2. LITERATURE REVIEW

2.1 GASTRIC ULCERS

2.1.1 Pathophysiology of Ulcer:

Peptic ulcer is basically a lesion located at the level of the stomach, duodenum or esophagus. Ulcer tends to affect the entire gastrointestinal tract, starting from the lining of the mouth and ending with the rectal region. Peptic ulcer suggests the involvement of hydrochloric acid and pepsin in the development of the disorder. When gastric acid is produced in excess, the mucosal membrane that protects the stomach and internal organs from danger is damaged, enabling the bacteria Helicobacter pylori to penetrate the barrier and cause internal infections. Therefore, in the case of peptic ulcer, both gastric acid and bacteria are responsible for the development of the disorder. Peptic ulcer located in the stomach is called gastric ulcer; peptic ulcer located at the level of the duodenum is called duodenal ulcer and peptic ulcer developed at the level of the esophagus is called esophageal ulcer.

Despite extensive research, the etiology of peptic ulcer disease remains unclear. Given the multiple processes that control acid and pepsin secretion and defense and repair of the gastroduodenal mucosa, it is likely that the cause of ulceration differs between individuals. Acid and pepsin appear to be necessary but not sufficient ingredients in the ulcerative process. It is clear that the majority of gastric ulcers and a substantial number of duodenal ulcers do not have increased gastric acid secretion. Recent research has focused more on protection and repair of the stomach and duodenum\textsuperscript{22}.

Historically, our understanding of the pathophysiology of peptic ulcer disease focused on abnormalities in the secretion of gastric acid and pepsin, and on the suppression of acid as a treatment strategy. Today, gastric hypersecretion—associated with gastrinoma in Zollinger–Ellison syndrome, antral G-cell hyperplasia, an increase in parietal-cell
mass, and a physiological imbalance between the antagonistic gastric hormones gastrin and somatostatin—is still an important issue in peptic ulcer disease. Moreover, it is known that cholinergic hypersensitivity and parasympathetic dominance are related to the stimulation not only of hydrochloric acid but also pepsin, which is often neglected as a cofactor in the development of erosive injury to the gastric mucosa. Psychologic stress, cigarette smoking, alcohol consumption, use of nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin, oral bisphosphonates, potassium chloride, immunosuppressive medications, and an age-related decline in prostaglandin levels have all been shown to contribute to peptic ulcer disease\textsuperscript{23}. It was, however, the isolation of \textit{H. pylori} and its identification as the most important cause of peptic ulcer disease that led to exploration of the role of inflammation and its associated cytokine cascade in gastric acid secretion.

\textit{H. pylori} evades attack by the host immune system and causes chronic, indolent inflammation by several mechanisms. \textit{H. pylori} can damage the mucosal defense system by reducing the thickness of the mucus gel layer, diminishing mucosal blood flow, and interacting with the gastric epithelium throughout all stages of the infection. \textit{H. pylori} infection can also increase gastric acid secretion; by producing various antigens, virulence factors, and soluble mediators, \textit{H. pylori} induces inflammation, which increases parietal-cell mass and, therefore, the capacity to secrete acid. The \textit{H. pylori} cytotoxin-associated gene \textit{CagA} also has an important role: it interferes with gastric epithelial cell-signaling pathways, thereby regulating cellular responses and possibly contributing to apical junction barrier disruption, interleukin-8 secretion and phenotypic changes to gastric epithelial cells\textsuperscript{24}.

Understanding the pathophysiology of peptic ulcer disease is at something of a crossroads: mechanisms of injury differ distinctly between duodenal and gastric ulcers. Duodenal ulcer is essentially an \textit{H. pylori}-related disease and is caused mainly by an increase in acid and pepsin...
load, and gastric metaplasia in the duodenal cap. Gastric ulcer, at least in Western countries, is most commonly associated with NSAID ingestion, although *H. pylori* infection might also be present. Chronic, superficial and atrophic gastritis predominate in patients with gastric ulcers, when even normal acid levels can be associated with mucosal ulceration. In both conditions, ulcer is associated with an imbalance between protective and aggressive factors, with inflammation being a leading cause of this imbalance.

**Fig 2.1.1 : Pathophysiology of Ulcer**

The isolation of *H. pylori* in the early 1980s was one of the most exciting advances in the history of peptic ulcer disease, and it has dramatically changed the management of peptic ulcer. Eradication of *H. pylori* infection is now the mainstay of treatment for peptic ulcer disease, and has resulted in very high ulcer healing rates and recurrence rates that have dropped dramatically, especially for individuals with a duodenal ulcer. The greater recognition of the role of NSAIDs and aspirin in gastrointestinal-tract injury has led to the development of therapeutic
and preventive strategies that rely on the use of antisecretory drugs, the prostaglandin analog misoprostol, or selective cyclo-oxygenase (COX)-2 inhibitors (coxibs).

**Figure 2.1.2 Pathogenesis of Peptic Ulcer**

**Diagnosis**

Peptic ulcers are always suspected in patients with persistent dyspepsia (bloating, belching and abdominal pain). A number of steps are needed to make an accurate diagnosis of ulcers.

**Medical and Family History**

The doctor will ask for a thorough report of a patient’s dyspepsia and other important symptoms, such as weight loss or fatigue, present and past medication use (especially chronic use of NSAIDs), family members with ulcers and drinking and smoking habits.
Ruling out Other Disorders

In addition to peptic ulcers, a number of conditions, notably gastroesophageal reflux disease and irritable bowel syndrome, cause dyspepsia. Often, however, no cause can be determined. In such cases, the symptoms are referred to collectively as functional dyspepsia.

Peptic ulcer symptoms, particularly abdominal pain and chest pain, may resemble those of other conditions, such as gallstones or heart attack. Certain features may help to distinguish these different conditions. However, symptoms often overlap and it is impossible to make a diagnosis based on symptoms alone. A number of tests are needed.

Noninvasive Tests for Gastrointestinal (GI) Bleeding

When ulcers are suspected, the doctor will order tests to detect bleeding. These may include a rectal exam, a complete blood count and a fecal occult blood test (FOBT). The FOBT tests for hidden (occult) blood in stools. Typically, the patient is asked to supply up to 6 stool specimens in a specially prepared package. A small quantity of feces is smeared on treated paper, which reacts to hydrogen peroxide. If blood is present, the paper turns blue.

Noninvasive Screening Tests for Helicobacter pylori

Simple blood, breath and stool tests can now detect Helicobacter pylori with a fairly high degree of accuracy.

Tests for diagnosing Helicobacter pylori.

The following tests are used to diagnose Helicobacter pylori infection. Testing may also be done after treatment to ensure the bacteria are fully eradicated.
1) **Breath Test.** A simple test called the carbon isotope-urea breath test (UBT) can identify up to 99% of people who harbor *Helicobacter pylori*. Up to 2 weeks before the test, the patient must discontinue taking any antibiotics, bismuth-containing agents such as Pepto-Bismol and proton-pump inhibitors (PPIs). As part of the test, the patient swallows a special substance containing urea (a compound in mammals metabolized from nitrogen) that has been treated with carbon atoms. If *Helicobacter pylori* are present, the bacteria convert the urea into carbon dioxide, which is detected and recorded in the patient’s exhaled breath after 10 minutes. This test can also be used to confirm that *Helicobacter pylori* have been fully treated.

2) **Blood Tests.** Blood tests are used to measure antibodies to *Helicobacter pylori*, with results available in minutes. Diagnostic accuracy is reported at 80 - 90%. One such important test is called enzyme-linked immunosorbent assay (ELISA). An ELISA test of the urine is also showing promise in children.

3) **Stool Test.** A test to detect genetic fingerprints of *Helicobacter pylori* in the feces appears to be as accurate as the breath test for initial detection of the bacteria and for detecting recurrences after antibiotic therapy. This test can also be used to confirm that the *Helicobacter pylori* infection has been fully treated.

4) **Tissue biopsy.** The most accurate way to identify the presence of *Helicobacter pylori* is a tissue biopsy from the lining of the stomach. However, this is clearly an invasive task and many patients are treated for *Helicobacter pylori* based on the above three noninvasive tests.

It should be noted that such tests are not as accurate as endoscopy, an invasive procedure, which is needed to confirm a diagnosis of *Helicobacter pylori*. The breath and stool tests, however, can be
particularly useful after treatment to determine if a patient has been cured.

If symptoms persist, endoscopy is usually performed. Though it is an invasive procedure, it is the only procedure in which a biopsy of stomach tissue can be taken, making it the most accurate test.

**Endoscopy**

Endoscopy is a procedure used to evaluate the esophagus, stomach and duodenum using an endoscope -- a long, thin tube equipped with a tiny video camera. When combined with a biopsy, endoscopy is the most accurate procedure for detecting the presence of peptic ulcers, bleeding and stomach cancer or for confirming the presence of *Helicobacter pylori*.

**The Procedure.**

Endoscopy may be performed in a hospital, doctor's office or outpatient surgery center and typically involves the following:

1) The doctor administers a local anesthetic using an oral spray and an intravenous sedative to suppress the gag reflex and relax the patient.
2) The doctor then places the thin, flexible plastic tube into the patient’s mouth and maneuvers it down the esophagus into the stomach.
3) A tiny camera in the endoscope allows the doctor to see the surface of the esophagus, stomach and duodenum and to search for abnormalities.
4) The doctor will remove about 10 small tissue samples (biopsies), which will be tested for *Helicobacter pylori*. 
2.1.2 Drug treatment for Ulcer:

The drugs used in the treatment of peptic ulcer are classified as

1. **H₂-receptor Blockers:**
   - Ranitidine (Zantac)
   - Cimetidine (Tagamet)
   - Famotidine (Pepcid)
   - Nizatidine (Axid)

2. **Proton pump Inhibitors**
   - Omeprazole (Losec)
   - Pantoprazole (Protium)
   - Rabeprazole (Pariet)
   - Lansoprazole (Zoton)

3. **Antibiotics**
   - Metronidazole (Flagyl)
   - Amoxycillin (Amoxil)
   - Clarithromycin (Klaricid)
4. Miscellaneous

Bismuth (De-Nol)
Sucralfate (Antepsin)
Misoprostol (Cytotec).

Deciding which treatment is best for patients with symptoms of dyspepsia or peptic ulcer disease depends on a number of factors.

**Approach to patients who are not taking NSAIDS**

1) If an ulcer is seen and the patient is infected with *Helicobacter pylori*, treatment for the infection is started, followed by four to eight weeks of treatment with a proton pump inhibitor. Most of these patients will improve with this treatment.

2) If an ulcer is seen but *Helicobacter pylori* are not present, patients are usually treated with proton pump inhibitors for 8 weeks.

3) If no ulcer is seen and the patient is not infected with *Helicobacter pylori*, the first treatment attempt will usually be with proton pump inhibitors. These patients do not need antibiotics to treat *Helicobacter pylori*. Other possible causes of their symptoms should also be considered.

4) Patients who test positive for *Helicobacter pylori* infection will receive an antibiotic regimen that eradicates *Helicobacter pylori*. Those who truly have an ulcer present are more likely to respond to such treatment. Unfortunately, since an endoscopy is not performed before treatment in the test and treat strategy, patients without an ulcer are also treated with antibiotics here. These patients, even if they are positive for *Helicobacter pylori* are less likely to have a full response.
5) When the test and treat approach is used, those who do not respond to treatment, or whose symptoms recur relatively quickly, will often need an upper endoscopy at that point.

**Antibiotic and Combination Drug Regimens for the Treatment of Helicobacter pylori**

The standard treatment regimen uses 2 antibiotics and a PPI:

1) **Proton pump inhibitors (PPIs).** These drugs include Omeprazole (Prilosec), Lansoprazole (Prevacid), Esomeprazole (Nexium) and Rabeprazole (Aciphex). PPIs are important for all types of peptic ulcers and are a critical partner in antibiotic regimens. They reduce acidity in the intestinal tract and increase the ability of antibiotics to destroy *H. pylori*.

2) **Antibiotics.** The standard antibiotics are Clarithromycin (Biaxin) and Amoxicillin. Some doctors substitute the antibiotic Metronidazole (Flagyl) for either Clarithromycin or Amoxicillin.

This combination treatment typically lasts for at least 14 days.

**Treatment of NSAIDs-induced ulcers**

If NSAID-caused ulcers or bleeding are identified, patients should

1) Get tested for *Helicobacter pylori* and, if they are infected, take antibiotics.

2) Possibly use a PPI. Studies suggest these medications lower the risk for NSAID-caused ulcers, although they do not completely prevent them.

**Healing Existing Ulcers.**

A number of drugs are used to treat NSAID-caused ulcers. PPIs -- Omeprazole (Prilosec), Lansoprazole (Prevacid), or Esomeprazole (Nexium)
are used most often. Other drugs that may be useful include H2 blockers, such as Famotidine (Pepcid AC), Cimetidine (Tagamet), and Ranitidine (Zantac). Sucralfate is another drug used to heal ulcers and reduce the stomach upset caused by NSAIDs.

A number of alternative medications may be tried for people with chronic pain, to minimize the risk of ulcers associated with NSAIDs.

1) **COX-2 Inhibitors (Coxibs).** Coxibs block an inflammation-promoting enzyme called COX-2. This drug class was initially thought to work as well as NSAIDs, while causing less gastrointestinal distress. However, following numerous reports of cardiovascular events, the FDA banned Rofecoxib (Vioxx) and Valdecoxib (Bextra) from use in the U.S. Celecoxib (Celebrex) is still available, but patients should discuss with their doctor whether this drug is appropriate and safe for them. The use of Cox-2 inhibitors may provide a decrease in uncomplicated ulcers, but more serious events do not seem to be reduced by the use of these medications.

2) **Arthrotec.** Arthrotec is a combination of Misoprostol and the NSAID Diclofenac. It may reduce the risk for gastrointestinal bleeding. This drug can cause miscarriage (abortion) at any stage of pregnancy and therefore should not be used during pregnancy.

3) **Acetaminophen.** Acetaminophen (Tylenol, Anacin-3) is the most common alternative to NSAIDs. Acetaminophen is inexpensive and generally safe. It poses far less of a risk of gastrointestinal problems than NSAIDs. It does have some adverse effects, however and the daily dose should not exceed 4 grams (4,000 mg); some studies suggest that ulcer risk is increased even in doses exceeding 2 grams (2,000 mg) a day, if the drug is used on a long-term basis. Patients who take high doses of Acetaminophen for long periods are also at risk for liver damage, particularly if they drink alcohol.
It may pose a small risk for serious kidney complications in people with preexisting kidney disease, although Acetaminophen remains the drug of choice for patients with impaired kidney function.

4) **Tramadol.** Tramadol (Ultram) is a pain reliever that has been used as an alternative to opioids. It has opioid-like properties, but is not as addictive. However, dependence and abuse have been reported. It can cause nausea, but does not cause severe gastrointestinal problems, as NSAIDs can. Some patients experience severe itching. A combination of Tramadol and Acetaminophen (Ultracet) provides more rapid pain relief than Tramadol alone and more durable relief than Acetaminophen alone. Side effects are the same as for each of these agents.

5) If continuation of NSAIDs is necessary, the lowest possible dose should be used

**MEDICATIONS**

The following drugs are sometimes used in the treatments of peptic ulcers caused by either NSAIDs or *Helicobacter pylori*

**Antacids**

Many antacids are available without prescription and are the first drugs recommended to relieve heartburn and mild dyspepsia\(^9\). They play no major role in either the prevention or healing of ulcers, but help in the following ways:

1) They neutralize stomach acid by relying on various combinations of three basic compounds -- magnesium, calcium or aluminum.
2) They may defend the stomach by increasing bicarbonate and mucus secretion. (Bicarbonate is an acid-buffering substance.)

**Basic Salts Used in Antacids.** There are three basic salts used in antacids:

1) **Magnesium.** Magnesium compounds are available in the form of magnesium carbonate, magnesium trisilicate and most commonly, magnesium hydroxide (Milk of Magnesia). The major side effect of these magnesium compounds is diarrhoea.

2) **Calcium.** Calcium carbonate (Tums, Titralac and Alka-Seltzer) is a potent and rapid-acting antacid, but it can cause constipation. There have been rare cases of hypercalcemia (elevated levels of calcium in the blood) in people taking calcium carbonate for long periods of time. Hypercalcemia can lead to kidney failure.

3) **Aluminum.** The most common side effect of antacids containing aluminum compounds (Amphogel, Alternagel) is constipation.

Maalox and Mylanta are combinations of aluminum and magnesium, which balance the side effects of diarrhea and constipation. People who take large amounts of antacids containing aluminum may be at risk for calcium loss and osteoporosis. Long-term use also increases the risk of kidney stones. People who have recently experienced GI bleeding should not use aluminum compounds.

**Antibiotics**

*Helicobacter pylori* are usually highly sensitive to certain antibiotics, particularly Amoxicillin and to antibiotics in the macrolide class, such as Clarithromycin. Either class of antibiotics serves effectively as a second antibiotic in a three-drug regimen. Other antibiotics that are sometimes used include Tetracycline, Metronidazole and Ciprofloxacin.
1) **Amoxicillin** is a form of penicillin. It is inexpensive, but some people are allergic to it.

2) **Clarithromycin (Biaxin)** is a macrolide and is the most expensive antibiotic used against *Helicobacter pylori*. It is very effective, but there is growing bacterial resistance to this drug. Resistance rates tend to be higher in women and increase with age. Researchers fear that resistance will increase as more people use the drug.

