilage (%)	Mg St (%)	*Ficus racemose* Powder (%)	Disintegration Time (min)	Hardness (kp)
1	7.5	7.5	28.7	2.8	3.8	26.4 ± 1.1	6.9 ± 0.8
2	7.5	7.5	28.7	2.8	3.8	26.5 ± 1.8	6.8 ± 0.9
3	0.2	3.2	37.1	4.2	6.2	36.7 ± 2.8	6.9 ± 0.8
4	0.3	15.3	28.7	4.3	2.9	30.8 ± 2.8	7.9 ± 0.9
5	15.5	0.5	32.3	2.1	2.1	38 ± 2.9	8 ± 1.7
6	7.5	7.5	28.7	2.8	3.8	26.9 ± 1.9	6.8 ± 0.9
7	11.9	2.3	29.5	1.7	5.6	29.9 ± 1	6.8 ± 0.9
8	0.0	0.0	44.3	4.0	1.7	46.9 ± 2.8	8.8 ± 0.8
9	5.7	11.1	30.5	1.6	1.6	25.9 ± 1.9	7.9 ± 0.9
10	0.0	11.4	35.8	1.6	1.6	33.9 ± 1.9	8.9 ± 0.9
11	7	2.8	33.9	2.9	3.9	34.8 ± 2.8	7.9 ± 0.9
12	15.0	1.1	24.0	4.0	6.0	28.8 ± 1.7	5.6 ± 0.8
13	0.0	0.0	42.8	1.6	5.9	40.7 ± 2.08	7.9 ± 0.8

Table 3. Batches of formula used to create final formulations:

Run	CMC. (%)	Lactose (%)	Okra Mucilage (%)	Mg St (%)	*Ficus racemose* Powder (%)	Disintegration Time (min)	Hardness (kp)
1	11.9	10.3	30.5	1.7	10%	30.4 ± 1.04	6.6 ± 0.9
2	0.3	15.3	28.7	4.3	2.9	30.9 ± 2.9	7.9 ± 0.8
3	15.5	0.5	32.3	2.1	2.1	38.09 ± 2.9	8 ± 1.7
4	0.0	0.0	42.8	1.6	5.9	40.00 ± 2.01	7.5 ± 0.5

Table 4. Optimised formula for the final batch of tablet of desired type.

Ingredients:	Quantity	Use or function.
1. CMC	11.5%	Binder.
2. Lactose	10.3%	Binder.
3. Okra mucilage  	30.5%	Binder.
4. Mg. st.	1.7%	Glidant or excipient.

"Mg. st." typically stands for "magnesium stearate," which is a commonly used pharmaceutical excipient. Magnesium stearate is a white, water-insoluble powder that is widely used in the pharmaceutical industry as a lubricant in tablet and capsule formulations. It helps prevent ingredients from sticking to the manufacturing equipment during the tablet compression process, thereby improving the flow properties of the powder blend and facilitating tablet formation.		
5. *Ficus racemose* powder. Can be substituted with Chanca Piedra. 	15%	API, diuretic, stimulant, coolant, blood cleaner, act to neutralise the urine and system. Replace vital nutrients and salts such as: potassium in the body. Dysuria, which is characterised by discomfort, burning, or pain during urination. This symptom can be indicative of various underlying medical conditions, such as: urinary tract infections, bladder inflammation (cystitis), sexually transmitted infections, kidney stones, or irritation of the urethra. It's important to consult a healthcare professional for proper diagnosis and treatment if experiencing painful urination. It is also anti-diabetic, and also used in some herbal treatment to treat diabetic condition. It cleanse body

toxins and is anti-oxidant in nature.

Some rare traditional treatments believe that the bark of the tree are quite potential in treating diabetes. So it can be given in water extracted form or made into formulation such as tablets, capsules and mouth films. But no special evidences are justified on its true potential and therefore must have specific research study that can give the clear idea of it.

In some cultural and traditional practices it is believed that the water collected form the cuts in the roots of this plant is quite good to restore human health as it is anti-oxidant and of many benefits to treat conditions such as chickenpox, smallpox and fever along with improving the vitality and immunity boosting of the body. However justification are must for its uses which are just traditional and no scientific

evidences are found.

The fruit is also used traditionally to treat chickenpox and smallpox. Its paste is applied on burns and honey bee, wasp, and ants bites. The fruit poultice is also utilised on the treatment of pimples and acne, treat wrinkles and tone skin properly. It is also used for making face packs and face cream as a skin tone improving agent. It lightens skin and the fruit along with honey, cucumber juice and lemon can be utilised on the skin lightening therapy along with lemon peel and orange peel powder.

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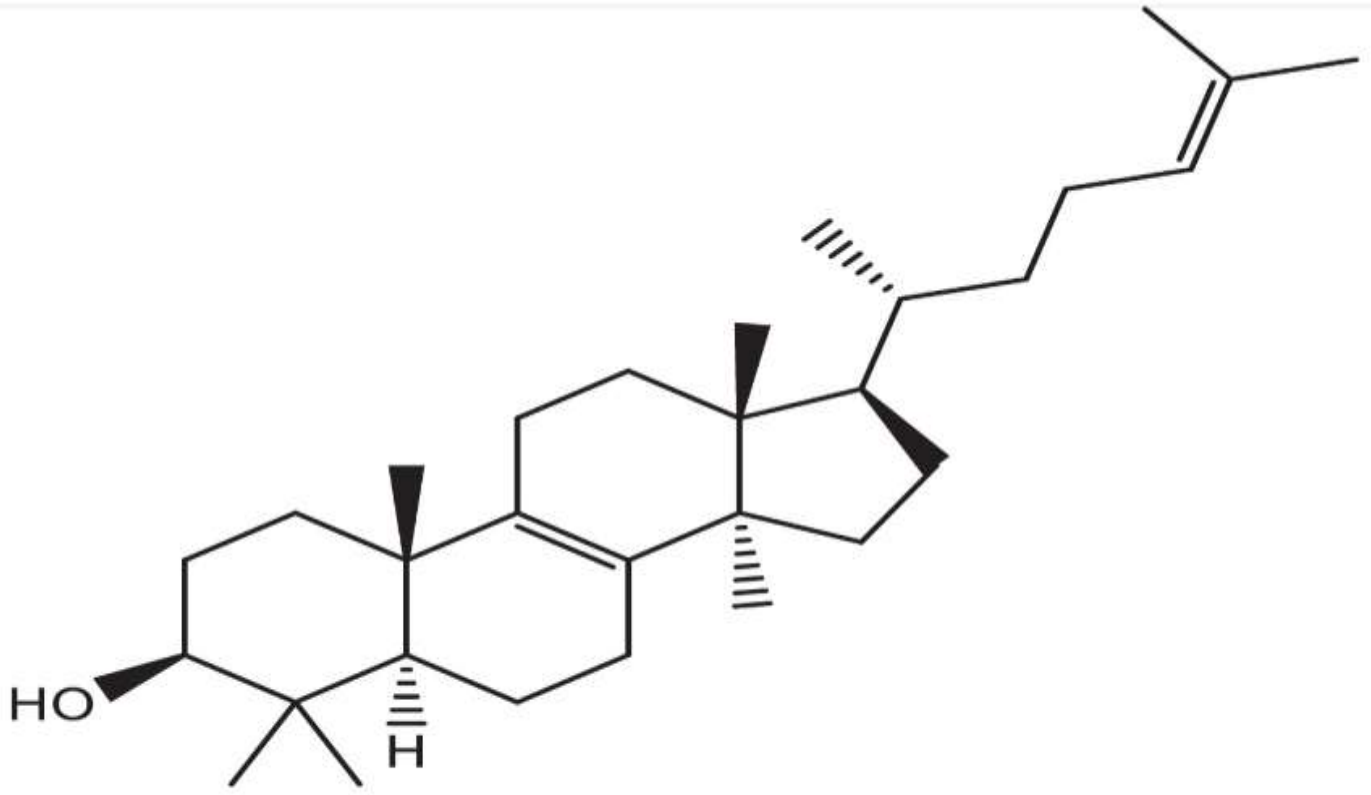
Ficus racemosa, commonly known as Cluster Fig, is a sizable shade tree characterised by its expansive canopy and dense clusters of vibrant yellow, orange, and green fig fruits, which are edible and grow directly on the trunk and larger branches. Typically found in moist environments such as: monsoon forests and coastal dunes, it serves as a reliable shade provider suitable for parks and larger estates. Additionally, it holds significance in Aboriginal Plant Knowledge. This tree can reach heights of 10-15 meters. [121] Excessive care must be taken while using and processing fig, as stated in a study stating that; in the midst of a study on nematodes associated with fig trees in eastern Australia, an uncommon diplogastrid nematode caught or gained attention, which we hereby introduce as *Teratodiplogaster fignewmani* gen. nov., sp. nov. This particular nematode was found among adult and juvenile specimens within the syconia of *Ficus racemose* trees in Queensland and Western Australia. It's likely linked to dispersal by the agaonid fig wasp, *Ceratosolen fusciceps*, to new phase-B sycones. Through molecular phylogenetic analysis utilising near-