3) **Tetracycline** is effective, but this medicine has unique side effects, including tooth discoloration in children. Pregnant women cannot take Tetracycline.

4) **Ciprofloxacin (Cipro)**, a fluoroquinolone, is also sometimes used in ulcer regimens.

5) **Metronidazole (Flagyl)** was the mainstay in initial combination regimens for *Helicobacter pylori*. As with Clarithromycin, however, there continues to be growing bacterial resistance to the drug. Today, about 25 - 35% of *Helicobacter pylori* bacteria are Metronidazole-resistant.

**Bismuth**

Compounds that contain bismuth are often used in the three-drug treatment programs. They destroy the cell walls of *H. pylori* bacteria. The only bismuth compound available in the U.S. has been Bismuth subsalicylate (Pepto-Bismol), although a drug combination of the H2 blocker Ranitidine and Bismuth Citrate (Tritec) has been released. High doses can cause vomiting and depression of the central nervous system, but the doses given for ulcer patients rarely cause side effects.

**Proton-Pump Inhibitors (PPIs)**

*Actions against ulcers.*

PPIs are the drugs of choice for managing patients with peptic ulcers, regardless of the cause. They suppress the production of stomach
acid by blocking the gastric acid pump -- the molecule in the stomach glands that is responsible for acid secretion\textsuperscript{30}.

PPIs can be used either as part of a multidrug regimen for \textit{Helicobacter pylori} or alone for preventing and healing NSAID-caused ulcers. They are also useful in treating ulcers caused by Zollinger-Ellison syndrome. They are considered to be more effective than H2 blockers.

\textbf{Standard Brands.}

Most PPIs are available by prescription as oral drugs. There is no evidence that one brand of PPI works better than another. Brands approved for ulcer prevention and treatment include:

1) Omeprazole (generic, Prilosec OTC)

2) Esomeprazole (Nexium)

3) Lansoprazole (Prevacid)

4) Rabeprazole (Aciphex)

\textbf{H\textsubscript{2} Blockers}

H\textsubscript{2} blockers interfere with acid production by blocking histamine, a substance produced by the body that encourages acid secretion in the stomach. H\textsubscript{2} blockers were the standard treatment for peptic ulcers until proton pump inhibitor and antibiotic regimens against \textit{H. pylori} were developed. These drugs cannot cure ulcers, but they are useful in certain cases. They are effective only for duodenal ulcers, however.

Four H\textsubscript{2} blockers are currently available over-the-counter in the U.S.: Famotidine (Pepcid AC), Cimetidine (Tagamet), Ranitidine (Zantac), and Nizatidine (Axid). All have good safety profiles and few side effects. There are some differences between these drugs:
1) **Famotidine (Pepcid AC)**. Famotidine is the most potent H2 blocker. The most common side effect is headache, which occurs in 4.7% of people who take it. Famotidine is virtually free of drug interactions, but it may have significant adverse effects in patients with kidney problems.

2) **Cimetidine (Tagamet)**. Cimetidine has few side effects; about 1% of people taking Cimetidine experience mild temporary diarrhea, dizziness, rash, or headache. Cimetidine interacts with a number of commonly used medications, including Phenytoin, Theophylline, and Warfarin. Long-term use of excessive doses (more than 3 grams a day) may cause impotence or breast enlargement in men. These problems resolve after the drug is discontinued.

3) **Ranitidine (Zantac)**. Ranitidine interacts with very few drugs. In one study, Ranitidine provided more pain relief and healed ulcers more quickly than Cimetidine in people younger than age 60, but there was no difference in older patients. A common side effect of Ranitidine is headache, which occurs in about 3% of people who take it.

4) **Nizatidine (Axid)**. Nizatidine is nearly free of side effects and drug interactions.

**Misoprostol**

Misoprostol (Cytotec) increases prostaglandin levels in the stomach lining, which protects against the major intestinal toxicity of NSAIDs.
**Actions against ulcers.**

Misoprostol can reduce the risk of NSAID-induced ulcers in the upper small intestine by two-thirds and in the stomach by three-fourths\textsuperscript{31}. It does not neutralize or reduce acid, so although the drug is helpful for preventing NSAID-induced ulcers, it is not useful in healing existing ulcers.

**Sucralfate**

Sucralfate (Carafate) seems to work by adhering to the ulcer crater and protecting it from further damage by stomach acid and pepsin. It also promotes the defensive processes of the stomach. Sucralfate has an ulcer-healing rate similar to that of H\textsubscript{2} blockers. Other than constipation, which occurs in 2.2\% of patients, the drug has few side effects. Sucralfate does interact with a wide variety of drugs, however, including Warfarin, Phenytoin and Tetracycline.
### 2.1.3 Plants showing Antiulcer activity:

#### Table 2.1.1 Plants showing Antiulcer activity

<table>
<thead>
<tr>
<th>S.No</th>
<th>PLANT NAME</th>
<th>CHEMICAL CONSTITUENTS</th>
<th>OTHER USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Acacia catechu</em></td>
<td>Tanins: catechutanic acid, catechin, l-epicatechin, catechu red, gum, flavonoids-quercitrin, quercitin.</td>
<td>Astringent, anthelmintic, antiseptic, antidysenteric, antipyretic, appetiser, anti-inflammatory, haemostatic, haematinic, cough, leprosy, leucoderma, skin diseases, foul ulcers, diarrhea, wounds, haemorrhages, pharyngodynia, splenomegaly, diabetes, anaemia</td>
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<tr>
<td>3</td>
<td><em>Andrographis paniculata</em></td>
<td>Lactones-diterpene lactone andrographolide diterpene lactones viz andrograpanin, deoxyxooandrographolide; glycosides viz neoandrographolide, andrographiside and flavanols</td>
<td>Laxative, vulnerary, antipyretic, antiperiodic, anti-inflammatory, expectorant, anthelmintic, digestive and stomachic, hyperdipsia, burning sensation, wounds, ulcers, chronic fever, malarial and intermittent fevers, inflammations, cough, bronchitis, skin</td>
</tr>
<tr>
<td></td>
<td><strong>Plant</strong></td>
<td>Secondary Metabolites</td>
<td>Medical Uses</td>
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<tr>
<td>4</td>
<td><strong>Bacopa monnieri</strong></td>
<td>Glycosides-sapon glycosides-triterpinoids saponins:bacosides A &amp; B, hersaponin, betulic acid, monnierin, alkaloids viz, herpestine, brahmine, flavanoids viz luteolin-7-glucoside, glucoronyl-7-apigenin &amp; glucoronyl-7-luteolin, common phytosteroids.</td>
<td>Astringent, carminative, digestive, antiinflammatory, anti convulsant, depurative, cardiotonic, bronchodilator, diuretic, febrifuge, neuralgia, inflammations, epilepsy, amentia, tumours, ulcers, splenomegaly, dyspepsia, flatulence, constipation, asthma, bronchitis, skin diseases, leprosy, leucoderma, syphilis, hoarseness, strangury, elephantiasis, dysmenorrhoea, sterility, fever &amp; general debility.</td>
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<tr>
<td>5</td>
<td><strong>Butea monosperma</strong></td>
<td>Fixed oils, water soluble albuminoid substances, glucose, fatty acids viz oleic, lenoleic, lenolenic, palmitic, stearic, arachidic, behenic &amp; lignoceric acid.</td>
<td>Emollient, Astringent, aphrodisiac, appetizer, digestive, constipation, antihelmintic, tonic, hepatopathy, anti inflammatory, pimples, flatulence, haemostatic, leprosy, swelling, arthriti s, purgative, ophthalmic, rubifacient, epilepsy, diabetes, hyperacidity &amp; abdominal disorders.</td>
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<tr>
<td>6</td>
<td><strong>Curcuma longa</strong></td>
<td>Curcuminoids, essential oil with high content of bisabolane derivatives, desmethoxycurcumin, bisdesmethoxycurcumin, dihydrocurcumin; common phytosterols, fatty acids &amp; polysaccharides viz., ukonan A, B, C, &amp; D</td>
<td>Thermogenic, emollient, anodyne, antiinflammatory, vulnerary, antiseptic, appetizer, carminative, stomachic, antihelmintic, laxative, diuretic, expectorant, haematinic, styptic, antiperiodic, alterative, alexetaric, detergent, stimulant, febrifuge, ophthalmic &amp; tonic, ulcers, wounds, leprosy, skin diseases, pruritus, allergic conditions, anorexia,</td>
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<tr>
<td></td>
<td><strong>Ficus racemosa</strong></td>
<td>Tannins, leucoanthocyanins, leucocyanidin-3-O-β-D-glucopyranoside, leucopelargonidine-3-O-α-L-rhamnopyranoside, β-sitosterol, stigmasterol, lupeol, ceryl behenate, α-amyrin acetate.</td>
<td>Astringent, antidiabetic, refrigerant, stomachic, refrigerant, carminative, menorrhagia, haemoptysis, aphrodisiac, diarrhea, haemorrhoids, diarrhoea, dyspepsia, haemorrhages,</td>
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<td>7</td>
<td><strong>Glycyrrhiza glabra</strong></td>
<td>Triterpinoid saponins – glycyrrhizin, a mixture of potassium and calcium salts of glycyrrhizic acid. Other triterpinoid saponins viz., glabranin A&amp;B, glycyrrhetol, glabrolide, isoglabrolide; isoflavones viz., formononetin, glabrone, neoliquiritin, hispaglabridin A&amp;B;</td>
<td>Refrigerant, emetic, tonic, diuretic, demulsant, mild laxative, aphrodisiac, trichogenous, expectorant, emmenagogue, alexipharmic, alterant, intellect promoting, gastralgia, cough, bronchitis, urelcosis, cephalgia, fever, skin diseases, ophthalmopathy and pharyngodynia.</td>
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<td>8</td>
<td><strong>Phyllanthus amarus</strong></td>
<td>Lignans—a diarylbutane, phyllanthin and an aryltetrahydronaphthalene, hypophyllanthin, hydrolysable tannins viz.,</td>
<td>Astringent, diuretic, deobstruante, stomachic, febrifuge and antiseptic, gastropathy, dropsy, jaundice, diarrhoea, dysentery, intermittent</td>
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<td><strong>phyllanthusiinD</strong>, <strong>amariin</strong>, <strong>amarulone</strong> and <strong>amarinic acid</strong>; <strong>alkaloids viz.</strong>, <strong>ent-norsecurinine</strong>, <strong>sobubbialine</strong>, <strong>epibubialine</strong>; <strong>a diarylbutane</strong>, <strong>nyrphyllin</strong> and <strong>a neolignan</strong>, <strong>phyllnirurin</strong>.</td>
<td><strong>fevers</strong>, <strong>ophthalmopathy</strong>, <strong>diseases of the urinogenital system,</strong> <strong>scabies,</strong> <strong>ulcers and wounds.</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>Piper cubeba</strong></td>
<td><strong>Cubebin, a lignin, hinokinin, clusin, dihydrocubebin, cubebinolide, cubebinone, 5-methoxy hinokinin; oxygenated cyclohexanesviz.</strong>, <strong>piperenol A</strong>, <strong>piperenol B</strong>, <strong>crotepoxide</strong> and <strong>zeylenol</strong>; <strong>sesquiterpene hydrocarbons viz.</strong>, <strong>bicyclosesquiphellandrene</strong> and <strong>1-epi bicyclosesquiphellandrene.</strong></td>
<td><strong>Thermogenic,</strong> <strong>stimulant,</strong> <strong>anodyne,</strong> <strong>dentifrice,</strong> <strong>anti-inflammatory,</strong> <strong>anthelmintic,</strong> <strong>deobstruant,</strong> <strong>vulnerary,</strong> <strong>appitiser,</strong> <strong>carminative,</strong> <strong>digestive,</strong> <strong>stomachache,</strong> <strong>cardiotonic,</strong> <strong>expectorant,</strong> <strong>diuretic,</strong> <strong>sedative,</strong> <strong>antineptic,</strong> <strong>flatulence,</strong> <strong>dyspepsia,</strong> <strong>anorexia,</strong> <strong>heamorrhoids,</strong> <strong>cardiac debility,</strong> <strong>cough,</strong> <strong>asthma,</strong> <strong>bronchitis,</strong> <strong>amenorrhea,</strong> <strong>dysmenorrhoea,</strong> <strong>cephalalgia,</strong> <strong>odontalgia,</strong> <strong>somaticgia,</strong> <strong>stangury,</strong> <strong>genito-urinary diseases.</strong></td>
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<td><strong>Plantago ovata</strong></td>
<td><strong>Mucilage polysaccharides,</strong> <strong>fixed oils viz.</strong>, <strong>linoleic, oleic, palmitic acid,</strong> <strong>iridoids</strong> &amp; <strong>proteins.</strong></td>
<td><strong>Astringent,</strong> <strong>refrigerant,</strong> <strong>emollient,</strong> <strong>diuretic,</strong> <strong>anti-inflammatory,</strong> <strong>laxative,</strong> <strong>expectorant,</strong> <strong>antidysenteric,</strong> <strong>aphrodisiac,</strong> <strong>robortant,</strong> <strong>burning sensation,</strong> <strong>constipation,</strong> <strong>strangury,</strong> <strong>gastritis,</strong> <strong>chronic diarrhea,</strong> <strong>dysentery,</strong> <strong>colonalgia,</strong> <strong>dry cough,</strong> <strong>nephropathy,</strong> <strong>gout,</strong> <strong>gonorrhea,</strong> <strong>bilious fever,</strong> <strong>duodenal ulcers,</strong> <strong>haemorrhoids,</strong> <strong>emaciation and general debility.</strong></td>
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<td><strong>Acacia leucophloea</strong></td>
<td>n- Hexacosanol, beta-Amyrin, beta-Sitosterol and Tannin</td>
<td>astringent, bitter, thermogenic, styptic, alexeteric, anthelmintic, vulnerary, demulcent, constipating, expectorant and antipyretic, vulnerary, demulcent, constipating, bronchitis, cough, vomiting, wounds, ulcers, diarrhoea, dysentery, internal and external haemorrhages.</td>
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<td>13</td>
<td><strong>Acacia nilotica</strong></td>
<td><strong>Arabin</strong>, a compound of Arabic acid with calcium, varying amounts of the magnesium and potassium salts of the same acid being present. It is believed, also, that small amounts of other salts of these bases occur.</td>
<td>Astringent, constipation, emollient, depurative, vulnerary, anthelmintic, diuretic, expectorant, alexeteric, emetic, nutritive, helminthiasis, haemorrhages, diarrhoea, skin diseases, burning sensation, aphrodisiac, cough, strangury, leprosy, leucorrhoea, haemorrhoids, proctoptosis.</td>
</tr>
<tr>
<td>14</td>
<td><strong>Acacia polyantha</strong></td>
<td>polyphenolics, especially tannins (proanthocyanidins or condensed tannins and hydrolysable tannins)</td>
<td>Astringent, acrid, thermogenic, depurative, anthelminthic, revulsive, leprosy, leucoderma, pruritus, skin diseases, diabetes, helminthiasis, ulcers, epilepsy, insanity, rheumatism &amp; obesity.</td>
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<td>15</td>
<td><strong>Albizia lebbeck</strong></td>
<td>tannins of condensed type, viz, D-catechin, isomers of leucocyanidin and melacacidin and a new leucoantho-cyanidin, lebbecacidin, friedelin and b-sittosterol, arginine, histidine, leucine, and isoleucine lysine.</td>
<td>Asthma, Thoracic pain, Skin diseases, Leprosy, Leucoderma, Sprains, Wounds, Ulcers, Neuralgia, Night blindness, Diarrhoea, antiinflammatory, aphrodisiac.</td>
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<tr>
<td></td>
<td><strong>Albizia odoratissima</strong></td>
<td>Tannins of condensed type, viz. D-catechin, isomers of leucocyanidin and melacacidin, leucoanthocyanidin, lebbecacidin, frienedelin and 3-sitosterol, arginine, histidine, leucine &amp; isoleucine lysine, methionine, phenylalanine, threonine, tyrosine, and valine.</td>
<td>Astringent, acrid, cooling, depurative, expectorant, ulcers, leprosy, skin diseases, erysipelas, cough, bronchitis, diabetes and burning sensation.</td>
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<td>16</td>
<td><strong>Allium sativum</strong></td>
<td>Volatile oil (0.1-0.4%) containing sulfur compounds: including allicin, diallyl disulfide, diallyl trisulfide, ajoene and others. • Other sulfur compounds: including allyl cysteine sulfoxide, methyl allyl thiosulfinate and related compounds. • Trace minerals: especially selenium, geranium • Enzymes: including alliinase, myrosinase, peroxidase.</td>
<td>Astringent, thermogenic, aperients, anodyne, oleagenous, aphrodisiac, anthelmintic, expectorant, febrifuge, diuretic, alexeretic, rubefacient, stimulant, anticholesterol, antibacterial, antifungal, tonic, emmenagogue, cough, bronchitis, asthma, fever, facial paralysis, flatulence, colic, constipation, atonic dyspepsia, helminthiasis, duodenal ulcers, pulmonary &amp; laryngeal tuberculosis, ophthalmopathy, cardiopathy, fatigue, leucodermia, leprosy, hysteria, haemorrhoids, sciatica, otalgia, lumbago, swellings, splenopathy, hepatopathy, pneumonopathy, arthralgia, dental caries.</td>
</tr>
<tr>
<td>17</td>
<td><strong>Alstonia scholaris</strong></td>
<td>It contains three alkaloids, Ditamine, Echitamine or Ditaine, and Echitenines, and several fatty and resinous substances- the second is the strongest base and resembles ammonia in chemical</td>
<td>Astringent, bitter, acrid, thermogenic, digestive, laxative, anthelmintic, febrifuge, antipyretic, depurative, galactagogue, stomachic, cardiotonic, tonic, malarial fevers, abdominal disorders, diarrhea, dysentery, dyspepsia, leprosy, skin diseases, pruritus, tumours, chronic, foul ulcers, asthma,</td>
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<td><strong>Amomum subulatum</strong></td>
<td>The essential oil in the seeds contain α-terpineol 45%, myrcene 27%, limonene 8%, menthone 6%, β-phellandrene 3%, 1,8-cineol 2%, sabinene 2% and heptane 2%.</td>
<td>Halitosis, constipation, stomachic, depurative, expectorant, diuretic, febrifuge, anorexia, dyspepsia, colic, flatulence, hyper acidity, vomiting, diarrhea, dysentery, skin diseases, pruritus, wounds, ulcers, cephalalgia, odontalgia, neuralgia, cardiac debility, liver congestion, splenomegaly.</td>
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<td></td>
<td><strong>Acalypha indica</strong></td>
<td>Kaempferol glycosides, mauritanin, clitorin, nicotiflorin &amp; biorobin, acalyphin, epiacalyphin, tannins, β-siloosterol, acalyphamide, aurantiamide, succinamide, flindersin, triacetonamine, n-octacosanol, qebrachiton, hydrocyanic acid</td>
<td>Diuretic, skin diseases, constipation, ulcers, bronchitis, otalgia, cough &amp; purgative</td>
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<td><strong>Aquilaria agallocha</strong></td>
<td>Selinene, dihydro selinene, sesquiterpene, hydrocarbons, agarol, a sesquiterpine alcohol, a hydroxylketone, s-isopropyl-7 methyl-5,5,5a,6.7.8-hexahydro-3H-naphtho, agar oil</td>
<td>Halitosis, dyspepsia, anorexia, cardiac debility, skin diseases, leprosy, foul ulcers, hypothermia, inflammations, rheumatoid arthritis, cough, asthma, hiccough, albuminuria &amp; general debility.</td>
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|   | **Argyreia nervosa** | Tannins, alkaloids, acids, minerals like potassium, calcium & | Astringent, emollient, thermogenic, roborant, cardiotonic, appetiser, digestive, carminative, antiinflammatory, expectorant, diuretic, rejuvenating, aph
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<th>Plant Name</th>
<th>Secondary Metabolites</th>
<th>Therapeutic Properties</th>
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<tr>
<td>23</td>
<td>Cassia occidentalis</td>
<td>2- methylanthraquinone, 1, 4, 5-trihydroxy-7-methoxy-3-methylanthraquinone, physcion, its contain 1, 8-dihydroxy glucoside, rhein, aloe-emodin, chrysophanol, its glycoside, N-methylmorpholine, glucose</td>
<td>Astringent, thermogenic, purgative, diuretic, cardiootonic, stomachic, emmenagogue, sudorific, febrifuge, antiperiodic, anodyne, depurative, anthelminitic, arthralgia, inflammations, leprosy, leucoderm a, skin diseases, flatulence, colic, strangury, cardiac debility, fever, cough, catarrh, amenorrhoea, dysmenorrhoea, dystocia, abdominal disorders, cholera, arthralgia &amp; dyspnoea.</td>
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<td>24</td>
<td>Aristolochia bracteolate</td>
<td>Nauseous volatile substance, an alkaloid and salts</td>
<td>Antihelmintic, cathartic, anti-inflammatory, emmenagogue, vulnerary, appetite, sudorific, antiperiodic, constipation, inflammations, amenorrhoea, dysmenorrhoea, foul ulcers, boils, syphilis.</td>
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<td>25</td>
<td>Bambusa aruninacea</td>
<td>Silica 90%, silacum, potash, lime, alumina, cholin, betain, hydrate of silicic acid, nuclease, urease, proteolytic enzyme, cyanogenic glucoside and an alkaloid.</td>
<td>Astringent, laxative, depurative, diuretic, leprosy, skin diseases, burning sensation, discolorations, strangury, ring worm, ulorrhrea, arthralgia, general debility, emmenagogue, ophthalmic, febrifuge, vulnerary, constipation, diarrhea, gonorrhoea, amenorrhoea, dysmenorrhoea, wounds.</td>
</tr>
<tr>
<td>26</td>
<td>Anethum graveolens</td>
<td>D-carvone, dillapiol, dhc, eugenol, limonene, terpinene and myristicin</td>
<td>Antispasmodic, carminative, digestive, disinfectant, galactagogue, sedative, stomachic</td>
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<td>No.</td>
<td>Plant Name</td>
<td>Secondary Metabolites</td>
<td>Medicinal Properties</td>
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<td>27</td>
<td><em>Anamirta cocculus</em></td>
<td>quaternary alkaloids, such as berberine, palmatine, magnoflorine and colunibamine, picrotoxin, menispermine and paramenispermine.</td>
<td>Astringent, thermogenic, expectorant, antifungal, anthelmintic, depurative, bronchitis, dermatophy osis, foul ulcers, inflammations, flatulence, chronic skin diseases &amp; ringworm</td>
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<td>28</td>
<td><em>Argemone mexicana</em></td>
<td>22–36% yellow non-edible oil, called argemone oil or katkar oil, which contains the toxic alkaloids sanguinarine and dihydrosanguinarine. 4 quaternary isoquinoline alkaloids, dehydrocorydalmine, jatrorrhizine, columbamine, and oxyberberine.</td>
<td>Anti-inflammatory, aphrodisiac, emetic, depurative, anodyne, anthelmintic, antipyretic, op hthalmic, stomachic, sedative, expectorant, vulnerary, diuretic, purgative, skin diseases, pruritus, constipation, flatulence, colic, malarial fever, vesicular calculus, cough, wounds, ulcers, rheumatalgia, dropsy, jaundice, conjuncti vitis, burning sensation, asthma &amp; pertussis.</td>
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<tr>
<td>29</td>
<td><em>Artocarpus heterophyllus</em></td>
<td>morin, dihydromorin, cynomacurin, artocarpin, isoartocarpin, cyloartocarpin, artocarpesin, oxydihydroartocarpesi n, artocarpetin, norartocarpetin, cycloartinone and artocarpanone.</td>
<td>Anti-diarrhoeal, fever, boils, wounds, skin diseases, astringent, carminative, tonic, dyspeps ia, debility, laxative, aphrodisiac, constipation, diuretic, nerve sedative, convulsions, ophthalmitis &amp; pharyngitis</td>
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<tr>
<td>30</td>
<td><em>Azadirachta indica</em></td>
<td>Azadirachtn, Azadirachtn, salannin, gedunin, azadirone, nimbin, nimbidine, nimbicidine.</td>
<td>Anti-inflammatory, antiarthritic, antipyretic, hypoglycaemic, Antifungal, spermicidal, antimalarial, antibacterial, Diuretic, antipyretic, intestinal disorders, skin diseases, wounds,</td>
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<td>31</td>
<td><strong>Bombax ceiba</strong></td>
<td>nimbol.</td>
<td>obesity &amp; arthritis.</td>
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<td>Glycosides and tannins ,alkaloids, proteins , lupeol and b-sitostrol, 3 naphthalene derivatives related to gossypol , b-sitosterol, traces of essential oil, kaempherol and quercetin.</td>
<td>Tonic,demulcent,dysentery,aphrodisiac,styptic ,demulcent,cooling,stimulant,astringent, burning sensation,strangury, haemorrhoids, pulmonary tuberculosis, influenza, menorrhagia,emetic,splenomegaly,calculation infections.</td>
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<td>32</td>
<td><strong>Boswellia serrata</strong></td>
<td>Oils, terpenoids, sugars, and volatile oils. Up to 16 percent of the resin is essential oil, the majority being alpha-thujene and p-cymene. Four pentacyclic triterpene acids are also present, with beta-boswellic acid being the major constituent.</td>
<td>Asthma,haemorrhoids,skin diseases, dysentery,ulcers,expectorant,diaphoretic,diuretic,diatonic,diaphoresis,convulsions,dysentery ,urethrorrhea,orchipathy,bronchitis, stomatis, cough,syphilic diseases,jaundice &amp; arthritis</td>
</tr>
<tr>
<td>33</td>
<td><strong>Basella alba</strong></td>
<td>Iodine, fluorine, carotenoids, organic acids, vitamin-K.</td>
<td>Aphrodisiac,laxative,haemostatic,appetiser,sedative,diuretic,demulcent,maturate,tonic,flatulence,anorexia,haemorrhages,haemoptysis,sleeplessness,pruritus,leprosy,urticaria,ulcers,dysentery,gonorrhea,balanitis,strangury,fatigue &amp; general debility.</td>
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<td>34</td>
<td><strong>Buchanania lanzan</strong></td>
<td>Bark contains 13.4% tannin ,Myricetin 3-rhamnose-3-galactoside.</td>
<td>Depurative,emollient,anti inflammatory,nervine tonic,cardiotonic,stomachic,laxative,diuretic,expectorant,aphrodisiac,rejuvenating,febrifuge,cardiac debility,cough,asthma,seminal weakness,</td>
</tr>
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<td>36</td>
<td><em>Callicarpa macrophylla</em></td>
<td>2-tetracyclic diterpenoids, calliterpenone and its mono-OAc., sitosterol; calliterpenone and its mono-OAc, luteolin, apigenin and its 7-glucuronides; ursolic acid, its 2-OH derivatives, crategolic acid, calliterpenone and its acetate.</td>
<td>Astringent, cooling, anodyne, deodorant, digestive, constipation, depurative, styptic, alexeteric, febrifuge, rheumatoid arthritis, burning sensation, cephalalgia, diaphoresis, foul ulcers, dyspepsia, flatulence, colic, diarrhoea, dysentery, haemorrhages, haemoptysis, poisonous bites, skin diseases, diabetes, vomiting, fever, gout, arthralgia &amp; general weakness.</td>
</tr>
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<td>37</td>
<td><em>Caesalpinia sappam</em></td>
<td>Brazilin &amp; brasilein, essential oil containing of D-a-phellandrene, ocinene, tannin, gallic acid &amp; saponins.</td>
<td>Astringent, refrigerant, vulnerary, depurative, constipation, sedative, haemostatic, burning sensation, wounds, ulcers, leprosy, skin diseases, diarrhea, dysentery, epilepsy, convulsions, menorrhagia, leucorrhoea, diabetes, haemoptysis, haemorrhages, stomatopathy &amp; odontopathy.</td>
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</table>
|   | **Calycopteris floribunda** | Caryophyllene oxide (13.79%),  
n-hexadecanoic acid (11.91%) and β-caryophyllene (10.45%) | Astringent, laxative, anthelmintic, depurative, diaphoretic, febrifuge, intestinal worms, colic, leprosy, malarial fever, dysentery, ulcers, vomiting, jaundice, ulcers, pruritus & skin diseases. |
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<td>38</td>
<td><strong>Canscora decussate</strong></td>
<td>16 xanthones (I-XVI), 6 of which (II, VII, IX, XII, XIII, XVI), mangiferin (1,5-dihydroxy-3-methoxy (X), 1-hydroxy-3,5-dimethoxy (VII), 1, 3, 5-trihydroxy-6-methoxy (II), 1, 3, 8-trihydroxy-7-methoxy (III), 1,8-dihydroxy-3,7-dimethoxy (XI), 1-hydroxy-3, 7, 8-trimethoxy (VIII), 1, 3, 8-trihydroxy-6,7-dimethoxy (XIII), 1,8-dihydroxy-3, 6, 7-trimethoxy (XII), 1-hydroxy-3, 6, 7, 8-tetramethoxy (IX).</td>
<td>Astringent, thermogenic, laxative, vulnerary, emollient, alexeteric, anthelmintic, appetizer, aphrodisiac, depurative, rejuvenating, tonic, leucoderma, abdominal disorders, intestinal worms, insanity, epilepsy, nervous debility, forgetfulness, tuberculosis, ulcers &amp; general debility.</td>
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<tr>
<td>39</td>
<td><strong>Capparis deciduas</strong></td>
<td>alkaloids, glycosides, terpenoids, sterols, flavanoids, phenols and fatty acids. Capparine, Cappariline, Capparinine, Isocodonocarpine,</td>
<td>Thermogenic, anodyne., sudorific, expectorant, digestive, carminative, anthelmintic, purgative, antibacterial, vulnerary, alexeteric, stimulant, emmenagogue, aphrodisiac, tonic, cough, hiccough, asthma, vomiting, haemorrhoids, intermittent fevers, arthritis, odontalgia, lumbago, dyspepsia, flatulence, constipation, intestinal worms, cardiac debility, gout, amenorrhoea, dysmenorrhoea, card</td>
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<td>Plant Name</td>
<td>Constituents</td>
<td>Medical Uses</td>
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<td>41</td>
<td><strong>Capsicum annum</strong></td>
<td>Capsaicin, capsaicin and solanine, capsaicinoids, essential oil, alkylmethoxy pyrazines, vitamin C. Capsicum or Cayenne (Capsicum Frutescens) is rich in vitamins A, C, iron and calcium.</td>
<td>Carminative, laxative, expectorant, sialagogue, stimulant, cardiotonic, antipyratic, antiperiodic, sudorific, rubefacient, cephalalgia, gout, arthritis, sciatica, hoarseness, anorexia, dyspepsia, flatulence, cough, cardiac debility, malarial &amp; intermittent fevers, dropsy, cholera, indolent ulcers.</td>
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<tr>
<td>42</td>
<td><strong>Cassia auriculata</strong></td>
<td>Tannin, di-(2-ethyl)hexylphthalate, alkaloids, resins, vitamins, minerals like calcium &amp; phosphorus.</td>
<td>Astringent, cooling, depurative, leprosy, tumours, asthma, urethrorrhoea, anthelmintic, skin diseases, ulcers, diabetes urethrorrhoea, nocturnal emissions and pharyngopathy, chronic purulent conjunctivitis.</td>
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<td>43</td>
<td><strong>Carthamus tinctorius</strong></td>
<td>Chalcone C-glucoside carthamin (up to 8.5%), fatty acids, the chalcone hydroxysaffl or yellow A; the nitrogenous chalcone tinctormine; the quinoid C-glycosides saffl or yellow A and safflor yellow B; the flavonoids neocarthamin, quercetin, rutin, kaempferol and related hydroxy derivatives and glycosides.</td>
<td>Diuretic, laxative, urorrhoea, ophthalmopathy, tonic, inflammations, boils, ring worm, scabies, leucoderma, haemorrhoids &amp; bronchitis, purgative, carminative, aphrodisiac, scabies, pectoralgia, pharyngodynia, arthritis &amp; constipation.</td>
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<td>44</td>
<td><strong>Citrus colocynthis</strong></td>
<td>Colocynthin, certain fixed or stable oils, resins, gums, pectins, certain minerals like calcium, magnesium,</td>
<td>Purgative, uteralgia, mammillitis, rheumatalgia, visceromegaly, ophthalmia, ascites, jaundice, uropathy, carminative, cooling, antipyretic, leucoderma,</td>
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<td>68</td>
<td>lignin, phytosterol glycosides, elaterin, albumin oils, β substances like colocynthetin, cucurbitacin, B &amp; E.</td>
<td>dyspepsia, constipation, asthma, ulcers, elephantiasis, tuberculosis &amp; splenomegaly.</td>
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<td>45</td>
<td>Careya arborea</td>
<td>maslinic acid, a triterpenoid lactone, careyagenolide, tannins, saponions, sapogenol, hexacosanol, quercetin, ellagic acid, taraxerol, β-sitosterol, α-spinasterol, valoneic acid, ellagic acid dimethylether, triterpene ester, careanorin and β-amyrin, terpenes like lupeol, betulin, methyl betulinate, β-sitosterol, and piperine.</td>
<td>Astringent, thermogenic, alexeric, anthelmintic, antipyretic, antipruritic, bronchitis, catarrh, dyspsia, colic, leucoderma, epileptic fits, anaphrodisiac, cough, bronchitis, haemorrhoids, intestinal worms, dysentery, urorrhoea.</td>
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<td>46</td>
<td>Cissus quadrangularis</td>
<td>Tetracyclic triterpenoids, onocer-7-ene-3alpha, 21 beta-diol and onocer-7-ene-3beta, 21 alpha-diol and two steriodal principles I and II, alpha-sitosterol, delta-amyrin</td>
<td>Astringent, thermogenic, alexeric, anthelmintic, antipyretic, antipruritic, bronchitis, catarrh, dyspsia, colic, leucoderma, epileptic fits, anaphrodisiac, cough, bronchitis, haemorrhoids, intestinal worms, dysentery, otourrhoea.</td>
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<td>47</td>
<td>Cinnamomum verum</td>
<td>Cinnamaldehyde, gum, tannin, mannitol, coumarins, and essential oils (aldehydes, eugenol, pinene).</td>
<td>antibacterial, anti-fungal, and uterine stimulant, emmenagogue, styptic, anorexia, inflammation, stomachalgia, odontalgia, vomiting, tubercular ulcers, diarrhea, bronchitis, asthma, nausea, flatulence, fever, cardiac diseases.</td>
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<td><strong>Catunaregam spinosa</strong></td>
<td>11,14-eicosadienoic acid, methyl ester (42.49%), palmitic acid (15.34%), stearic acid (10.54%), myristic acid (6.26%), hexadecanoic acid, ethyl ester (5.84%)</td>
<td>Astringent, emetic, abortifacient, anodyne, constipation, antiseptic, dysentery, bruises, diarrhoea, carminative, anti-inflammatory, expectorant, febrifuge, vulnerary, antispasmodic, depurative, cough, asthma, bronchitis, flatulence, colic, constipation, fever.</td>
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<td><strong>Delphinium denudatum</strong></td>
<td>Alkaloids, fixed oil, delphonin and kaempferol, ajacine, ajainine, ajaconine. Fixed oil, resin, gallic and aconitic acids.</td>
<td>Thermogenic, anodyne, digestive, carminative, anti-inflammatory, anthelmintic, diuretic, lithotriptic, stimulant, odontalgia, dyspepsia, flatulence, jaundice, amenorrhoea, strangury, obesity, leprosy, skin diseases, cough, asthma, cardiac debility, fever.</td>
</tr>
<tr>
<td></td>
<td><strong>Datura metel</strong></td>
<td>Scopolamine, (b)-sitosterol, daturadiol, tropine, daturilin</td>
<td>Narcotic, anodyne, antispasmodic, emetic, asthma, cough, fever, ulcers, skin diseases, ophthalmodynia, otalgia, lumbago, sciatica, neuralgia, mumps, painful swellings, epilepsy, cephalalgia, dandruff, gastropathy.</td>
</tr>
</tbody>
</table>
2.1.4 Description of plants selected for Antiulcer activity:

1. **Wedelia calendulacea**

   **Plate 2.1.4.1 wedelia calendulacea**

   Botanical Name:  *wedelia calendulacea*
   
   Family:  Asteraceae

   **Vernacular names**

   Synonyms:  Solidago chinensis
   
   Common name:  Chinese Wedelia
   
   Hindi:  Pilabhangara, Bhanra
   
   Marathi:  Pivala-Bhangra
   
   Sanskrit:  Pitabhrnga, Pitabhrngarajah
   
   Tamil:  Manjalkarilamkanni, Patalai kayyantakarai
   
   Telugu:  Guntagalagara
   
   Kannada:  Gargari, Kalsarji
   
   Malayalam:  Mannakkannunni
   
   Konkani:  Birimgarsi

   **Geographical distribution**  Assam, Arunachal Pradesh, Uttar Pradesh in India The species generally occurs in wet places near seacoasts.
**Chemical constituents:** wedelolactone and demethylwedelolactone, Vitamin A

**Medicinal uses:**

The leaves are used in dyeing grey hair and in promoting the growth of hair. They are considered tonic, alternative, and useful in coughs, cephalalgia, skin diseases, and alopecia. The juice of the leaves is much used as a snuff in cephalalgia. The seeds and flowers, as well as the leaves, are used in decoction, in the quantity of half of teacupful twice daily, as a deobstruent. In decoction, the plant is used in uterine haemorrhage and menorrhagia.

**Earlier work done on this Plant**

1. *wedelia calendulacea* was investigated on ischemia and reperfusion-induced cerebral injury. Cerebral ischemia was induced by occluding right and left common carotid arteries (global cerebral ischemia) for 30 min followed by reperfusion for 1 h and 4 h individually. Various biochemical alterations, produced subsequent to the application of bilateral carotid artery occlusion (BCAO) followed by reperfusion viz. increase in lipid peroxidation (LPO), hydrogen peroxide (H2O2), and decrease in reduced glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD), level in the brain tissue, Western blot analysis (Cu-Zn-SOD and CAT) and assessment of cerebral infarct size were measured. *wedelia calendulacea* was markedly decrease cerebral infarct damages but results are not statistically significant. It can be concluded that *wedelia calendulacea* possesses a neuroprotective activity against cerebral ischemia in rat.

2. The neuropharmacological activities of the methanolic and aqueous extract of Wedelia calendulacea stem were screened in rats and mice. The extracts effect on pentobarbital-induced sleeping time, pentylenetetrazole-and styrychnine-induced seizure, spontaneous motor activity, exploratory behaviour, and rota-rod performance (motor coordination) were evaluated. The methanolic extract (20 and 50
mg/kg, i.p.) and aqueous extract (200 and 500 mg/kg, i.p.) produced a significant (P < 0.001) prolongation of pentobarbital-induced sleeping time, and reduced the SMA and exploratory behaviour. The extract prolonged onset of the phases of seizure activity but did not protect mice against lethality induced by pentylentetrazole and strychnine. It also failed to affect the motor coordination test. These results suggest that the extract contained an agent with neuropharmacological activity that may be sedative in nature. In addition, from the crude methanolic extract of *Wedelia calendulacea* stem a HPLC fingerprint profile and liquid chromatography/sequential mass spectrometry (LC/MS) were performed.

3. The cytotoxicity and antibacterial activity of petroleum ether, chloroform and methanol extracts of *Wedelia calendulacea* were assayed by brine shrimp lethality bioassay and standardized disk diffusion method against 19 bacterial strains. Three diterpenes isolated from the plant were also evaluated for in vitro antibacterial activities. The LC$_{50}$ for the crude extracts against the brine shrimp nauplii were found to be 4.59 μg/ml, 7.99 μg/ml and 14.88 μg/ml, respectively, whereas the positive control, vincristine sulfate showed an LC$_{50}$ of 0.58 μg/ml. Among the crude extracts and pure compounds tested, (−)-kaur-16-en-19-oic acid isolated from the chloroform extract showed the highest inhibitory activity against most of the bacterial strains with mean zone of inhibition of 10–21 mm at 200 μg/disc.

4. The hepatoprotective activity of ethanolic extract of *Wedelia calendulacea* was studied against CCl$_4$ induced, acute hepatotoxicity in rats. Hepatoprotective activity of the ethanolic-leaf extract of *Wedelia calendulacea* (EEWC) was studied by estimating serum enzyme activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), protein and bilirubin. The treatment with EEWC showed a dose-dependent reduction of CCl$_4$ induced elevated serum levels of enzyme activities with parallel increase in total protein and bilirubin, indicating the extract could preserve the normal functional status of the liver. The weight
of the organs such as liver, heart, lung, spleen and kidney in CCl induced experimental animals administered with EEWC showed an increase over CCl control group.

2. *Pongamia Pinnata*

![Image of Pongamia Pinnata](image)

**Plate 2.1.4.2 Pongamia Pinnata**

Botanical name : *Pongamia Pinnata*

Family : Fabaceae (Leguminaceae)

**Vernacular names**

Common name : Indian Beech, Poongam Oil Tree, Honge, Ponge.

Hindi : dithodi

Sanskrit : karanj

**Geographical distribution:** a leguminous tree, which is native to Northern Australia, India, Pongamia is widely distributed in tidal and beach forests of India.

**Chemical constituents:** sterols, fatty acids, polyhydroxylated chalcones, isoflavonoids, quercetin, amino acids, triterpinoids, karanjin, pongamol.

**Medicinal uses:** Pongamia seeds and oil is anthelmintic, styptic, and depurative. It is useful in rheumatism arthritis, whooping cough, skin ailments and scabies. Seed oil is mainly used in cosmetics, in soap making
and as a lubricant. Seed oil is also used as insecticidal, nematicidal and bactericidal. Flowers are useful to quench dipsia in diabetes and for alleviating vata and kapha. Leaves are digestive, laxative and useful in flatulence, dyspepsia, diarrhea, leprosy and cough. Bark is anthelmintic and used in pesticides. Dried leaves are used in stored grains to repel insects. The bark also yields a black gum that is used to treat wounds caused by poisonous fish.

**Earlier work done on this Plant**

1) Oil analysis and antimicrobial activity from seeds of elite genotype of *Pongamia pinnata* was carried out in the current study. The highest oil yield (33%) from seeds was recovered in n-Hexane. Physico-chemical properties of crude oil established suitability of *P. pinnata* for its use as a potential biofuel crop. The total mono unsaturated fatty acid (oleic acid 46%) present in seed oil was more in comparison to polyunsaturated fatty acid (33%) as analyzed by GC–MS. Seed oil also showed inhibition against the tested fungal and bacterial cultures. However, the efficacy of antimicrobial activity of the seed oil at four concentration levels (50%, 80%, 90% and 100%) against various pathogenic indicators was found to be concentration-dependent. The obtained results confirmed the use of seed oil from well characterized elite genotype of *Pongamia* as diesel fuel and in pharmaceuticals.

2) In the present study, the anti-inflammatory activity of 70% ethanolic extract of *Pongamia pinnata* leaves (PLE) in acute, subacute and chronic models of inflammation was assessed in rats. Per os (p.o.) administration of PLE (300, 1000 mg/kg) exhibited significant anti-inflammatory activity in acute (carrageenin, histamine, 5-hydroxytryptamine and prostaglandin E₂-induced hind paw edema), subacute (kaolin-carrageenin and formaldehyde-induced hind paw edema) and chronic (cotton pellet granuloma) models of inflammation. PLE did not show any sign of toxicity and mortality up to a dose level of 10.125 g/kg, p.o. in mice. Both acute as well as chronic administration of PLE (100, 300 and 1000 mg/kg, p.o.) did not produce any gastric lesion in rats. These results indicate that PLE possesses significant

3) Our aim was to evaluate the antihyperglycemic and antilipid peroxidative effect of ethanolic extract of *Pongamia pinnata* (Linn.) *Pierre* (Leguminosae) flowers (PpEt) in normal rats and alloxan induced diabetic rats. Hyperglycemia, elevated lipid peroxidation [thiobarbituric acid reactive substances (TBARS)] and disturbed nonenzymatic [Vitamin E, Vitamin C and glutathione] and enzymatic antioxidants status were noticed in alloxan induced diabetic rats. The oral administration of ethanolic extract of *Pongamia pinnata* flowers (300 mg/kg bw) showed significant antihyperglycemic, and antilipidperoxidative effects and enhancement in antioxidants defense system in alloxan induced diabetic rats. However, no significant characteristic changes were noticed in blood glucose level as well as in lipid peroxidation and antioxidant status in normal rats treated with “PpEt” alone. We have also observed that the “PpEt” considerably reduced the blood glucose concentration in a similar extent to that of the reference drug glibenclamide (600 μg/kg bw) in alloxan induced diabetic rats. Our results thus suggested that the “PpEt” could be used as a safe alternative antihyperglycemic drug for diabetic patients.

4) White Spot Syndrome Virus (WSSV) is an extremely virulent, contagious, causative agent of the White spot syndrome of shrimp and causes high mortality and affects most of the commercially important cultured marine crustacean species globally. Oral administration of ethanolic extract and purified compound from the leaves of *Pongamia pinnata*, an indigenous Indian “medicinal plant” “has increased the survival of WSSV infected *Penaeus monodon*”. Pelletized feed impregnated with ethanolic extract of the leaves of *P. pinnata* was fed to shrimp prior and after WSSV infection at 200 and 300 μg/g of body weight of shrimp/day. The survival rate for the WSSV-infected shrimp that were fed with 200 and 300 μg extract/g were 40% and 80%, respectively. The active WSSV antiviral
compound 1 that was isolated from the leaves of *P. pinnata* was identified as bis(2-methylheptyl)phthalate. Thus, the present work revealed that oral administration of the crude and purified compound from the leaves of *P. pinnata* effectively inhibited WSSV pathogenesis and reduced the mortality of infected shrimp.

5) Diabetes mellitus is a major metabolic syndrome characterized by derangement in carbohydrate metabolism associated with defect in insulin secretion or action. Alloxan is widely used to induce diabetes mellitus in experimental animals, owing to its ability to destroy the β-cells of pancreas possibly by generating excess reactive oxygen species\(^40\). Free radical-mediated biomembrane lipid peroxidation has been implicated in the pathogenesis of many pathological conditions including diabetes mellitus and its complications. Overproduction of lipid peroxidation by-products and insufficient antioxidant potential have been reported in both experimental and human diabetes mellitus.

### 3. *Selaginella bryopteris*

**Plate 2.1.4.3 - *Selaginella bryopteris***

Botanical Name: *Selaginella bryopteris*

Family: Selaginellaceae
**Common name:** sanjeevani

**Geographical distribution:** Sanjeevani grows on the hills of tropical areas, particularly the Arawali Mountain terrains from east to west in India. The dry plants have traditionally been used as a remedy for several human health complications for centuries in India, particularly by tribal peoples.

**Chemical constituents:** flavones, bioflavones, alkaloidal glycosides, phenylpropanones, lignans.

**Medicinal uses:** heart stroke, dysuria, irregular menstruation, and jaundice

**Earlier work done on this Plant**

1. The chemopreventive and anticarcinogenic potential of *Selaginella bryopteris*, a traditional Indian herb referred to as ‘Sanjeevani’ in the Ayurvedic system of medicine, was examined study. Comprehensive *in vitro* and *in vivo* studies were conducted on the flavonoid-rich benzene fraction of the aqueous extract that demonstrated a significant cytoprotective activity\(^1\). Biomarkers of chemoprevention such as proliferative index and status of cell-cycle regulatory proteins, antioxidant property, anti-inflammatory effect, reversal of stress-induced senescence and genoprotective effect were investigated in human and murine cell cultures

2. A series of eleven biflavonoids containing amentoflavone and hinokiflavone derivatives from the Indian medicinal herb *Selaginella bryopteris* has\(^2\) been investigated for their antipROTOzoal activity using *in vitro* assays against the K1 strain of *Plasmodium falciparum*, *Leishmania donovani*, *Trypanosoma brucei rhodesiense* and *Trypanosoma cruzi*. 

Plate 2.1.4.4 - Cissampetos mucronata

Botanical Name:  *cissampetos mucronata.*
Family                :  Menispermaceae

**Vernacular names**
English      :  Heart-leaved vine
Sanskrit     :  Nyakuta

**Geographical distribution:** Origin and *geographic distribution* *Cissampelos mucronata* is distributed throughout tropical Africa, except the most humid areas, from Senegal east to Ethiopia

**Chemical constituents:** bisbenzyliisoquinoline alkaloids, proteins, lipids, sugars.

**Medicinal uses:** Antimalarial, antimicrobial, antibacterial, antiulcer

**Earlier work done on this Plant :**

1)The leaves and roots of *Cissampelos mucronata* A. Rich (Menispermaceae) are widely used in the tropics and subtropics to manage various ailments such as gastro-intestinal complaints, menstrual problems, venereal diseases and malaria. In the Coast region, Tanzania, roots are used to treat wounds due to extraction of jigger. Leaves of *Tephrosia villosa* (L) Pers (Leguminosae) are reported to be used in the treatment of diabetes
mellitus in India. In this study, extracts from the roots and aerial parts of *C. mucronata* and extracts from leaves, fruits, twigs and roots of *T. villosa* were evaluated for larvicidal activity, brine shrimps toxicity and antimicrobial activity.

2) The ethanolic root extract of Cissampelos mucronata was investigated for sedative activity. Phytochemical analysis indicated the presence of alkaloids: sterols/triterpenes, tannins, carbohydrates, glycosides, and flavonoids. Acute lethality test gave an LD50 of 282.84 mg/kg. The study of the effect of the extract on the behavioural pattern of mice showed changes indicative of central nervous system depression. The results further revealed that the extract progressively reduced ephedrine-induced spontaneous motor activity in rats, and prolonged pentobarbitone-sleeping time in mice. Pre-treatment of mice with the extract also protected 40% of the animals against pentylenetetrazole-induced convulsions. The mechanism of action is not precisely known but may probably be attributed to central nervous system depressant action.

5. *Ginkgo biloba*.

**Plate 2.1.4.5 - Ginkgo biloba**

Botanical Name:   *Ginkgo biloba*

Family :   Ginkgoaceae

**Common names:** Ginkgo; Maidenhair tree
Geographical distribution: Origin and geographic distribution *Cissampelos mucronata* is distributed throughout tropical Africa, except the most humid areas, from Senegal east to Ethiopia ...


Medicinal uses: Antihypoxic (increases peripheral and cerebral blood flow), antioxidant, cardiovascular tonic, cerebrovascular trophorestorative, Platelet Activating Factor (PAF) antagonist, vasodilator.

Earlier work done on this Plant

1) This study investigates the cardioprotective activity of a combined treatment of *Ginkgo biloba* phytosomes (GBP) and Ocimum sanctum extract (Os) in isoproterenol (ISO)-induced myocardial necrosis in rats. Significant myocardial necrosis, depletion of the endogenous antioxidants superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), and glutathione (GSH), and increases in the serum marker enzymes aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine phosphokinase (CPK) were observed in ISO-treated rats compared with normal rats.

2) The present study relates to a methanol extract of the seed coat of *Ginkgo biloba*, and tested particularly on the third instar larvae of *Spodoptera exigua*. The extract was found to have an inhibitory effect on the growth of the larvae besides bringing a change in the nutrient reserves in the body of the insect. Topical application of five different doses of the methanol extract resulted in a mortal effect to third instar larvae of *S. exigua* that is very much dependent on the dose as well as duration of exposure.