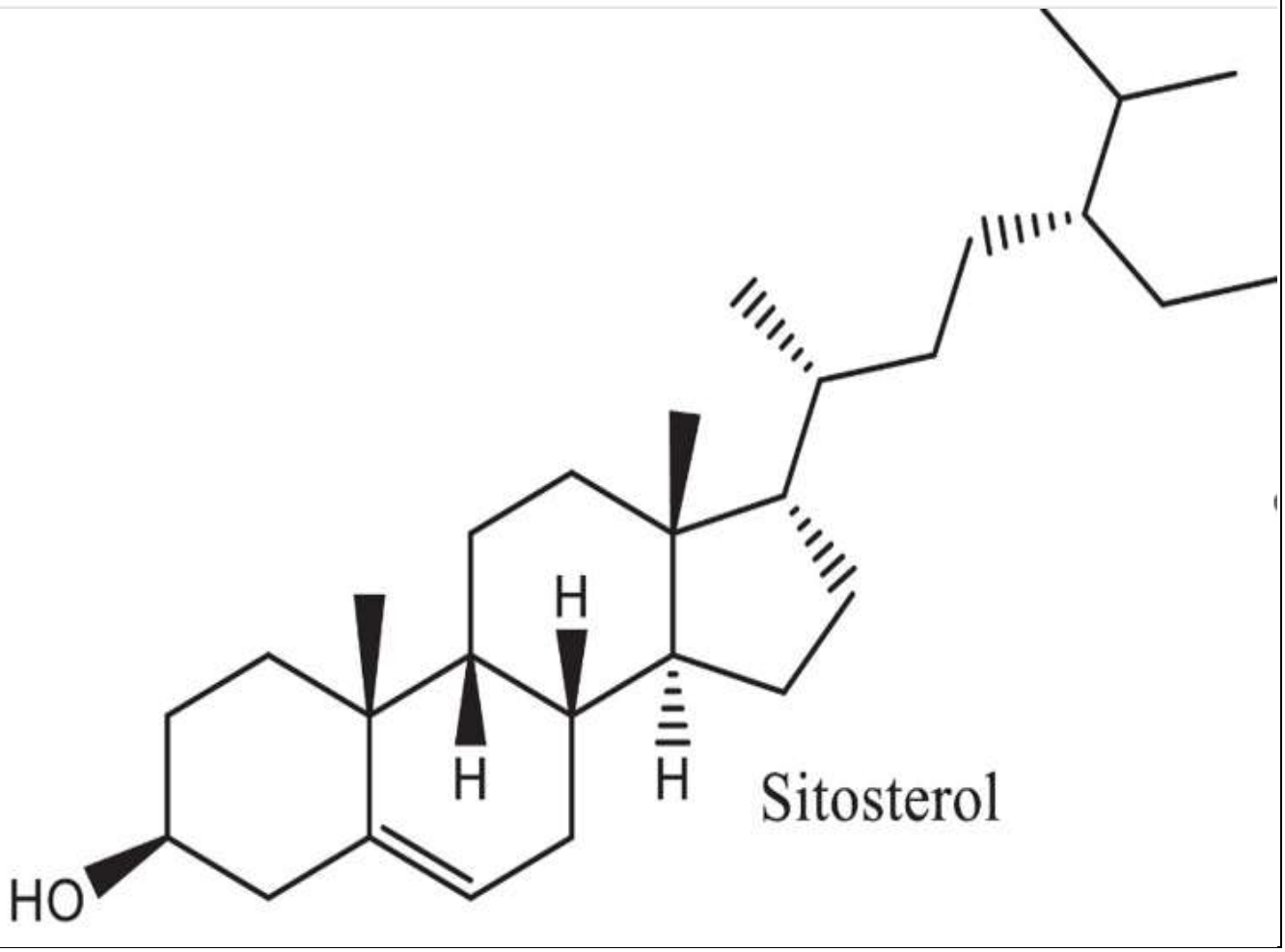
complete sequences of the SSU and D2/D3 LSU ribosomal RNA genes, we established *Teratodiplogaster fignewmani* gen. nov., sp. nov. as closely related to the *Parasitodiplogaster* genus. Its distinct morphology, characterised by numerous unique features, supports the justification for its classification as a new genus comprising a single species. Anticipate that further exploration of sycones from different *Ficus* species across tropical Australasia and potentially Africa may reveal additional species belonging to the *Teratodiplogaster* gen. nov. [117] *Ficus racemosa*, also known as cluster fig, red river fig, or gular, umbar, belongs to the *Moraceae* family and is indigenous to Australia and tropical regions of Asia. This plant exhibits rapid growth, featuring large, coarse leaves that typically reach the size of a sizable shrub, although mature specimens can develop into substantial and intricately shaped trees. Notably, it showcases an uncommon characteristic called cauliflory, wherein its figs grow directly on or near the tree trunk. The fruits of *Ficus racemosa* are commonly consumed as a vegetable, typically prepared in stir-fries and curries after removing the seeds. They are particularly favoured by the common Indian macaque as a dietary staple. Additionally, this plant serves as a vital food source for the caterpillars of the two-brand crow butterfly (*Euploea sylvester*) found in northern Australia. [118] [119] [120]

Traditional practices: Since ancient times, traditionally every part of this plant has been utilised for its medicinal properties. The fruits exhibit efficacy against a range of ailments, including leprosy, menorrhagia, leucorrhoea, blood disorders, burns, intestinal worms, dry cough, and urinary tract infections. In the herbal system of medicine, leaves are employed for treating bronchitis, irritable bowel syndrome, and piles. Leaf buds are known for their effectiveness against skin infections, while a decoction of the leaves aids in wound healing and washing. The bark decoction finds use in treating conditions such as: piles, ulcerative colitis, diarrhoea, and dysentery, along with diabetes and asthma. The latex, when applied externally, reduces inflammation, pain, and edema, facilitating wound healing. Additionally, when combined with sugar, it alleviates diarrhoea and dysentery, particularly in children, and enhances male sexual potency. The roots are utilised in addressing dysentery, pectoral complications, and diabetes, and are applied for inflammatory glandular enlargement, mumps, and hydrophobia. It possesses anti-diabetic properties and is incorporated into herbal remedies for diabetes treatment. Known for its ability to detoxify the body and act as an antioxidant, some traditional methods suggest using the bark of the tree for diabetes management. These treatments can take various forms such as water extracts, tablets, capsules, and mouth films. However, while cultural practices suggest that water collected from root cuts of the plant aids in restoring health by enhancing immunity and treating ailments like: chickenpox, smallpox, and fever, scientific evidence is lacking. Similarly, the fruit is employed in traditional medicine for treating conditions like: chickenpox, smallpox, burns, and insect bites, as well as for skincare purposes like: treating pimples, acne, and wrinkles. Its skin-lightening properties are utilized in face packs and creams, often combined with ingredients like: honey, cucumber juice, lemon, lemon peel, and orange peel powder. Nevertheless, there remains a lack of substantial scientific validation for these traditional medicinal practices, leaving uncertainty regarding their efficacy and potential to either bolster or undermine confidence in their therapeutic benefits. Therefore, extensive research is imperative to provide robust scientific evidence supporting or refuting the medicinal claims associated with these practices.