3) The standardized extract of *Ginkgo biloba* (EGb 761) has been widely employed for its significant benefit in neurodegenerative disorders. Although antioxidative actions have been attributed to this extract, the
mechanisms of the multiple principles involved in this pharmacological activity are not completely established. Parkinson's and Alzheimer's diseases are frequently associated with oxidative stress and defects in the cellular protective mechanisms. In this study, the lipid peroxidation (LPO) and the activity of the antioxidant enzymes, catalase (CAT) and superoxide dismutase (SOD) were evaluated in the hippocampus, striatum and substantia nigra (SN) of rats treated with EGb 761.

4) The antibacterial activity of methanol, ethanol, chloroform, and hexane extracts of the leaves of Himalayan gymnospermous plant Ginkgo biloba L. was assessed against five animal and plant pathogenic strains (Agrobacterium tumefaciens, Bacillus subtilis, Escherichia coli, Erwinia chrysanthemi, and Xanthomonas phaseoli) employing disc-diffusion and broth-dilution assays. The methanol extract showed the highest activity (zone of inhibition of 15-21 mm) followed by ethanol (14-19 mm), chloroform (15-20 mm), and hexane (14-19 mm) extracts at 250 μg/mL. A minimum inhibitory concentration (MIC) of 7.8 μg/mL was found for the methanol extract against most of the pathogens tested.


**Plate 2.1.4.6 - Vitex negundo**

Botanical name : *Vitex negundo*

Family : Verbenaceae
**Vernacular names**

- **English**: five-leaved chaste tree
- **Chinese**: Huang jing zi
- **Spanish**: Agno-casto
- **Tamil**: nochhi
- **Sanskrit**: nirgundi
- **Telugu**: Sindhuvara; Vavili; Nalla-vavili; Tella-vavili
- **Kannada**: Bile-nekki
- **Malayalam**: Indrani

**Geographical distribution:** *Vitex negundo* is native to tropical Eastern and Southern Africa and Asia. It is widely cultivated and naturalized elsewhere. Countries it is indigenous to include Afghanistan, Bangladesh, Bhutan, Cambodia, China, India, Indonesia, Japan, Kenya, Madagascar, Malaysia, Mozambique, Myanmar, Nepal, Pakistan, the Philippines, Sri Lanka, Taiwan, Tanzania, Thailand, and Vietnam. *Vitex negundo* are commonly found near bodies of water, recently disturbed land, grasslands, and mixed open forests.

**Chemical constituents:** Hentriacontane, sterols, β-sitosterol, β-sitosterol acetate, stigmasterol, ascorbic acid, p-hydroxybenzoic acid, carotene and amino acids have also been isolated from this plant. Leaves contain a pale greenish yellow essential oil, an alkaloid, nishindine and a glucoside. Stem bark contains flavonoid glycosides of wogonin, aurosin, vitexin, myricetin, also luteolin, leucodelphinidin, luecocyanidin rhammoside, β-sitosterol, vanillic acid and p-hydroxybenzoic acid.

**Medicinal uses:** Leaves are tonic, vermifuge, antiparasitic, alterative and anodyne; relieve catarrh and headache and effective against inflammatory swellings of the joints due to acute rheumatism. Leaf Juice removes foetid discharges and worms from ulcers. A decoction of the leaves along with long pepper is given in catarrhal fever with heaviness of head and dullness of hearing. Leaf juice mixed with oil is applied to sinuses and scrofulous sores. A vapour bath prepared from the leaves is used for treating febrile, catarrhal and rheumatic affections. Leaves are used for diarrhoea in Rema-Kalenga.
Leaf-boil water is used for bath to relieve post-partum pains in Jointiapur of Sylhet. Leaves are used for asthma and hair growth in Khagrachari. Roots are tonic, febrifuge, expectorant and diuretic. Fruits are nerveive, cephalic and emmenagogue; dried fruit acts as a vermifuge. Flowers are astringent and cooling. Chloroform extract of the leaf possesses strong antibacterial properties against wide range of human pathogenic bacteria.

**Earlier work done on this Plant:**

1) This study confirmed the oral anti-inflammatory, analgesic and antihistamine properties of mature fresh leaves (MFL) of *Vitex negundo* L. (Verbenaceae) claimed in the Ayurveda medicine by orally treating a water extract of the leaves to rats. The early phase (2 h) of carrageenan-induced rat paw oedema was significantly (*P*<0.01) suppressed in an inversely dose-dependent (*r*²=1, *P*<0.01) manner by MFL. The observations revealed that the fresh leaves of *Vitex negundo* have anti-inflammatory and pain suppressing activities possibly mediated via PG synthesis inhibition, antihistamine, membrane stabilising and antioxidant activities. The antihistamine activity can produce the anti-itching effect claimed in Ayurveda medicine.

2) Maximal electroshock seizures (MES) in albino rats and pentylenetetrazole (PTZ) induced seizures in albino mice were used to study anticonvulsant activity of *Vitex negundo* leaf extract. The ethanolic leaf extract of *Vitex negundo* was administered orally in graded doses (250, 500 and 1000 mg/kg p.o) in both the experimental models and the effects were compared with diphenylhydantoin in MES method and valporic acid in PTZ induced seizures method as standard control respectively.
7. *Picrasma quassioides*

**Plate2.1.4.7- Picrasmaquassioides**

Botanical name : *Picrasma quassioides*

Family : Simaroubaceae

**Vernacular names**

English : Quassia, Quassia Wood, macary bitter
Hindi : *Karui, Baringi, Bharangi, Charangi, Kashshing,*
Sanskrit : *Bhargangi, Bharangi, Vicharniya, Asranasini*
Urdu : *Karwiya*

**Geographical distribution:** native to temperate regions of southern Asia, from the northeast of Pakistan east along the Himalaya and through southern, central and eastern China to Taiwan and Japan.

**Chemical constituents:** simaroubolides, picrasin A, B, C, D, E, F and G

**Medicinal uses:** The bark is used in herbal medicine as a bitter flavouring and antibacterial agent. Extracts from the wood are also used as a natural insecticide in organic farming.
Earlier work done on this Plant:

1) A new alkaloid, 4,5-dimethoxy-10-hydroxycanthin-6-one (1), was isolated from the stem of Picrasma quassioides Bennet (Simaroubaceae) together with four known canthin-6-one alkaloids, 8-hydroxycanthin-6-one (2), 4,5-dimethoxycanthin-6-one (3), 5-hydroxy-4-methoxycanthin-6-one (4), and 3-methylcanthin-5,6-dione (5). Their structures were elucidated on the basis of spectroscopic data.

2) Investigations of Picrasma quassioides BENNET, four new bis-β-carboline alkaloids, quassidines E-H (1-4), and three new β-carboline alkaloids, canthin-16-one-14-butyric acid (5), 3-(1,1-dimethoxylmethyl)-β-carboline (6), and 6,12-dimethoxy-3-formyl-β-carboline (7), were isolated from its anti-inflammatory CHCl(3)-soluble fraction. Structures of new compounds were elucidated and characterized by MS and NMR analysis. A plausible biogenetic pathway for quassidine E (1), the first bis-β-carboline alkaloid in which a canthin-6-one moiety and a β-carboline moiety were connected together by a single carbon-carbon bond from the nature, was proposed.

8. Solanum xanthocarpum

Plate 2.1.4.8 - Solanum xanthocarpum

Botanical Name: Solanum xanthocarpum
Family: Solanaceae
**Vernacular names**

English : Yellow-berried Nightshade  
Hindi : Kateli  
Sanskrit : Kantakari  
Kannada : Nelagulla

**Geographical distribution:**

**Chemical constituents:** Solasodine is the main constituent isolated from the berries of the plant, together with solanine in the unripe fruits and solacarpidin.

**Medicinal uses:**

**Allergic Rhinitis:** Roots and seeds are used as an expectorant in asthma, Bronchitis, cough and pain in chest. Kantakari is beneficial in curing catarrh and phlegm from the bronchial tube.

**In Skin diseases:** The herb is beneficial in the treatment of cardiac diseases associated with edema, since it is a stimulant to the heart and act as a blood purifier. The shoots and fruits of Kantakari possess antibacterial activity.

**Paralysis:** The plant is used in treating paralysis, and all type of nervous disorders.

**Muscular pain:** Its seeds are analgesic in property. The herb is made to a paste and applied on swollen and painful joints to reduce the pain and swelling in arthritis.

**Asthmatic cough:** It is bitter, pungent, hot, digestant, carminative, diuretic, expectorant and used in cough, asthma, dyspnoea, fever, pleurisy, heart diseases, hoarseness of voice, calculus. Kantkari is useful in treating worms, cold, hoarseness

**Fatigue, General Weakness:** Kantakari used in the general low vitality (energy) of the system. In women for irregular menstruation and dysmenorrhreal. The white flowered variety of kantakari (Laksmana) helps to
promote conception in females. As the herb is a stimulant to the heart and is a blood purifier.

**Earlier work done on this Plant:**

**1) Nonsteroidal and steroidal drugs are generally used as a part of drug therapy in inflammation. However, these drugs have severe side-effects like nausea and vomiting. Therefore, there is a need to identify anti-inflammatory compounds that will be effective with a better safety profile.** *Solanum xanthocarpum* Schrad and Wendl and *Cassia fistula* Linn has many therapeutic uses mentioned in Ayurveda and therefore we aimed to study its anti-inflammatory activity both alone and in combination.

**2) Aqueous extract of the fruits of *Solanum xanthocarpum* Schrad. & Wendl. (Solanaceae) was investigated for hypoglycaemic activity in rats and mice. Screening for the hypoglycaemic activity was assessed on normoglycaemic, alloxan treated hyperglycaemic and glucose loaded rats along with in vitro study on glucose utilization by isolated rat hemidiaphragm. The toxicity studies report safety usage of the plant extract.**

**3) Chronic administration of solasodine (20 mg/kg alt. day for 30 days) caused testicular lesions resulting in a severe impairment of spermatogenic elements. Cholesterol and phospholipid levels were elevated after solasodine treatment to intact dogs. Simultaneous administration of TP to solasodine treated castrated dogs failed to stimulate the epididymal growth. Antispermatogenic/antiandrogenic activity of the compound solasodine is discussed. Solasodine administration in dogs definitely rendered the male infertile as evidenced by the absence of sperms in the cauda epididymis and ductus deferens.

**4) The combination activities of temephos, fenthion and petroleum ether extract of *Solanum xanthocarpum* were observed for their larvicidal activities against *Culex quinquefasciatus*. The combination of**
temephos and S. xanthocarpum was studied at ratios of 1:1, 1:2, and 1:4. Similar ratios were also used for the combination of fenthion and S. xanthocarpum.

9. **Pueraria tuberosa**

**Plate 2.1.4.9 - Pueraria tuberosa**

Botanical Name: *Pueraria tuberosa*

Family: Fabaceae

**Vernacular names**

Common name: Indian kudzu

Hindi: Sural, Bilaikand, Bharda, Tirra, Bankumra

Sanskrit: Bhukushmandi

Gujarati: Vidarikand

Telugu: Nela Gummadi, Dari Gummadi, Vidari Kanda.

Kannada: Gumadigida

Malayalam: Mutukku

Nepali: Baraali kund

**Geographical distribution**

It is native to India, Pakistan, and Nepal. Indian Kudzu is found in the Himalayas, from Kashmir to Nepal, at altitudes of 300-1500 m. It is also
found in Western Ghats and some other parts of India. Flowering: March-April

**Chemical constituents:** Isoflavonoids, pterocarpene, puminicarpene, flavones.

**Medicinal uses:** In Ayurveda, this herb is used as a general tonic, for headaches, and as an aphrodisiac. The roots are said to be used in medicine as a demulcent and refrigerent in fevers, as cataplasm for swelling of joints, and as lactagogue. It is also emetic, galactogogue and tonic. Now a days it is used in preparing sexual potency enhancement pills.

**Earlier work done on this Plant**

1) Antioxidant activity of *Pueraria tuberose* DC, (PT) *Leguminosae (Fabaceae)* has already been reported by us and here an active compound has been isolated and its action on expression of iNOS protein has been explored by using LPS induced changes in attached rat peritoneal macrophage cell culture\(^56\).

2) *In vitro* antimicrobial and chemical properties of petroleum ether, ethyl acetate and ethanol extracts of *Pueraria tuberosa* were evaluated. Among the test samples ethyl acetate extract showed pronounced antimicrobial activity, while ethanol extract exhibited the least activity and petroleum ether extract failed to inhibit the test pathogens\(^57\). Preliminary phytochemical analysis of extracts revealed the presence of antimicrobial compounds such as alkaloids, flavonoids, coumarins, volatile oils and glycosides.
2.2 LIVER DISEASES

2.2.1 Pathophysiology of Liver diseases

The liver is the vital largest glandular organ of the body. The liver is necessary for survival; there is currently no way to compensate for the absence of liver function long term, although liver dialysis can be used short term. It weighs about 3 lb (1.36 kg). It is reddish brown in color and is divided into four lobes of unequal size and shape. It is located in the right upper quadrant of the abdominal cavity, resting just below the diaphragm.

Diseases of the Liver

Several diseased states can affect the liver. Some of the diseases are:

- Wilson’s disease
- Hepatitis (inflammation of liver)
- Liver cancer and
- Cirrhosis (a chronic inflammation that progresses ultimately to organ failure).

Alcohol alters the metabolism of the liver, if taken over long periods of time. Hemochromatosis can cause liver problems.\(^{58}\)

Table 2.2.1. Disease and signs of Liver diseases

The classic signs of liver damage include the following.\(^{59}\)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Disease sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stercobilin, a brown pigment, is absent in the stool.</td>
<td>Pale stool</td>
</tr>
<tr>
<td>Bilirubin mixes with urine</td>
<td>Dark urine</td>
</tr>
<tr>
<td>Bilirubin deposits under skin</td>
<td>Itching</td>
</tr>
<tr>
<td>Liver fails to make Albumin</td>
<td>Swelling of abdomen, ankles and feet</td>
</tr>
<tr>
<td>Loss of nutrients, minerals nad vitamins</td>
<td>Excessive fatigue</td>
</tr>
<tr>
<td>Liver fails to produce clotting agents</td>
<td>Bruising and easy bleeding</td>
</tr>
</tbody>
</table>
**Hepatotoxicity**

Hepatotoxicity is hepatic toxicity which is caused by some chemicals leading to liver damage. The liver plays a central role in transforming and clearing chemicals and is susceptible to the toxicity from these agents. Certain medical agents, when taken in over doses and sometimes even when introduced within therapeutic ranges, may injure the organ.

![Figure 2.2.1 - Hepatic liver](image)

**Epidemiology**

In the United States, approximately 2000 cases of acute liver failure occur annually and drugs account for over 50% of the (39% are due to Acetaminophen, 13% of Idiosyncratic reactions due to other medications). Drugs account for 2 – 5% of cases of patients hospitalized with jaundice and approximately 10% of all cases of acute hepatitis.

The prognosis is highly variable depending on the patient’s presentation and stage of liver damage. In a prospective study conducted in the United States from 1998 – 2001, the overall survival rate of patients (including those who received a liver transplant) was 72%. The outcome of acute liver failure is determined by etiology, the degree of hepatic encephalopathy present upon admission and complications such as infections.
Etiology

There is a great diversity of individual P 450 gene products which allows liver to perform oxidation on vast array of chemicals in Phase 1 reactions. Genetic variations (polymorphism) in CYP450 metabolism should be considered when patients exhibit unusual sensitivity or resistance to drug effects at normal doses.

- Change in enzyme activity
- Congenital birth defects or abnormalities of the liver present at birth.
- Metabolic disorders or defects in basic body processes.
- Viral or bacterial infections.
- Alcohol or poisoning by toxins.
- Certain medications that is toxic to liver.
- Nutritional deficiencies.
- Trauma or injury.

Symptoms of hepatotoxicity

- Nausea
- Vomiting
- Abdominal pain in upper right part of stomach
- Loss of appetite
- Unusual weight gain or loss
- Diarrhoea
- Feeling tired or weak
- Jaundice (yellowing of the skin and eyes)
- Darkened urine
- Hepatomegaly (liver enlargement)
- Varicose veins (enlarged blood vessels)

Mechanism of liver damage

Drugs continue to be taken off the market due to late discovery of hepatotoxicity. Due to its unique metabolism and close relationship with the gastrointestinal tract, the liver is susceptible to injury from drugs and other
substances. 75% of blood coming to the liver arrives directly from gastrointestinal organs and then spleen via portal veins which bring drugs and xenobiotics in concentrated form. Several mechanisms are responsible for either inducing hepatic injury or worsening the damage process. Many chemicals damage mitochondria, an intracellular organelle that produces energy. Its dysfunction releases excessive amount of oxidants which in turn injure hepatic cells. Activation of some enzymes in the cytochrome P – 450 systems such as CYP2E1 also leads to oxidative stress. Injury to hepatocytes and bile duct cells lead to accumulation of bile acid inside liver. This promotes further liver damage of non–parenchymal cells such as Kupffer cells, fat storing stellate cells and leukocytes (i.e. neutrophil and monocyte) also have role in the mechanism.