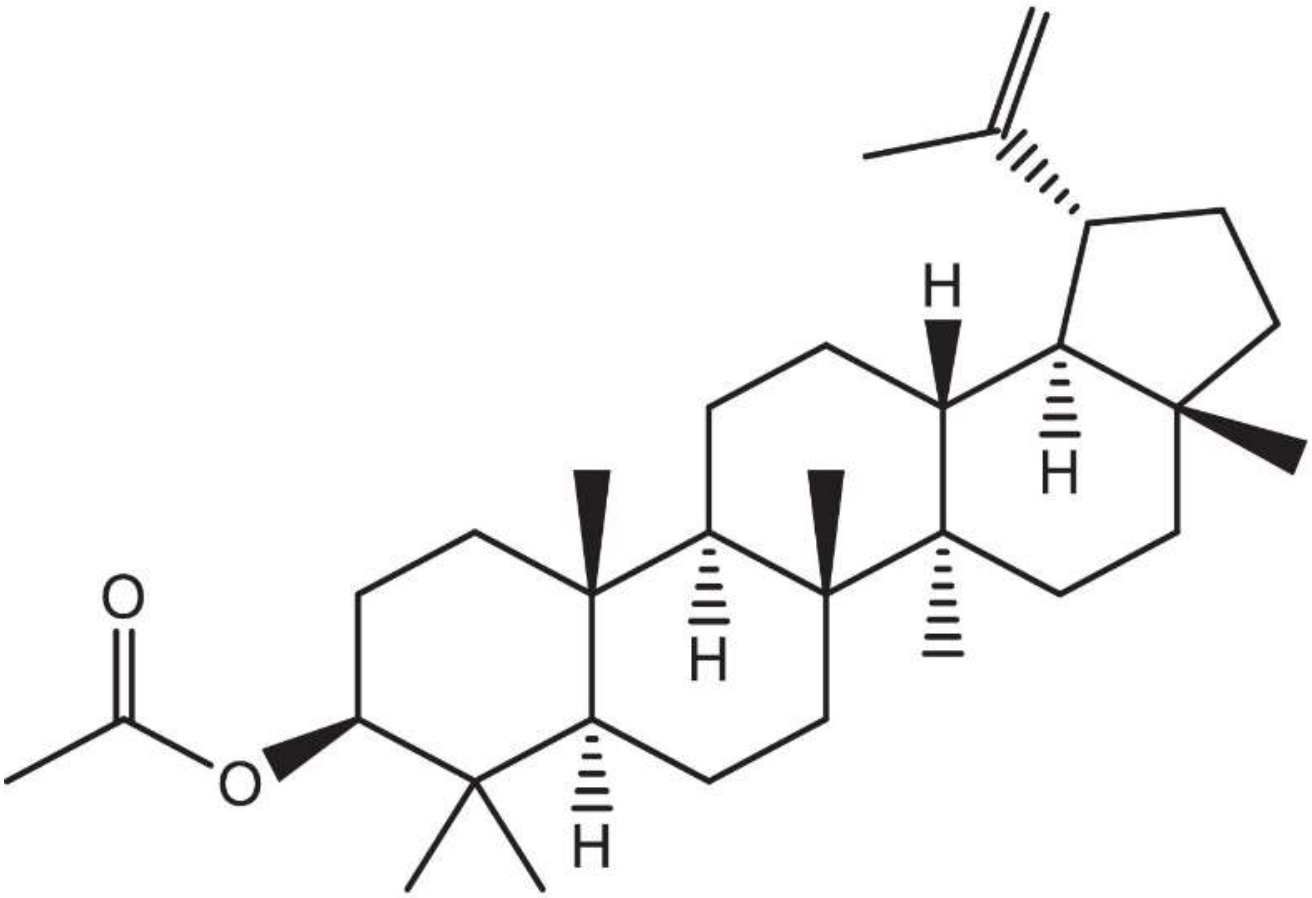
Phytochemistry or phytoconstituents: [122]