Agents that cause liver damage

- Carbon tetrachloride
- D–Galactosamine
- Thioacetamide
- Paracetamol and
- Antitubercular drugs (INH, Rifampicin, Pyrazinamide)

D – Galactosamine induced hepatotoxicity

Galactosamine produces diffuse type of liver injury simulating viral hepatitis. It presumably disrupts the synthesis of essential uridylate nucleotides resulting in organelle injury and ultimately cell death. Depletion of those nucleotides would impede to the normal synthesis of RNA and consequently would produce a decline in protein synthesis. This mechanism of toxicity brings about an increase in cell membrane permeability leading to enzyme leakage and eventually cell death. The Cholestasis caused by D – Galactosamine may be from its damaging effects on bile ducts or ductules or canalicular membrane of hepatocytes. Galactosamine reduces the bile flow and its content that is bile salts, cholic acid and deoxycholic acid. Galactosamine reduces the number of viable hepatocytes as well as rate of oxygen consumption. Dose of D – Galactosamine is 400 mg/kg, i.p.63
Hepatitis

Hepatitis (plural hepatitides) is a medical condition defined by the inflammation of the liver and characterized by the presence of inflammatory cells in the tissue of the organ. The condition can be self-limiting (healing on its own) or can progress to fibrosis (scarring) and cirrhosis.

Hepatitis may occur with limited or no symptoms, but often leads to jaundice, anorexia (poor appetite) and malaise. Hepatitis is acute when it lasts less than six months and chronic when it persists longer. A group of viruses known as the hepatitis viruses cause most cases of hepatitis worldwide, but it can also be due to toxins (notably alcohol, certain medications, some industrial organic solvents and plants), other infections and autoimmune diseases.

Viral hepatitis

It is liver inflammation due to a viral infection. It may present in acute (recent infection, relatively rapid onset) or chronic forms. The most common causes of viral hepatitis are the five unrelated hepatotropic viruses Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E. In addition to the hepatitis viruses, other viruses that can also cause hepatitis include Herpes simplex, Cytomegalovirus, Epstein-Barr virus, or Yellow fever.

A virus previously called Hepatitis G virus is now classified as GB virus C because it does not appear to cause hepatitis.

![Hepatitis B infected hepatocytes](image)

**Figure 2.2.2 - Hepatitis B infected hepatocytes**
Acute Hepatitis

Initial features are of nonspecific flu-like symptoms, common to almost all acute viral infections and may include malaise, muscle and joint aches, fever, nausea or vomiting, diarrhea, and headache.

More specific symptoms, which can be present in acute hepatitis from any cause, are: profound loss of appetite, aversion to smoking among smokers, dark urine, yellowing of the eyes and skin (i.e., Jaundice) abdominal discomfort. Physical findings are usually minimal, apart from jaundice in a third and tender Hepatomegaly (swelling of the liver) in about 10%. Some exhibit lymphadenopathy (enlarged lymph nodes, in 5%) or splenomegaly (enlargement of the spleen, in 5%).

Acute viral hepatitis is more likely to be asymptomatic in younger people. Symptomatic individuals may present after convalescent stage of 7 to 10 days, with the total illness lasting 2 to 6 weeks. A small proportion of people with acute hepatitis progress to acute liver failure, in which the liver is unable to clear harmful substances from the circulation (leading to confusion and coma due to hepatic encephalopathy) and produce blood proteins (leading to peripheral edema and bleeding). This may become life-threatening and occasionally requires a liver transplant.

Chronic Hepatitis

Chronic hepatitis often leads to nonspecific symptoms such as malaise, tiredness and weakness, and often leads to no symptoms at all. It is commonly identified on blood tests performed either for screening or to evaluate nonspecific symptoms. The occurrence of jaundice indicates advanced liver damage. On physical examination there may be enlargement of the liver.

Extensive damage and scarring of liver (i.e. cirrhosis) leads to weight loss, easy bruising and bleeding tendencies, peripheral edema (swelling of the legs) and accumulation of Ascites (fluid in the abdominal cavity).
Eventually, cirrhosis may lead to various complications: esophageal varices (enlarged veins in the wall of the esophagus that can cause life-threatening bleeding) hepatic encephalopathy (confusion and coma) and hepatorenal syndrome (kidney dysfunction). Acne, abnormal menstruation, lung scarring, inflammation of the thyroid gland and kidneys may be present in women with autoimmune hepatitis.

**Risk factors for liver injury**

- Race
- Age
- Sex
- Alcohol ingestion
- Liver disease
- Patients with HIV infection who are co-infected with hepatitis B or C virus are at increased risk
- Patients with Cirrhosis are at increased risk by toxic drugs
- Genetic factors
- Long – acting drugs may cause more injury than shorter – acting drugs.
- Pregnancy

**Pathophysiology of liver injury**

- Disruption of the hepatocytes.
- Disruption of the transport proteins.

- **Cytolytic T – cell activation:** Covalent binding of a toxic agent to the P – 450 enzyme acts as an immunogen, activating T cells and cytokines and stimulating a multifaceted immune response

- **Apoptosis of hepatocytes:** Activation of the apoptotic pathways by the tumor necrosis factor – alpha receptor of Fas may trigger the cascade of intercellular caspases, which results in programmed cell death.
• **Mitochondrial disruption**: Certain drugs inhibit mitochondrial function by a dual effect on both beta – oxidation energy production by inhibiting the synthesis of Nicotinamide adenine dinucleotide and flavin adenine dinucleotide, resulting in decreased ATP production.

• **Bile duct injury**: Toxic metabolites excreted in bile may cause injury to the bile duct epithelium.

**Diagnosis**

- The diagnosis of liver function is made by blood tests. If infection is suspected, then other serological tests are done.
- A complete blood count (CBC)
- Abdominal X - rays
- Ultrasound
- ERCP or Endoplastic Retrograde Cholangio Pancreatography
- Abdominal CT scan or Abdominal MRI

**2.2.2 Drug treatment for Liver diseases**

Drugs which are used in the treatment of Liver diseases are known as Hepatoprotective agents. Hepatoprotective agents are those compounds, which mitigate the liver injury caused by hepatotoxic agents. Hepatoprotective effects of plant drugs and herbal formulations are studied against chemicals (alcohol, CCl₄, D-Galactosamine Thioacetamide) and drugs (Paracetamol, Nimesulide, Antitubercular drugs like Isoniazid, Rifampicin etc.) that induce hepatotoxicity in rats and mice as they virtually mimic any form of naturally occurring liver diseases.

Silymarin is the standard drug for hepatoprotection which shows action by different ways.
**Table 2.2.2 - Hepatic function tests**

<table>
<thead>
<tr>
<th>Agents</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (total)</td>
<td>Jaundice</td>
</tr>
<tr>
<td>Bilirubin (unconjugated)</td>
<td>Hemolysis</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>Cholestasis and infiltrative disease</td>
</tr>
<tr>
<td>AST</td>
<td>Hepatocellular disease and progression of disease</td>
</tr>
<tr>
<td>ALT</td>
<td>ALT relatively lower than AST in persons with alcoholism</td>
</tr>
<tr>
<td>Albumin</td>
<td>Severity of liver injury (HIV infection and malnutrition)</td>
</tr>
<tr>
<td>Gamma globulin</td>
<td>Autoimmune hepatitis, Cirrhosis</td>
</tr>
<tr>
<td>Prothrombin time after vitamin K</td>
<td>Severity of liver disease</td>
</tr>
<tr>
<td>Antimitochondrial antibody</td>
<td>Primary of liver disease</td>
</tr>
<tr>
<td>ASMA</td>
<td>Primary Sclerosing cholangitis</td>
</tr>
</tbody>
</table>

**Figure 2.2.3 - Mechanism of Silymarin**

Many of the conventional drugs have the potential to cause hepatic damage, in such circumstances herbal medicine provide better therapy than conventional medicine when it comes to the adverse drug reactions which are caused by conventional medicine.
### 2.2.3 Plants showing Hepatoprotective activity

**Table 2.2.3 Plants showing Hepatoprotective activity**

<table>
<thead>
<tr>
<th>S.No</th>
<th>PLANT NAME</th>
<th>CHEMICAL CONSTITUENTS</th>
<th>OTHER USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Andrographis panuiculata</em></td>
<td>Lactones-diterpene lactone andrographolide(0.5%-0.9%),andrograpanin,deoxyoxoandrographolide;glycosides,neoandrographolide and andrographiside and flavonols,oroxyl,flavonins,andrographidine s A,B,C,D,E,F</td>
<td>Antiallergic,Immunpmodulatory, hepatoprotective,antipyretic,antithrombotic,anticholestatic,antidote for snake bite</td>
</tr>
<tr>
<td>2</td>
<td><em>Boerhavia diffusa</em></td>
<td>Punarnavoside,antifibrolytic glycoside,0.03-0.05%,retinoids viz.,boeravine and hypoxantine-9-L-arabinofuranoside</td>
<td>Antifibrinolytic and anti-inflammatory,hepatoprotective,diuretic, cardiotonic,antiviral,anticholinesterase and anticonvulsant</td>
</tr>
<tr>
<td>3</td>
<td><em>Crataeva nualia</em></td>
<td>Bioactive triterpenoids-lupeol,about 0.6%,alkaloids viz.,cadabacine,cadabacine diacetate; tannins viz.,(−)-catechin,(−)-epicatechin-5-glucoside and (−)-epifzelechin</td>
<td>Anticomplement,hepatoprotective,antibacterial,antiurolithiatic</td>
</tr>
<tr>
<td></td>
<td><strong>Eclipta prostrata</strong></td>
<td>Coumestan derivatives, wedelolactone and demethylwedelolactone, thiophene derivatives - ecliptal, saponins viz., ecalbosaponins I-IV; common sterols</td>
<td>Hepatoprotective, antinociceptive, antiinflammatory, bronchodilator, antibacterial, antiviral</td>
</tr>
<tr>
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<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td><strong>Emblica officinalis</strong></td>
<td>Vitamin-C(=L-(+)-threo-ascorbic acid, ~2%); tannins (~5%) viz., gallic acid, ellagic acid, phyllembic acid and emblicol, alkaloids viz., phyllantidine and phyllantine; pectin and minerals.</td>
<td>Hepatoprotective, antioxidant, antimutagenic, cytoprotective, antitumour, antifungal, antimicrobial</td>
</tr>
<tr>
<td></td>
<td><strong>Nardostachys jatamansi</strong></td>
<td>Essential oil valeranone (jatamansone), a sesquiterpinenoid, 0.02-0.1% viz., spirojatamol, patchouli alcohol, norseychelanone and α,β patchoulenes, jatamol A&amp;B, jatamansic acid, virolin etc.</td>
<td>Hepatoprotective, sedative, antimicrobial activity, analgesic activity</td>
</tr>
<tr>
<td></td>
<td><strong>Phyllanthus amarus</strong></td>
<td>Lignans - a diarylbuto, phyllanthin, aryltetrahydrocarbonaphthalene, hypophyllanthin, hydrolysable tannins, alkaloids.</td>
<td>Diuretic, antibacterial, antifungal, hepatoprotective, antidiarrhoeal, antimutagenic, anticarcinogenic, contraceptive &amp; antiviral</td>
</tr>
<tr>
<td></td>
<td><strong>Picrorhiza kurroa</strong></td>
<td>Iridoid glycosides, picroside I, kutkoside, picroside III, veronicoside, minecoside; phenol glycosides viz., picein, androsin and 4-hydroxy-3-methoxyacetophenone.</td>
<td>Antidiabetic, antiulcer, antioxidant, iron chelating, hepatoprotective, cardioprotective, antiasthmatic, anticholestatic, antihealing, antiradicals, antileishmaniasis, bittertonic.</td>
</tr>
<tr>
<td></td>
<td><strong>Species</strong></td>
<td><strong>Compounds</strong></td>
<td><strong>Activities</strong></td>
</tr>
<tr>
<td>---</td>
<td>-------------</td>
<td>---------------</td>
<td>---------------</td>
</tr>
<tr>
<td>9</td>
<td><em>Piper longum</em></td>
<td>Piperine, volatile oil, piperlongumunine, pipilartine, waxy alkaloid N-isobutyldecatrans-2-trans-4-dienamide, piperidine alkaloids- pipernonaline, pipernundecalidine, sesamin, lignin derivative, terpenoids, resin, dihydrostigmasterol.</td>
<td>Antiallergic, antiasthmatic, hepatoprotective, antifertility, antiamoebic, cholagogue, emmenagogue, abortifacient, anthelmintic, carminative.</td>
</tr>
<tr>
<td>10</td>
<td><em>Ricinus communis</em></td>
<td>Lipids-fixed oil, triricinolein, common fatty acids with carbon numbers from C14 to C20, ricinine, N-demethylricinine, 3-O-β-D-glucopyranosides and 3-O-β-D-rutinosides of kaempferol and quercetin.</td>
<td>Purgative, hepatoprotective</td>
</tr>
<tr>
<td>12</td>
<td><em>Swertia Chirata</em></td>
<td>Amarogentin, amaroswerin, xanthone derivatives viz, chiratol, methyl belliifolin, decussatin, mangiferin, swertianin, swertinin, chiratanin, triterpinoids viz., masilinic acid, chiratenol, swertenol, episwertenol, secoiridoid glycosides</td>
<td>Anti-inflammatory, Anti-hepatotoxic, Anti-ulcerogenic, Anti-cholinergic, CNS depressant, Anti-malarial, Hypoglycemic, Bitter tonic and febrifuge.</td>
</tr>
<tr>
<td>No.</td>
<td>Species</td>
<td>Chemical Components</td>
<td>Properties</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>13</td>
<td><em>Terminalia Belerica</em></td>
<td>Tannins, gallic acid, ellagic acid, ethyl galate, galloyl glucose and chebulagic acid, phyllemblin, β-sitosterol, mannitol, glucose, fructose, rhamnose.</td>
<td>Hepatoprotective, Hypolipidemic, Purgative, Astringent, Expectorant, Laxative, Bile stimulant activity.</td>
</tr>
<tr>
<td>14</td>
<td><em>Terminalia Chebula</em></td>
<td>Tannins, anthraquinones, chebulinic acid, chebulagic acid, ellagic acid, gallic acid, β-D-glucogallin, glucose, sorbitol, polyphenolic compounds, triterpene glycosides, terflavin A, flavonoids, reducing sugars and starch.</td>
<td>Laxative, Hypolipidemic, Antioxidant, Hepatoprotective, Adaptogenic, Cardiac Activities, Anti viral, Anti-bacterial, Astringent.</td>
</tr>
<tr>
<td>15</td>
<td><em>Acorus calamus</em></td>
<td>Main chemical components are acorenone, b-gurjunene, isoshyobunine, b-asarone, calamendiol, a-selinene, a-calacorene, calamusenone, camphone and shyobunone.</td>
<td>Thermogenic, laxative, carminative, stomachic, antihelminthic, diuretic, expectorant, antispasmodic, hepatodynia, antipyretic, antiinflammatory, anticonvulsion, nephropathy.</td>
</tr>
<tr>
<td>16</td>
<td><em>Allium sativum</em></td>
<td>Volatile oil (0.1-0.4%) containing sulfur compounds: including allicin, diallyl disulfide, diallyl trisulfide, ajoene and others. • Other sulfur compounds: including allyl cysteine sulfoxide, methyl allyl thiosulfinate</td>
<td>Haemorrhoids, sciatica, otalgia, lumbago, swellings, splenopathy, hepatopathy, pneumonia, monopathy, arthralgia, dental caries.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>
|   | **Aloe barbadensis** | and related compounds.  
• Trace minerals: especially selenium, geranium  
• Enzymes: including alliinase, myrosinase, peroxidase.  
<p>| 17 |   |   |   |
| 18 | <strong>Asparagus racemosus</strong> | The main chemical components of dill oil are d-carvone, dillapiol, dhc, eugenol, limonene, terpinene and myristicin. | Digestive, carminative, stomachic, antihelminthic, anodyne, anti-inflammatory, diuretic, expectorant, cardiotonic, amenorrhoea, hiccoughs, asthma, bronchitis |
| 19 | <strong>Anethem graveolens</strong> | Edible oils, proteins, carbohydrates, calcium, iron, potassium, phosphorus, ascorbic acid, tartaric acid, oxalic acid, alpha-keto glutaric acid and | Antipruritic, antipyretic, antihelminthic, intermittent fevers, intestinal worms, various types of poisoning, pruritus, constipating and |
| 20 | <strong>Averrhoa carambola</strong> |   |   |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td><em>Azadirachta indica</em></td>
<td>Azadirachtin, Azadirachtin, salannin, gedunin, azadione, nimbin, nimbidine, nimbicide, nimbinol.</td>
<td>Anti-inflammatory, antiarthritic, antipyretic, hypoglycaemic, Antifungal, spermicidal, antimalarial, antibacterial, Diuretic, antipyretic, intestinal disorders, skin diseases, wounds, obesity &amp; arthritis.</td>
</tr>
<tr>
<td>22</td>
<td><em>Butea monosperma</em></td>
<td>The main constituent of the flower is butrin (1.5%) besides butein (0.37%) and butin (0.04%). Also contains flavonoids and steroids, coreopsin, isocoreopsin, sulphurein (glycoside) and other two with monospermoside and isomonospermoside.</td>
<td>Astringent, emollient, aphrodisiac, diarrhoea, dysentery, anorexia, bone fractures, gonorrhea, ulcers, astringent, antiinflammatory.</td>
</tr>
<tr>
<td>23</td>
<td><em>Caesalpinia bonduc</em></td>
<td>They yield bergenin (vakerin). A novel spermidine alkaloid, caesalpinine A (C25H31O3N3) has also been isolated.</td>
<td>Expectorant, antihelminthic, stomachic, amenorrhoea, fevers, elephantiasis, splenomegaly, hepatomegaly, anti-inflammatory, digestive, contraceptive, antipyretic.</td>
</tr>
<tr>
<td>24</td>
<td><em>Curcuma longa</em></td>
<td>Curcuminoinds, essential oil with high content of bisabolane derivatives, desmethoxycurcumin, bisdesmethoxycurcumin, dihydrocurcumin; common phytosterols, fatty acids &amp; polysaccharides viz., ukonan A, B, C, &amp; D</td>
<td>Thermogenic, emollient, anodyne, hepato megaly, splenomegaly, fever, giddiness, elephantiasis, dropsy, hysteria, fever, epilepsy, chronic otorrhoea, gonorrhea, amenorrhoea, jaundice, conjunctivitis &amp; diabetes.</td>
</tr>
<tr>
<td>25</td>
<td><strong>Cichorium intybus</strong></td>
<td>The active compounds in chicory are inulin, sesquiterpene lactones, vitamins, minerals, fat, mannitol and latex. Fructans have been extracted from chicory roots. Alpha-amyrin, taraxerone, baurenyl acetate and beta-sitosterol. Twelve compounds were isolated from the root of <strong>Cichorium intybus</strong> including 2, 3, 4, 9-tetrahydro-1H-pyrido-(3,4-b)indole-3-carboxylic acid.</td>
<td>Anti-inflammatory, appetiser, digestive, stomachic, liver tonic, cardiotonic, hepatomegaly, insomnia, jaundice, splenomegaly</td>
</tr>
</tbody>
</table>
2.2.4 Description of Plants selected for Hepatoprotective activity

1. *Achillea millefolium*

   **Plate 2.2.4.1 - Achillea millefolium**

   ![Achillea millefolium](image)

**Plant Profile**

Botanical name: *Achillea millefolium*

Family: Asteraceae

**Vernacular names**

- **English**: Yarrow, gordaldo, nosebleed plant, old man's pepper, devil's nettle, sanguinary, milfoil, soldier's woundwort, thousand-leaf
- **Hindi**: Gandrain, Puthkanda, Bhut Kesi
- **Marathi**: Rojmaari
- **Tamil**: Achchilliya
- **Urdu**: Tukhm gandana, Buiranjasif, Brinjasuf
- **Konkani**: Rajmar

**Geographical distribution**: Native to the Northern Hemisphere. In New Mexico and southern Colorado

**Chemical constituents**: Ketones, essential oils, *chemical components* of yarrow oil are tricyclene, a-pinene, camphene, b-pinene, sabinene, borneol acetate, alkaloids.