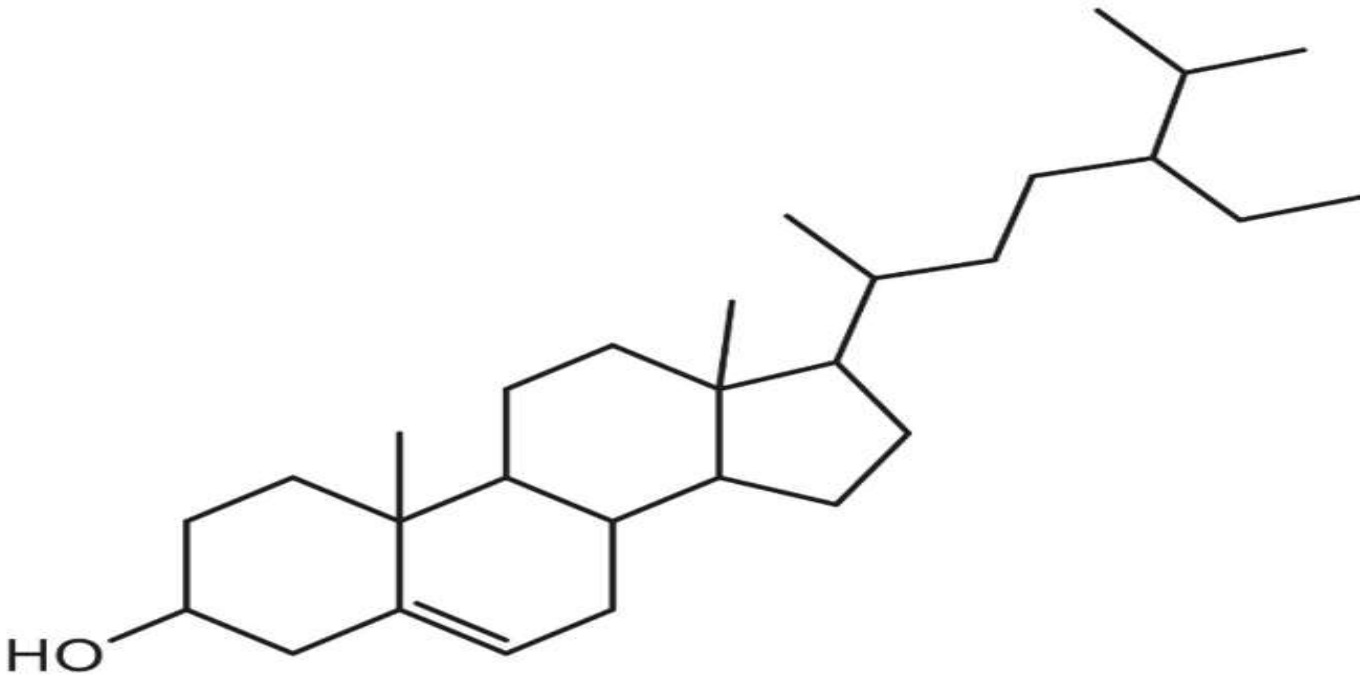
Lanosterol



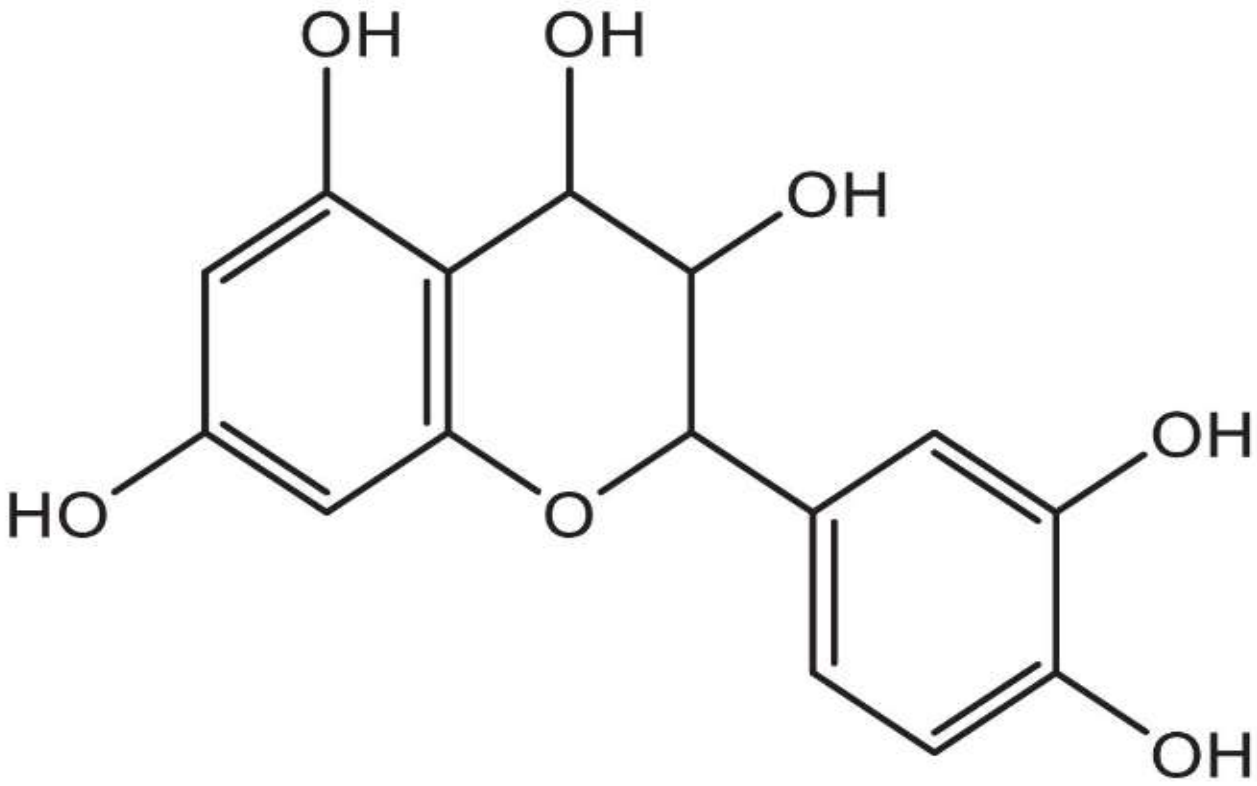
Sitosterol



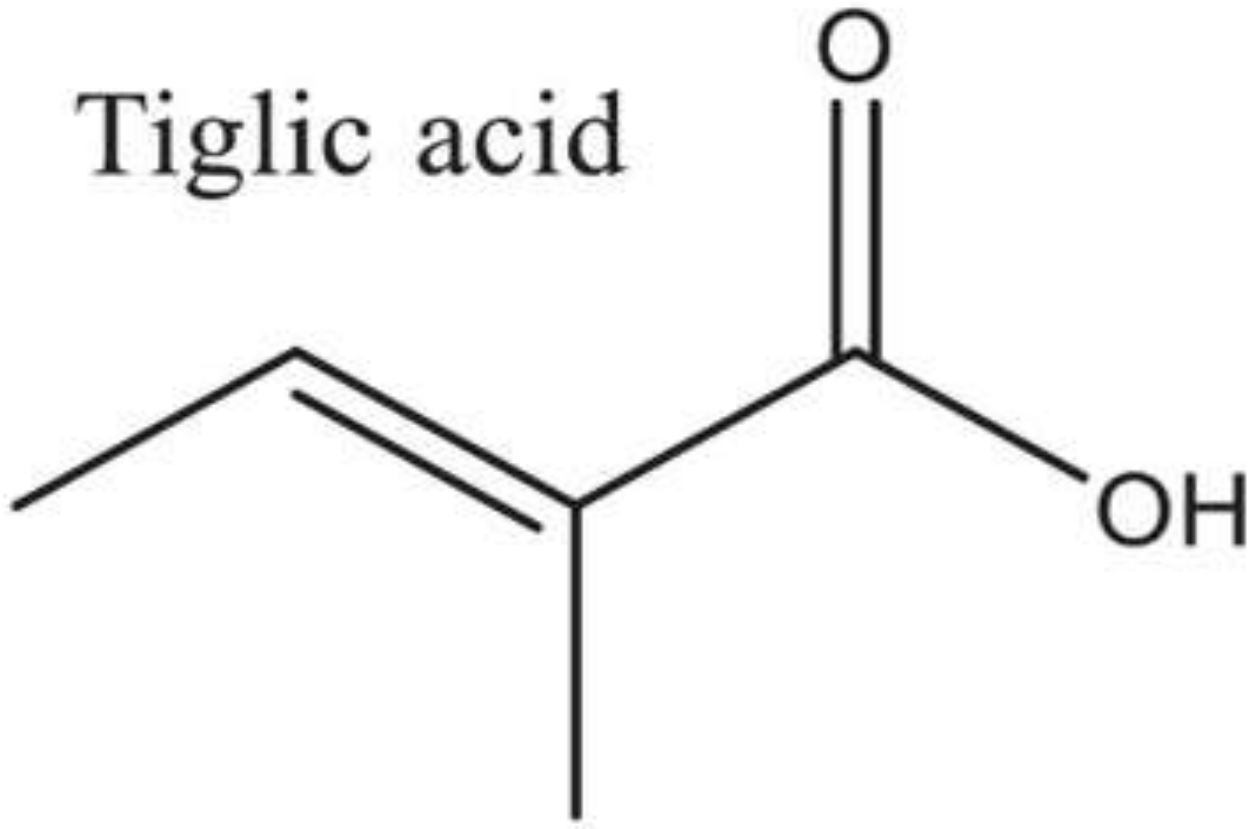
Lupeol acetate



beta-sistosterol



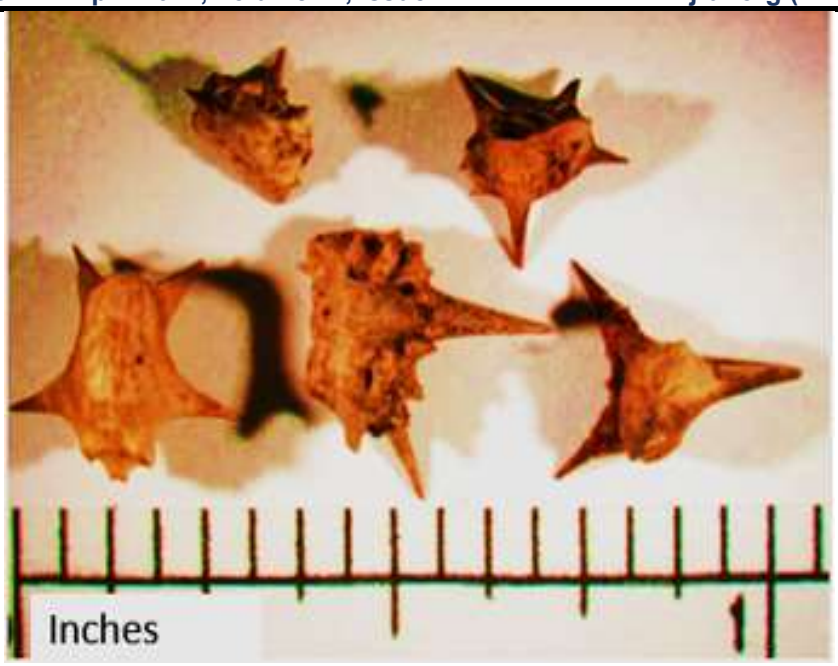
Leucocyanidin



6. Extract of cathedral bells or *Kalanchoe pinnata*. Dried.	25%	API

Dried powder of API, herbal drug substance or plant leaf, *Kalanchoe pinnata*. Dried.

7. Aqueous vehicle; coconut water + *Tribulus terrestris*, (puncture vine). *Tribulus terrestris* collected from the ground, and forest covered area of CHALISGAON, Bhadgaon, Dhule, were utilised for extraction. (Year 2021.) 20.48615, 74.97681. 	q.s.	Vehicle + API; diuretic. 70% tincture. Or 70% aqueous extract. Water of 20 Tender green coconut + *Tribulus terrestris*, (puncture vine). Boiled to 70% and the remanent portion used as a concentrated extract of it which was sonicated to take the active proportion out of it.



Within the *Zygophyllaceae* family, the genus *Tribulus* encompasses approximately 20 species globally. In India, three prevalent species are *Tribulus cistoides, Tribulus terrestris,* and *Tribulus alatus.* Of these, *Tribulus terrestris* (TT) stands out as a widely utilised medicinal herb, cherished by both Ayurvedic practitioners from ancient times and contemporary herbalists. *Tribulus terrestris,* belonging to the

Zygophyllaceae family and commonly referred to as Gokshur or puncture vine, has a rich history of utilisation in traditional Indian medicine systems for treating various ailments. Its different parts harbour a diverse array of chemical compounds, including: flavonoids, flavonol glycosides, steroidal saponins, and alkaloids, all of which possess medicinal significance. The plant exhibits a wide range of pharmacological properties, including diuretic, aphrodisiac, antiurolithic, immunomodulatory, antidiabetic, absorption-enhancing, hypolipidemic, cardiotonic, central nervous system stimulant, hepatoprotective, anti-inflammatory, analgesic, antispasmodic, anticancer, antibacterial, anthelmintic, larvicidal, and anticariogenic activities. *Tribulus terrestris* (TT) has a rich history of usage in folk medicine, where it is esteemed as a tonic, aphrodisiac, palliative, astringent, stomachic, antihypertensive, diuretic, lithotriptic, and urinary disinfectant. The dried fruit of this herb is particularly esteemed for its effectiveness in addressing various genitourinary tract disorders. It plays a pivotal role in formulations such as: Gokshuradi Guggul, a potent Ayurvedic medicine renowned for supporting the proper functioning of the genitourinary system and facilitating the elimination of urinary stones. Throughout centuries, TT has been a staple in Ayurvedic treatments for impotence, venereal diseases, and sexual debility. In recent decades, significant research efforts have been directed towards elucidating its biological activities and the pharmacological mechanisms underlying the effects of its extracts. *Tribulus Terrestris*, also known as puncture vine, is a Mediterranean plant recognised for its spiny fruit production. It is utilised for medicinal purposes, with various formulations incorporating its fruit, leaf, or root along with other ingredients. Historically, individuals have turned to *tribulus* to potentially enhance athletic performance, aid in bodybuilding, and address a spectrum of health concerns including heart and circulatory conditions, as well as sexual issues. While limited studies suggest potential benefits such as: alleviating symptoms of angina and improving athletic performance, there's also some evidence indicating positive effects on sexual problems and infertility. However, further research