**Medicinal uses**: Use in staunching the flow of blood from wounds, the herb is purported to be a diaphoretic, astringent, tonic, stimulant and mild aromatic. It
contains isovaleric acid, salicylic acid, asparagin, sterols, flavonoids, bitters, tannins, and coumarins. The plant also has a long history as a powerful 'healing herb' used topically for wounds, cuts and abrasions.

**Earlier work done on this Plant:**

1) Isolation and biological characterization of pure compounds was used to identify and characterize estrogenic activity and estrogen receptors (ER) preference in chemical components of Achillea millefolium. This medicinal plant is used in folk medicine as an emmenagogue. In vitro assay, based on recombinant MCF-7 cells, showed estrogenic activity in a crude extract of the aerial parts of A. millefolium.

2) An ethanol extract of Achillea millefolium L. showed repelling properties against the mosquito, Aedes aegypti L. Prepared fractions from the extract contained several active compounds which were characterized by thin layer chromatography, high performance liquid chromatography, gas chromatography and mass spectroscopy. Of 35 compounds tested, the most active were the nitrogen containing compound stachydrine, the carboxylic acids, caffeic, chlorogenic, and salicylic acids, and the phenolic compound pyrocatechol.

3) The in vitro antimicrobial and antioxidant activities of the essential oil and methanol extracts of Achillea millefolium subsp. millefolium Afan. (Asteraceae) were investigated. GC-MS analysis of the essential oil resulted in the identification of 36 compounds constituting 90.8% of the total oil. The oil showed antimicrobial activity against *Streptococcus pneumoniae, Clostridium perfringens, Candida albicans, Mycobacterium smegmatis, Acinetobacter lwoffi* and *Candida krusei* while water-insoluble parts of the methanolic extracts exhibited slight or no activity.

4) Potential anxiolytic-like effect of hydroalcoholic extract of Achillea millefolium L. was evaluated the in animal models the effects of the hydroalcoholic extract from the aerial parts of Achillea millefolium L. in mice.
subjected to the elevated plus-maze, marble-burying, and open-field tests\textsuperscript{71}. Additionally, the GABA(A)/benzodiazepine (BDZ) mediation of the effects of Achillea millefolium was evaluated by pretreatment with the noncompetitive GABA(A) receptor antagonist picROTOXIN and the BDZ antagonist flumazenil and by [(3)H]-flunitrazepam binding to the BDZ site on the GABA(A) receptor. Achillea millefolium exerted anxiolytic-like effects in the elevated plus-maze and marble-burying test after acute and chronic (25 days) administration at doses that did not alter locomotor activity.

5) Functional dyspepsia (FD) is a highly prevalent Background gastrointestinal disorder characterized by alterations in gastric motility. Yarrow (Achillea millefolium L., Fam Asteraceae) preparations are traditional remedies used to treat dyspeptic complaints. Herein, we investigated the effect of a standardized dry water extract obtained from A. millefolium flowering tops (AME) on gastric motility\textsuperscript{72}. Methods The effect of AME on motility was evaluated on the resting tone of the isolated gastric antrum and on gastric emptying in vivo (phenol red meal method) both in control mice and in the model of cancer chemotherapy

2. Ficus bengalensis

Plate 2.2.4.2 - Ficus bengalensis

Botanical Name: *Ficus bengalensis*

Family: Moraceae
Geographical distribution: A remarkable tree of India and tropical Africa.

Chemical constituents: Ketones, The stem bark contains β-sitosterol, α-D-glucose and meso-inositol. The leaves contain petunidin di-glycoside.

Medicinal uses: Therapeutically valuable tree is attributed with tonic, astringent, cooling and diuretic properties in Ayurveda.

Earlier work done on this Plant:

1) The stem bark and fruits of Ficus bengalensis L. and Ficus racemosa L. are used in India for the treatment of diabetes and a number of other diseases. Since these effects may be correlated with the presence of antioxidant compounds, methanol and 70% acetone (acetone:water, 70:30) extracts of F. bengalensis (aerial root) and F. racemosa (stem bark) were evaluated for their antioxidant activity and radical scavenging capacity in comparison with Camellia sinensis (L.) O. Kuntz (green tea)\textsuperscript{73}. Methanol extracts of green tea and F. bengalensis and 70% acetone extract of F. racemosa contained relatively higher levels of total phenolics than the other extracts.

2) The extract of jaman pulp from fruit of Eugenia jambolana showed hypoglycemic activity. The effect of pulp was seen in 30 min, while the seeds of the same fruit required 24 hr\textsuperscript{74}. The extracts of bark of Ficus bengalensis...
caused reduction in blood sugar level. These results were confirmed in streptozotocin-induced diabetic animals.

3) The antidiabetic potential of Ficus bengalensis aerial roots was evaluated. Effect of variable doses of aqueous extract of Ficus bengalensis aerial roots on blood glucose level (BGL) of normal-, sub- and mild-diabetic models have been studied and the results were compared with the reference drug Glipizide and elemental Mg and Ca intake as glycemic elements. The hypoglycemic effect in normoglycemic and antidiabetic effect in sub- and mild-diabetic models of aqueous extract of aerial roots of Ficus bengalensis are due to the presence of these glycemic elements in high concentration with respect to other elements.

4) One month treatment of alloxan diabetic dogs with a glycoside, viz. leucopelargonin derivative (100 mg/kg/day) isolated from the bark of F. bengalensis decreased fasting blood sugar and glycosylated haemoglobin by 34% and 28% respectively. Body weight was maintained in both the treated groups while the same was decreased significantly by 10% in the control group. In cholesterol diet fed rats, as the atherogenic index and the hepatic bile acid level and the faecal excretion of bile acids and neutral sterols increased, the HMGCoA reductase and lipogenic enzyme activities in liver and lipoprotein lipase activity in heart and adipose tissue and plasma LCAT activity and the incorporation of labelled acetate into free and ester cholesterol in liver decreased significantly.

5) Pharmacognostical parameters for the leaves of Ficus bengalensis were studied with the aim of drawing the pharmacopoeial standards for this species: macroscopical and microscopical characters, physio-chemical constants, extractive values with different solvents, fluorescence analysis of dry powder, its reaction after treatment with chemical reagents under visible light, and UV light at 254 nm and 366 nm. Preliminary phytochemical studies on the Ficus bengalensis leaves were conducted.
3. *Sida cordifolia*

**Plate 2.2.4.3 - Sida cordifolia**

![Image of Sida cordifolia plant](image)

**Plant Profile**

**Botanical Name:** *Sida cordifolia*

**Family:** Malvaceae

**Vernacular names**

**Common Name:** Bala, Country Mallow

**Geographical distribution:**

*S.cordifolia* is found in moist places throughout tropical and sub-tropical India and Nepal ascending to an altitude of 1,050 m.

**Chemical constituents:**

Ephedrine is one of the alkaloids reported to be present. It contains phytosterol and potassium nitrate. The phytosterols have estrogenic activity. Alkaloid ephedrine, Pseudoephedrines, palmitic, stearic and hexacosanoic acids. The flavones: 5,7-dihydroxy-3-isoprenyl flavone (1) and 5-hydroxy-3-isoprenyl flavone (2), β-sitosterol and stigmasterol have been isolated from the
The analgesic alkaloid (5’-Hydroxymethyl-1’-(1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-1-yl)-heptan-1-one) has also been found. Sterculic, malvalic and coronaric acids have been isolated from the seed oil, along with other fatty acids.

**Medicinal uses:** It is used traditionally in cases of spermatorrhea, polyurea, leucorrhea and certain nerve disorders such as monoplegia, sciatica, palsy, etc.

**Earlier work done on this Plant:**

1) Ethanol extract of roots of *Sida cordifolia* was evaluated for antistress, adaptogenic activity using cold restraint stress and swim endurance in mice\(^7^8\). Mice pretreated with extract of *Sida cordifolia* showed significant improvement in the swim duration and reduced the elevated WBC, blood glucose and plasma cortisone.

2) *Sidacordifolia* L. (Malvaceae) is used in folk medicine for the treatment of inflammation of the oral mucosa, blenorrhea, asthmatic bronchitis and nasal congestion. The anti-inflammatory, analgesic effects and acute toxicity of an aqueous extract of *S. cordifolia* were evaluated in animal models. The aqueous extract (AE) showed a significant inhibition of carrageenan-induced rat paw edema at a dose of 400 mg/kg administered orally, but did not block the edema induced by arachidonic acid\(^7^9\). The AE also increased the latency period for mice in the hot plate test, and inhibited the number of writhes produced by acetic acid at the oral dose of 400 mg/kg. The aqueous extract of *S. cordifolia* showed low acute toxicity in mice.

3) The methanol leaf extracts of *Acacia nilotica*, *Sida cordifolia*, *Tinospora cordifolia*, *Withania somnifer* and *Ziziphus mauritiana* showed significant antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas fluorescens*, *Staphylococcus aureus* and *Xanthomonas axonopodis pv. malvacearum* and antifungal activity against *Aspergillus flavus*, *Dreschlera turcica* and *Fusarium verticillioides* when compare to root/bark extracts. *A. nilotica* and *S. cordifolia* leaf extract showed highest
antibacterial activity against *B. subtilis* and *Z. mauritiana leaf* extract showed significant activity against *X. a. pv. Malvacearum*.

4) *Sida cordifolia*. Linn. (Malvaceae) is commonly known as *bala*. and widely used in Ayurveda. The comparative antioxidant potential of ethanol extracts of *Sida cordifolia*. leaf, stem, root, and whole plant was studied. Anti–lipid peroxidation, free-radical scavenging, reducing power, nitric oxide scavenging, superoxide scavenging antioxidant assay, and further estimation of total phenolic content and HPTLC studies were carried out. Various antioxidant activities were compared with standard antioxidants such as BHA, α-tocopherol, and ascorbic acid.

5) Acute toxicity of Sidacordifolia and its action on the central nervous system (CNS) was evaluated because no data in the literature have been found about of pharmacological activity of this plant in the CNS. The hydroalcoholic extract of Sidacordifolia leaves (HESc) was used and the psychopharmacology approach began with the determination of LD$_{50}$, where a low toxicity was observed in mice. Depressive activity on CNS was demonstrated by several alterations in mice’s behavior in the pharmacological screening. In the motility test, the HESc showed significant reduction of spontaneous activity at a dose of 1000 mg/kg (i.p.) at 30 and 60 min. The same form the HESc also decreased the ambulation and rearing in open-field test at 30, 60 and 120 min at a dose of 1000 mg/kg (i.p.).
4. *Tephrosia purpuria*

**Plate 2.2.4.4 - Tephrosia purpuria**

Botanical name: *Tephrosia purpuria*

Family: Fabaceae

** Vernacular names **

English: Fish Poison, Wild Indigo

Hindi: Sarphonk, Sharpunkha

** Geographical distribution:**

The plant commonly flowers from May through June. Common yarrow is frequently found in the mildly disturbed soil of grasslands and open forests, In North America, Europe and Asia, the plant grows abundantly in the upper Gangetic plains, and western Himalayas, in India, South Africa.

**Chemical constituents:**

Aromatic ester, a sesquiterpene and prenylated flavonoid, flavones, flavanones and prenylated flavonoids, chalcones, and rotenoids.

**Medicinal uses:**

Used as a fish poison; the leaves and seeds contain tephrosin, which paralyzes fish. Larger doses are lethal to fish, but mammals and amphibians...
are unaffected. It is also used traditionally as folk medicine. According to Ayurveda, the plant is anthelmintic, alexiteric, alterative, and antipyretic; it is used in the treatment of leprosy, ulcers, asthma, and tumors, as well as diseases of the liver, spleen, heart, and blood. A decoction of the roots is given in dyspepsia, diarrhea, rheumatism, asthma and urinary disorders, dental pains and stop bleeding, deobstruent, diuretic and useful in treating bronchitis, bilious febrile attacks and obstructions of the liver, spleen and kidneys. It is also recommended as a blood purifier.

**Earlier work done on this Plant:**

1) To evaluate the antiinflammatory activity of orally administered ethanolic extract of Tephrosia purpurea in acute and subacute inflammation in rats. Methods: An ethanolic extract of Tephrosia purpurea was prepared. Carrageenan induced paw edema and cotton pellet granuloma were the models for acute and subacute inflammation respectively. Four groups of rats in each model were treated orally with 2% gum acacia, 100 mg /kg of aspirin, 500 mg/kg and 1 000 mg/kg of ethanolic extract of Tephrosia purpurea respectively.

2) The flavonoid fraction of Tephrosia purpurea (FFTP) was studied for its effect on cellular and humoral functions and on macrophage phagocytosis in mice. Oral administration of FFTP (10–40 mg/kg) significantly inhibited sheep red blood cells (SRBC)-induced delayed-type hypersensitivity reactions. It also produced a significant, dose-related decrease in sheep erythrocyte-specific haemagglutination antibody titre. However, the fraction failed to show a significant change in the macrophage phagocytic activity.

3) Panus giganteus, a culinary and medicinal mushroom consumed by selected indigenous communities in Malaysia, is currently being considered for large scale cultivation. The study was undertaken to investigate the hepatoprotective effects of P. giganteus against thioacetamide- (TAA-) induced liver injury in Sprague-Dawley rats. The rats were injected intraperitoneally with TAA thrice weekly and were orally administered freeze-dried fruiting bodies of P. giganteus (0.5 or 1 g/kg) daily for two months, while control rats were given vehicle or P.
giganteus only. After 60 days, rats administered with P. giganteus showed lower liver body weight ratio, restored levels of serum liver biomarkers and oxidative stress parameters comparable to treatment with the standard drug silymarin.

4) Chemopreventive potential and antilipidperoxidative effects of ethanolic root extract of Tephrosia purpurea (Linn.) was evaluated on 7,12-dimethylbenz(a)anthracene (DMBA)- induced hamster buccal pouch carcinoma. TpEt showed potent antilipidperoxidative effect, as well as enhanced the antioxidant status in DMBA- painted animals86.

5. Trichopus zeylanicus

Plate 2.2.4.5 - Trichopus zeylanicus

Botanical name : Trichopus zeylanicus

Family : Trichopodaceae

Geographical distribution: India, Tamil Nadu, herb grows on sandy soil near rivers and streams in shady places in lowlands

Chemical constituents:

Alkaloids, essential oils
Medicinal uses:

To treat sexual performance problems. Trichopus zeylanicus is also used to increase sex drive, stimulate the immune system, reduce swelling (inflammation). Liver disease. Stomach ulcers. Obesity. Fatigue, Improving stamina.

Earlier work done on this Plant:

1) Administration of Trichopus zeylanicus leaf (ethanol extract) to male mice stimulated their sexual behaviour as evidenced by an increase in number of mounts and mating performance. This activity of the ethanol extract was concentration dependent and destroyed by heat treatment at 100°C for 15 min. Although oral administration of a single dose (200 mg/kg) was effective, daily administration of the extract for 6 days was found to be more effective.