is warranted to establish conclusive evidence. The natural consumption of *tribulus* from its spiny fruit should be approached cautiously. While short-term supplementation is likely safe for healthy individuals who are not pregnant or breastfeeding, potential side effects may include sleep disturbances, gastrointestinal discomfort, and menstrual irregularities. It's essential to note potential risks, particularly for pregnant or breastfeeding individuals, as animal studies have suggested links between *tribulus* and foetal development issues. Men, especially those with prostate cancer concerns, should be cautious due to potential impacts on male hormones. Interactions with certain medications used to treat diabetes, high blood pressure, and blood clot prevention have been noted. *Tribulus* may affect blood sugar levels, particularly when combined with diabetes medications, and could potentiate the effects of steroids. As with any supplement, it's crucial to inform healthcare providers about its use, especially considering potential interactions with medications, foods, or other supplements. Despite regulation by the FDA, dietary supplements are not subject to the same rigorous testing as pharmaceuticals, necessitating cautious consumption and communication with healthcare professionals. [123]

8. Perfume. Rose oil.	q.s.	Perfume
9. *Butea monosperma* and *Crocus sativus* extract dried. In coconut water. 	6%	API

 		
10. Preservatives.	q.s.	Pharmaceutical agent. An excipient.

Herbal tablets are typically prepared through either wet granulation or direct compression methods. Wet granulation is often favoured due to its ability to impart sufficient strength to the tablets. These tablets undergo thorough assessment to ensure their quality, encompassing examinations of various physical attributes such as: hardness, friability, weight consistency, thickness, disintegration time, resistance to abrasion, and uniformity of mass.

Methods: To prepare the dry powder of *Kalanchoe pinnata* leaves, fresh leaves were collected from the local area of Nashik, India, and cleaned with distilled water. Subsequently, the leaves were dried at room temperature for several days, followed by further drying in a hot air oven to ensure complete dehydration due to their highwater content; (as they are very succulent.). The dried leaves were then ground into a fine powder using a mixer and passed through a sieve to obtain a microfine consistency.

For the preparation of the binder solution, carboxymethyl cellulose (CMC), lactose, and okra mucilage were used in optimised concentrations of 11.5%, 10.3%, and 30.5%, respectively. Distilled water was taken in a beaker, and the binder components were added and mixed thoroughly until a uniform solution was obtained, which exhibited a jelly-like appearance.

Next, the dry powder of *Kalanchoe pinnata* leaves and *Ficus racemose* powder were added to the binder solution, and the mixture was blended in a blender at high speed to achieve optimal blending results, resulting in a dry powder with a fine particle size. The remaining herbal tincture and coconut water-alcohol solution

were then added to the blend and mixed thoroughly until a cohesive dough with a partially dried and firm consistency was formed. Sieve no. 22. was used in the preparation process. Prepared granules are dried at room temperature. Granules that have dried well are prepared for compression.

Evaluation:

Pre-formulation study: [115]

Bulk density: Bulk density measurements were conducted using a 100 ml dried measuring cylinder. Granules were poured into the cylinder, and the bulk density was calculated by dividing the mass of the granules by the bulk volume.

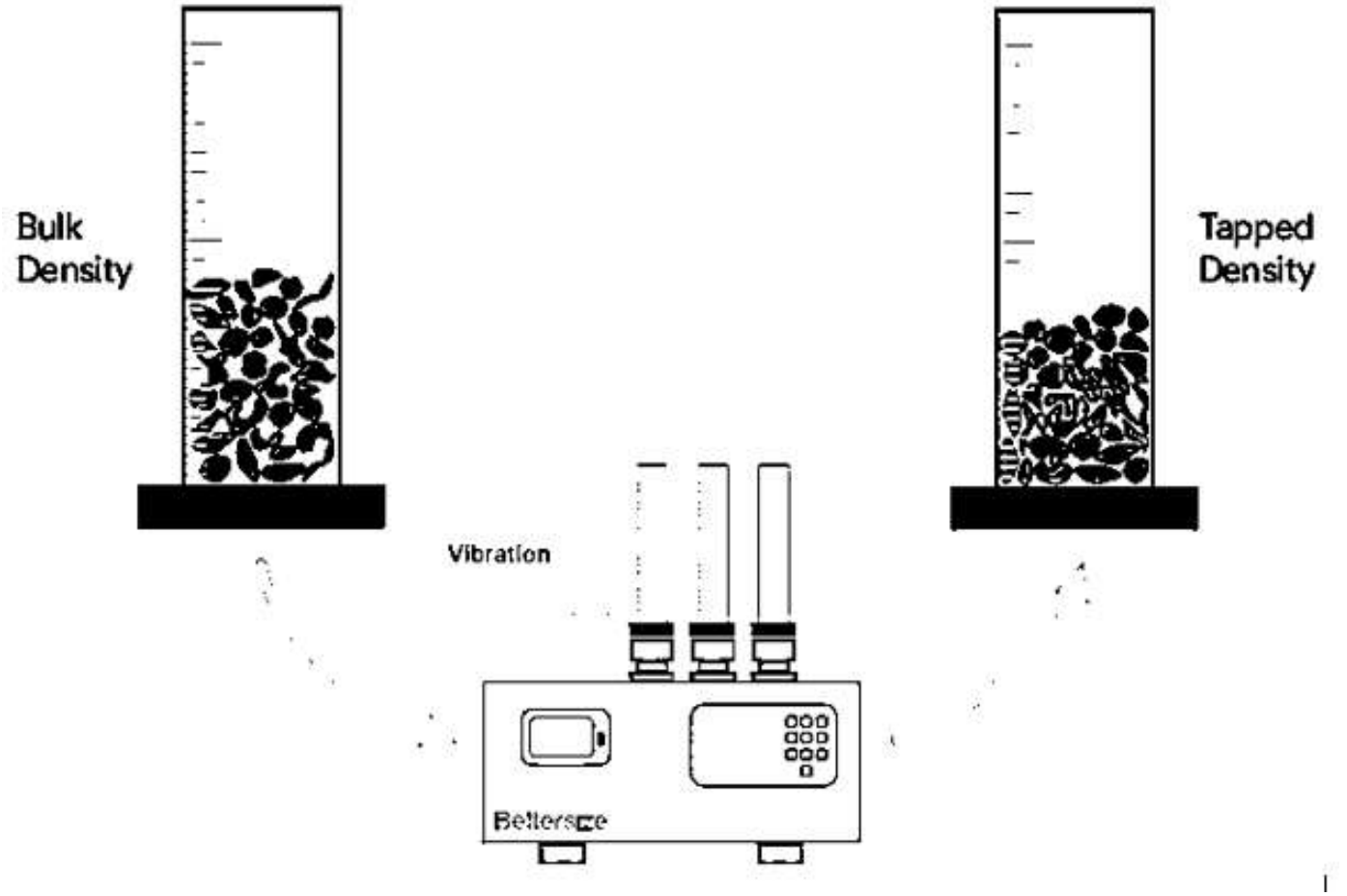


Figure 9. Bulk density. Experimental tapped density.

Tapped density: Tapped density was determined by pouring dried granules into a 100 ml measuring cylinder and tapping it 100 times. The volume after tapping was recorded, and the tapped density was calculated by dividing the weight of the granules by the volume of the tapped granules.

Figure 10. Tapped density.

Hausner's ratio: Hausner's ratio, indicating the flowability of the granules, was calculated as the ratio of tapped density to bulk density.

Carr's index: Carr's index, or compressibility index, was calculated using the formula [(Tapped density - Bulk density) / Tapped density] × 100; the flow properties of the granules.

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

$$Compressibility\ Index = 100 \times \left(\frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} \right)$$

$$Hausner\ \ Ratio = \left(\frac{\rho_{tapped}}{\rho_{bulk}} \right)$$

Angle of repose: The angle of repose was determined using the funnel method, and the formula Θ = Tan-1[h/r] was used to calculate it, where h represents the height of the granule cone formed and r represents the radius of the granule cone formed. Illustrates the flow property of the granules.

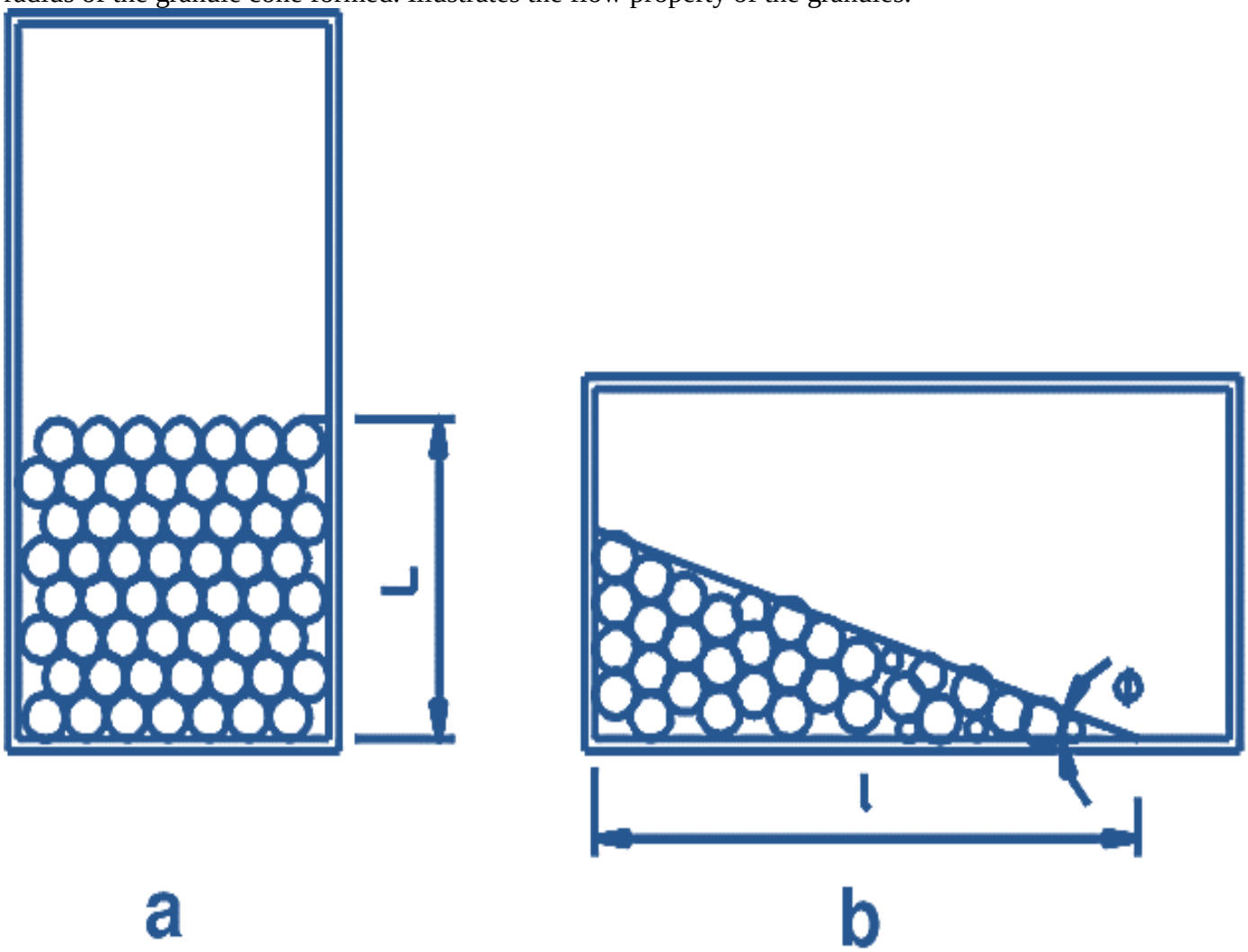


Figure 11. The bulk density and the experimental.

The tablets underwent several evaluation tests as follows:

General appearance: The visual appearance and colour of the tablets were assessed.

Weight variation test: This test involved individually weighing 20 tablets (X1, X2, X3, ..., X20). The average weight (X) of the 20 tablets was calculated as the sum of individual weights divided by 20. Each tablet's weight was compared with the upper and lower limits. The results, displayed in table 5, indicated that no more than two tablets deviated from the average weight by the specified percentage error, and none differed by more than double that percentage.

Hardness and thickness test:

Figure 12. Hardness test.

The hardness and thickness of 20 tablets for each formulation were determined using a Monsanto hardness tester and Vernier calipers, respectively.

Friability test:

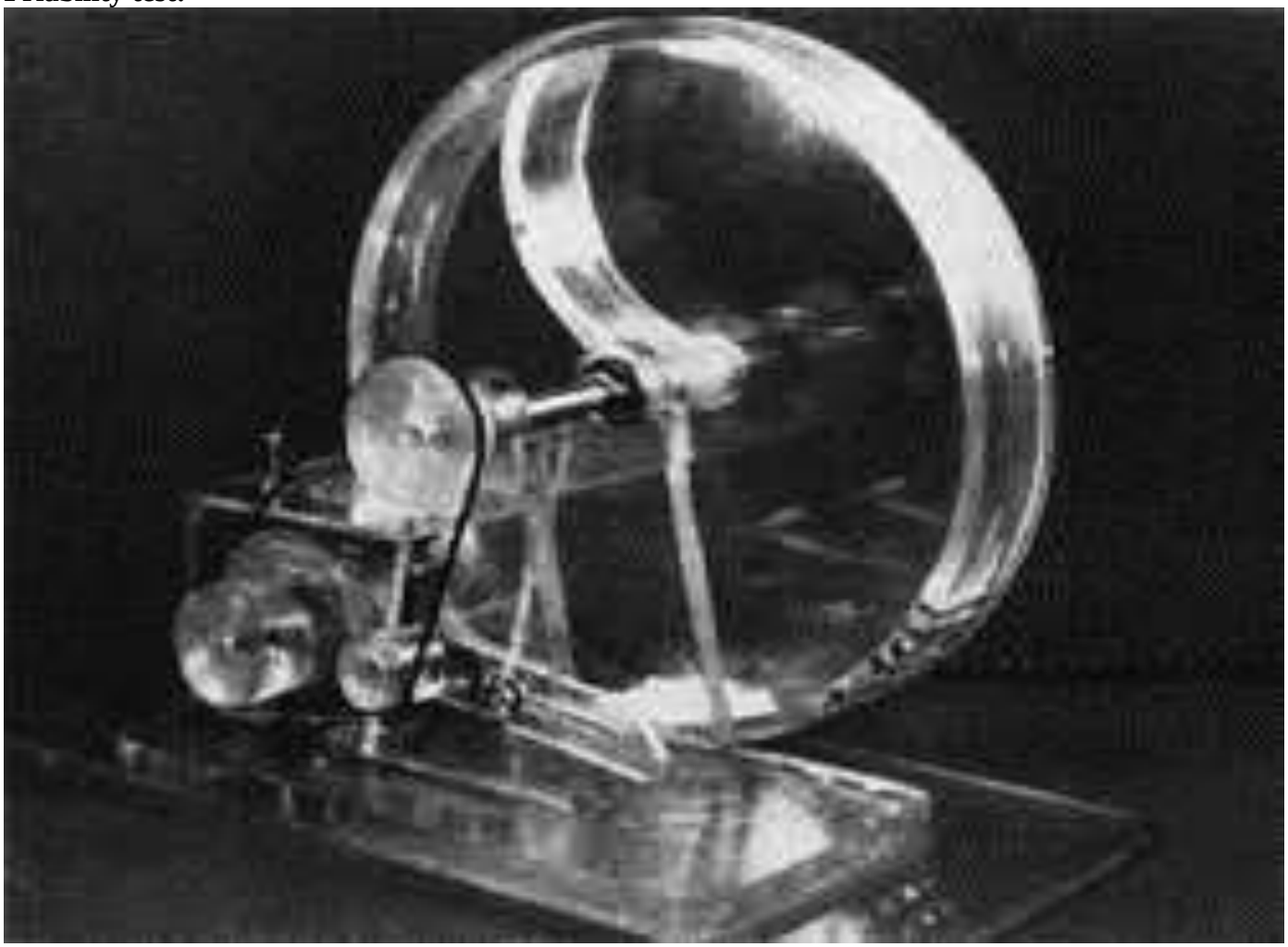


Figure 13. Friability test.

Friability of tablets was assessed using a Roche friabilator in a laboratory setting. Tablets were subjected to 100 revolutions in a plastic chamber rotating at 25 rpm, dropping them through a distance of six inches. After the test, tablets were reweighed. Tablets that lost less than 0.5% to 1.0% of their initial weight were considered acceptable. (USP)

Disintegration time:

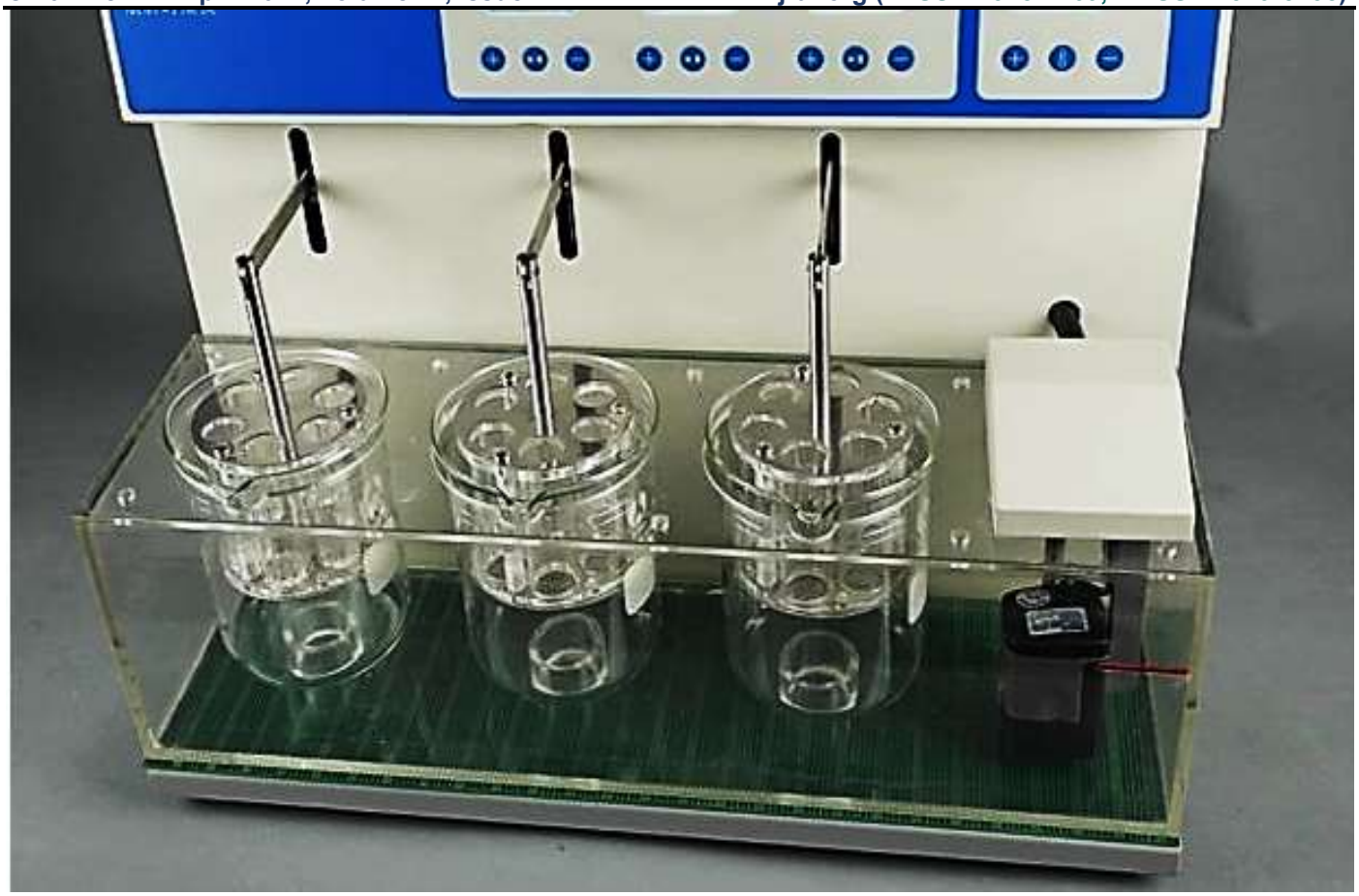


Figure 14. Disintegration time.

The disintegration time refers to the duration it takes for a tablet to break into particles under specific conditions. This test was conducted to determine the disintegration of tablets within a defined time frame. (As per USP).

Table 5. Scale to measure of flowability and tolerance for weight variation.

Flow character	Hausner's ratio	Carr's index (%)	Angle of repose (°)
Excellent	1.00-1.11	≤10	25-30
Good	1.12-1,18	11-15	31-35
Fair	1.19-1.25	16-20	36-40
Passable	1.26-1.34	21-25	41-45
Poor	1.35-1.45	26-31	46-55
Very poor	1.46-1.59	32-37	56-65
Very, very poor	>1.60	>38	>66

Average weight of tablets(mg)	Max.% difference is allowed
80 or less	10%
80-250	7.5%
More than 250	5%

Result: The preformulating studies performed showed excellent compressibility tablet required properties that are suitable for compression thus making it a great optimisable batch. Tablets formulated from the dry powder of *Kalanchoe pinnata* leaves exhibited excellent tablet-forming characteristics and demonstrated stability under various conditions according to ICH GCP guidelines. The tablets were prepared with uniform weight, adhering to a variation scale of ±0.02. After complete oven drying, the tablets maintained uniform weight without variation. Disintegration time for the tablets was observed to be within 30 minutes, with initial swelling followed by disintegration. Additionally, the tablets displayed satisfactory hardness and exhibited minimal friability, with less than 0.5% weight loss when subjected to 100 revolutions at 25 rpm. Therefore, they are suitable for packaging and capable of withstanding stress.

Figure 15. Formulated tablets.

Conclusion:

The preliminary studies conducted demonstrated excellent compressibility of the tablet, indicating properties conducive to compression and making it an ideal candidate for further optimisation in batch production. Therefore, in conclusion, tablets formulated from the dry powder of *Kalanchoe pinnata* leaves exhibit promising characteristics for the treatment of renal calculus or kidney stones. The observed excellent tablet-forming properties, stability, uniform weight, and optimal disintegration time suggest that these tablets have the potential to deliver the healing properties of *Kalanchoe pinnata* effectively. Additionally, the satisfactory hardness and minimal friability indicate that the tablets are suitable for packaging and can withstand the stresses encountered during handling and transportation. Overall, these findings support the potential of *Kalanchoe pinnata* tablets as a viable option for managing renal calculus or kidney stones, offering hope for improved therapeutic outcomes in patients suffering from these conditions. In addition to treating renal calculus, formulations containing *Kalanchoe pinnata* have the potential to be utilised across a broad spectrum of therapeutic areas, given its medicinal properties and therapeutic index. Jaggery and concentrated extracts are employed to formulate syrup containing *Kalanchoe pinnata* and *Tribulus terrestris*, aiding in the preparation of other medicinal concoctions. Other syrup bases can also be utilised such as: sugar. The tablets containing *Kalanchoe pinnata* and *Tribulus terrestris* can be consumed alongside distilled or boiled and cooled water, coconut water, or orange or lemon juice. It can also be taken with pineapple juice or with apple juice to increase it healing ability.

Label:

Tablet "Νεφρολιθολυτικός" (Nefrolitholytikós).

Ingredients:	Quantity
CMC	11.5%
Lactose	10.3%
Okra mucilage	30.5%
Mg. st.	1.7%
Ficus racemose powder. Can be substituted with Chanca Piedra.	15%
Extract of cathedral bells or *Kalanchoe pinnata*. Dried.	25%
Aqueous vehicle; coconut water + *Tribulus terrestris*, (puncture vine).	q.s.
Perfume. Rose oil.	q.s.
Butea monosperma and *Crocus sativus* extract dried.	6%

Batch no: A67
Mfg. Date: Jan 2024
Exp Date: Jan 2026
MRP: 650 Indian rupees.

Acknowledgment: I extend my sincere gratitude to respectable Prof. Dr. Saurabh D. Bhandare, sir for providing me with the invaluable opportunity to undertake this project on *Kalanchoe pinnata* tablets for renal health and other therapeutic index. His guidance and support have been instrumental in enriching my knowledge and research experience throughout this endeavour. I am profoundly thankful to my mentor for his invaluable assistance, without which this project would not have been possible. Thank you. - Antra Jadhav R.

Conflict of interest: None. There are no conflicts of interest to declare.
Electronic media:

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ii. Saurabh D. Bhandare. *Citrullus lanatus* polymer and tablet binders or as an excipient. *YouTube*. https://www.youtube.com/watch?v=7hoaZdx4_MQ
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iv. Saurabh D. Bhandare. *Ficus racemosa*. *YouTube*. Published online March 18, 2024. https://www.youtube.com/watch?v=96Cz2se-K-4
v. Saurabh D. Bhandare. *Tribulus terrestris*, puncture vine. *YouTube*. Published online April 7, 2024. https://www.youtube.com/watch?v=n2DmPo3KsK8
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Ingredients:	Quantity
1. CMC	11.5%
2. Lactose	10.3%
3. Okra mucilage	30.5%
4. Mg. st. **"Mg. st." typically stands for "magnesium stearate," which is a commonly used pharmaceutical excipient. Magnesium stearate is a white, water-insoluble powder that is widely used in the pharmaceutical industry as a lubricant in tablet and capsule formulations. It helps prevent ingredients from sticking to the manufacturing equipment during the tablet compression process, thereby**	1.7%

improving the flow properties of the powder blend and facilitating tablet formation.	
5. *Ficus racemose* powder. Can be substituted with Chanca Piedra.	15%
6. Extract of cathedral bells or *Kalanchoe pinnata.* Dried.	25%
7. Aqueous vehicle; coconut water + *Tribulus terrestris*, (puncture vine).	q.s.
8. Perfume. Rose oil.	q.s.
9. *Butea monosperma* and *Crocus sativus* extract dried.	6%