2) Treatment of mice with Trichopus zeylanicus leaf resulted in inhibition of antigen-induced degranulation of sensitized peritoneal mast cells. Further, it reduced the ratio of mast cells in the peritoneal exudate cells. The plant drug treatment did not protect mice from E. coli-induced abdominal sepsis. Studies in rats using mesenteric mast cells confirmed the above mast cell-stabilizing property of T. Zeylanicus. This activity was found in the butanol fraction of methanol extract of T. zeylanicus leaf. The treatment with this fraction also reduced the number of rat mesenteric mast cells. However, the in vitro treatment of the mast cells with the butanol fraction did not inhibit antigen-induced degranulation of the mast cells.

3) The alcoholic extract of seeds of Trichopus zeylanicus showed a potent adaptogenic or antistress properties against a variety of stresses in both rats and mice. The extract increased the swimming performance of normal and adrenalectomized mice. Significantly; prevented a variety of stress and chemical induced ulcerations in rats and also prevented milk-induced leucocytosis in mice. The extract further reduced the gastric secretory clume, PH and acid output in pylorusligated rat stomach. No mortality was observed.
upto a dose of 3 g/kg per oral in mice. The study indicated that trichopus zeylanicus seeds induce a state of nonspecific increased resistance against a variety of stress induced biological changes in animals.

5) Chronic fatigue is a complex and little understood symptom for which there is no safe and effective pharmacotherapy. The present study was conducted to investigate the effectiveness of Trichopus zeylanicus whole plant powder on fatigue in young Sprague Dawley rats, and aged normal and long-living mutant Ames dwarf mice. Fatigue was evaluated by subjecting the animals to a forced swim test. Trichopus zeylanicus (250 and 500 mg/kg) treated young Sprague-Dawley rats resisted fatigue at a significant level (p < 0.005) compared with controls by an extended swim time in the forced swim test.

6. Withania somnifera

Plate 2.2.4.6 - Withania somnifera

Botanical name : Withania somnifera
Family : Solanaceae

Vernacular names

Hindi - Asgandh
English - winter cherry
Latin - WITHANIA somnifera  
Sanskrit - Ashwagandha  
Tamil - Amukira  
Kannada - Keramaddinagaddi  
Telgu - Vajigandha, Pennerugadda  
Malayalam:Amukkuram, Trittavu  
Marathi : Askandha  
Chinese :Shui Qie

**Geographical distribution:**  *Withania somnifera* is cultivated in many of the drier regions of India, such as Mandsaur District of Madhya Pradesh, Punjab, Sindh, and Rajasthan.[4] It is also found in Nepal.

**Chemical constituents:** The main active constituents are alkaloids and steroidal lactones. These include tropine and cuscohygrine. The leaves contain the steroidal lactones, withanolides, notably withaferin A, which was the first withanolide to be isolated from *W. somnifera*.

**Medicinal uses:** anti-metastatic activity, Alzheimer's disease, tumors, tubercular glands, carbuncles, and ulcers

**Earlier work done on this Plant:**

1) Antioxidant activity of active principles of *Withania somnifera*, consisting of equimolar concentrations of sitoindosides VII-X and withaferin A, was investigated for their effects on rat brain frontal cortical and striatal concentrations of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX)^91^. Antioxidant effect of active principles of *W. somnifera* may explain, at least in part, the reported antistress, immunomodulatory, cognition-facilitating, anti-inflammatory and anti-aging effects produced by them in experimental animals, and in clinical situations.
2) The roots of Withania somnifera (WS) are used extensively in Ayurveda, the classical Indian system of medicine, and WS is categorized as a rasayana, which are used to promote physical and mental health, to provide defence against disease and adverse environmental factors and to arrest the aging process\textsuperscript{92}. WS has been used to stabilize mood in patients with behavioural disturbances.

3) Administration of an extract from the powdered root of the plant Withania somnifera was found to stimulate immunological activity in Babl/c mice\textsuperscript{93}. Treatment with five doses of Withania root extract (20 mg/dose/animal; i.p.) was found to enhance the total WBC count (17 125 cells/mm\textsuperscript{3}) on 10th day. Bone marrow cellularity (27×10\textsuperscript{6} cells/femur) as well as α-esterase positive cell number (1800/4000 cells) also increased significantly (\textit{P} < 0.001) after the administration of Withania extract.

4) The \textbf{antibacterial activity} of \textit{Withania somnifera} was tested on clinically isolated bacterial pathogens, i.e., \textit{Staphylococcus aureus}, \textit{Escherichia coli}, \textit{Pseudomonas aeruginosa} and \textit{Bacillus subtilis} causing infections in human beings. Different solvents as ethanol, ethyl acetate, dichloromethane, hexane (from higher polarity to lower polarity) extracts was used for the study of \textbf{antibacterial activity}, by agar well diffusion method.

The bacterial plates were prepared by nutrient agar. The extracts at different concentration from 10 to 40 mg mL\textsuperscript{-1} were loaded in the wells prepared in nutrient agar\textsuperscript{94}. Zone of inhibition was measured around the wells to check the \textbf{antibacterial activity} of extracts.

5) As such, the adaptogenic activity of a standardised extract of WS roots was investigated against a rat model of chronic stress (CS). The stress procedure was mild, unpredictable footshock, administered once daily for 21 days to adult male Wistar rats. CS induced significant hyperglycaemia, glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression.
These CS induced perturbations were attenuated by WS (25 and 50 mg/kg po) and by PG (100 mg/kg po), administered 1 h before footshock for 21 days\textsuperscript{95}. The results indicate that WS, like PG, has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda.

7. \textit{Daucus carota}

\textbf{Plate 2.2.4.7 - Daucus carota}

Botanical Name : \textit{Daucus carota}

Family : Apiaceae

\textbf{Vernacular names}

English : Wild carrot, Bird’s nest, Bishop’s lace
Geographical distribution: 
Mostly occurring in the Mediterranean. A Eurasian native, *Daucus carota* is found from Norway and central. Sweden to North Africa and the Canary Islands and east

Chemical constituents:
a-pinene, camphene, b-pinene, sabinene, myrcene, y-terpinene, limonene, b-bisabolene, geranyl acetate and carotol.

Medicinal uses:
Thermogenic, appetizer, carminative, digestive, anthelmintic, stomachic, constipation, diuretic, expectorant, cardiotonic, stimulant, flatulence, dyspepsia, colic, strangury, wounds, cough, asthma, bronchitis, indolent ulcers, leprosy, cataract, nyctalopia, tumours, inflammation, haemorrhoids, jaundice.

Earlier work done on this Plant:

1) Hypolipidemic activity of ethanolic extract of Daucus carota seeds in Normal rats. Standard and test (400mg/kg DCSE) groups were showed significant (P <0.001) reduction in the total cholesterol, triglyceride HDL and VLDL as compared control group. Test group (200mg/kg) was showed significant (P <0.05) reduction as compared control group. The antioxidant potential of Daucus carota seeds has contributed to the reduction of oxidative stress and Lipid levels in experimental rats.

2) Cyclooxygenase (COX) enzymes inhibitory assay directed investigation of *Daucus carota* seed extracts resulted in the isolation and characterization of compounds, 2,4,5-trimethoxybenzaldehyde (1), oleic acid (2), trans-asarone (3) and geraniol (4). Compounds 1–4 showed 3.32, 45.32, 46.15, and 3.15% of prostaglandin H endoperoxide synthase-I (COX-I) inhibitory activity and 52.69, 68.41, 64.39 and 0% prostaglandin H endoperoxide synthase-II (COX-II) inhibitory activity, respectively at 100 mg mL⁻¹.
8. *Glycosmis pentaphylla*

**Plate 2.2.4.8 - Glycosmis pentaphylla**

Botanical name : *Glycosmis pentaphylla*

Family : Rutaceae

**Vernacular names**

Malayalam : *Kurumpannal, Panal, Panchi*

Malaysia : Merapi, Nerapi, Terapi

Indonesia : Gongseeng, Jerukan, Totoan

Philippines : Gingging

Cambodia : Dom phlang, Laos, Som Sum, Om Chune

**Geographical distribution:**

Tropical Asia and Australia. Has gained popularity as an edible fruit in parts of the Caribbean. In India, Srilanka, Burma (Myanmar), Thailand, Southern China, Indo-China, Philippines, Peninsular Malaysia, Sumatra and Java.

**Chemical constituents:**

Alkaloids- glycolone, glycozoline, glycozolidine, dictamine, vanillic acid, syringic acid, ferulic acid, acridone-alkaloid-glycoquinone, glycocitrine-lll; noracronycine, arborinine, 5-hydroxy arborinine, isoflavones etc
**Medicinal uses:**

Treat intestinal ailments, diarrhoea, coughs, rheumatism, anaemia, jaundice, anthelmintic, eczema & other skin infections.

**Earlier work done on this Plant:**

1) The study aims to determine the *in vitro* anticancer and apoptosis inducing activity of Glycosmis pentaphylla in hepatocellular carcinoma cell line, Hep3 B. The cytotoxic and apoptosis inducing activity of the crude extract and active fractions were estimated on Hep3 B and RAW264.7. The study showed that major active component in the ethanol extract of Glycosmis pentaphylla is a flavonoid which induces apoptosis on cancer cell line, Hep3 B, by increasing the expression ratio of Bax/Bcl2 genes in a time and dose dependent manner.

2) Acetone extracts of *Glycosmis pentaphylla* [*G. pentaphylla*] combined with equal amounts of extracts of *Catharanthus roseus*, *Salvadora oleododes* and *Breneya* species exhibited a significant increase in ovipositional deterrence activity against *Phthorimaea operculella* compared with the activity of the individual extracts. It is suggested that there are important practical implications of this synergism.

3) The growth of larval *Diaprepes abbreviatus* L. was measured after rearing them on roots of rutaceous seedlings for 35 or 42 days. Larvae were fed on seedlings of two common citrus rootstocks, two new hybrids that are under development as rootstocks, and one citrus relative. Live weights of larvae reared on Carrizo or Swingle rootstocks for 42 days increased an average of 10.3- and 10.2-fold, respectively; weight increases on the citrus hybrids HRS-802 and HRS-896 for 35 days averaged 7.6- and 6.1-fold, respectively; and weight increase on Glycosmis pentaphylla Retzius for 42 days averaged 2.5-fold.
9. Mikania cordata

Plate 2.2.4.9 Mikania cordata

Botanical name: Mikania cordata
Family: Asteraceae

Vernacular names

Common names: mile-a-minute, African mile-a-minute
English: heartleaf hempvine
French: liane marzoge

Geographical distribution:

African tropics and South Africa, Indian subcontinent and China through Southeast Asia to the Pacific Islands. Native to Southeast Asia and the Pacific Islands.

Chemical Constituents:

Beta-cubebene (12.95%), allo-aromadendrene (11.67%), beta-caryophyllene (9.17%), 1H-inden-1-one, 5-(1, 1-dimethylethyl)-2, 3-(6.23%), beta-himaohalene (4.56%), trans-alpha-bergamotene (4.09%), limonene
(3.68%), beta-ocimene (2.53%), a-pinene (20%), germacrene D (19.8%), beta-pinene (8.7%) and alpha-thujene (7.1%).

**Medicinal uses:**

Anticarcinogenic, Anti-Inflammatory, Anti-Stress Activity, Analgesic, Antioxidant, Anti-Ulcer.

**Earlier work done on this Plant:**

1) The alkaloidal fraction obtained from an ethanolic extract of the leaves of Mikania cordata exhibited significant *in vivo* antiulcer activity in diclofenac sodium-induced gastric erosions in Long Evans rats

2) The methanolic fraction of the root extract of *Mikania cordata* was found to possess an inhibitory effect on carrageenin and other mediator—induced oedema; there was a significant inhibition of protein exudation, an increase in peritoneal capillary permeability and leucocyte migration in inflammatory conditions. The extract significantly inhibited both cotton pellet and carrageenin—induced granuloma formation, was effective in experimentally induced arthritic conditions and turpentine—induced joint oedema.

3) *Effects of Mikania cordata* root extract were investigated on stress-induced alterations in central neurotransmitters, viz., adrenaline (Ad), noradrenaline (NA), dopamine (DA) and 5-hydroxytryptamine (5-HT), and enzymatic activities of monoamine oxidase (MAO) in brain and succinic dehydrogenase (SDH) in brain and liver of mice. Both 5 h swimming and 24 h immobilization stress elicited a decrease in the levels of Ad and NA whereas they increased those of DA and 5-HT. Pretreatment with *M. cordata* root extract for 15 days prevented the decrement in Ad and NA and increment in 5-HT while the level of DA was further increased. There was a marked inhibition in brain MAO and stimulation in brain and liver SDH activities following both types of stress. The extract restored MAO activity towards normalization whereas it facilitated stress-induced changes in SDH activities. These dose-
dependent biochemical responses may be the possible mechanism of anti-stress activity of this plant extract.

4) The chemopreventive role of an Indian medicinal plant Mikaniacordata (Compositae), which is consumed as vegetable and advocated in folk-medicine, has been evaluated through its effects on Phase 1 and 2 of the hepatic drug-detoxifying enzyme system in rats\textsuperscript{104}. Although oral administration of a methanolic extract of this plant root (50, 100 or 150 mg/kg for 4, 8 or 12 weeks) has been found to have very little or no effect on hepatic microsomal cytochrome P-450 and cytochrome b\textsubscript{5} contents as well as NADPH cytochrome c reductase activity, it afforded a marked induction of uridine diphosphoglucuronyl transferase activities of liver microsomes.

10. Moringa oleifera

Plate2.2.4.10- Moringa oleifera

Botanical Name:  

\textit{Moringa oleifera}  

Family : Moringaceae

\textbf{Geographical distribution:}

The southern foothills of the Himalayas in northwestern India. Cultivation in Hawai‘i, for commercial distribution in the United States, is in its early stages. "India is the largest producer of moringa, with an annual production of
1.1 to 1.3 million tonnes of tender fruits from an area of 380 km². Among the states, Andhra Pradesh leads in both area and production (156.65 km²) followed by Karnataka (102.8 km²) and Tamil Nadu (74.08 km²). In other states, it occupies an area of 46.13 km². Tamil Nadu, Sri Lanka, in Thailand, Philippines, it is commonly grown for its leaves, which are used in soup. It is also widely cultivated in Africa, Cambodia, Nepal, Indonesia, Malaysia, Mexico, Central and South America, and Sri Lanka.

**Chemical constituents:**

Vitamin B₆, vitamin C, provitamin A as beta-carotene, magnesium and protein, Carbohydrates, Fat, Thiamine, Riboflavin (vit. B₂), Niacin (vit. B₃), Pantothenic acid (B₅), Folate (vit. B₉), Calcium, beta-carotene, amino acids and various phenolics. The Moringa plant provides a rich and rare combination of zeatin, quercetin, beta-sitosterol, caffeoylquinic acid and kaempferol.

**Medicinal uses:**

Act as cardiac and circulatory stimulants, possess antitumor, antipyretic, antiepileptic, antiinflammatory, antiulcer, antispasmodic, diuretic, antihypertensive, cholesterol lowering, antioxidant, antidiabetic, hepatoprotective, antibacterial and antifungal activities, and are being employed for the treatment of different ailments in the indigenous system of medicine.
2.3 MEMORY IMPAIRMENT:

2.3.1 Pathophysiology of Memory Impairment:

Memory is the ability of an individual to record sensory stimuli, events, information etc., retain them over short or long periods of time and recall the same at a later date when needed. Poor memory, lower retention and slow recall are common problems in today’s stressful and competitive world. Age, stress, emotions are conditions that may lead to memory loss, amnesia, anxiety, high blood pressure, dementia, to more ominous threat like schizophrenia and Alzheimer’s disease.

Alzheimer’s disease (AD) is a neurodegenerative disorder, which according to world health organization (WHO) affects 22 million people world wide, out of which, over 3 million are in India. Its prevalence rises sharply from about 5% at the age of 65 to 90% or more at the age of 95 years. Though there are drugs available that aim at slow progression of disease, an affirmative cure to AD still eludes researchers.

Memory loss is unusual forgetfulness that can be caused by brain damage due to disease or injury, or it can be caused by severe emotional trauma.

Common causes:-

- Aging
- Alzheimer’s disease
- Neurodegenerative illness
- Head trauma or injury
- Hysteria often accompanied by confusion
- Seizures
- General anaesthetics such as Halothane, Isoflurane and Fentanyl
- Alcoholism
- Stroke or transient ischemic attack
- Transient global amnesia
- Drugs such as Barbiturates or Benzodiazepines
Electro Convulsive Therapy (Especially if prolonged)
Temporal lobe brain surgery
Brain masses (Caused by tumors or infection)
Herpes Encephalitis
Other brain infections
Depression

Alzheimer’s disease (AD) is a neurodegenerative disorder that robs patients of their memory and cognitive abilities and even their personalities and is the most common form of senile dementia^{105}.

Memory impairment is a necessary feature for the diagnosis of this or any type of dementia. Changes in one of the following areas must also be present: Language, decision-making ability, judgment, attention and other areas of mental function and personality.

There are 2 types of AD early-onset and late-onset. In early-onset AD, symptoms first appear before age 60. Early onset AD is much less common, accounting for only 5-10% of cases. However, it tends to progress rapidly. Early-onset disease can run in families and involves autosomal dominant, inherited mutations that may be the cause of the disease. So far three early-onset genes have been identified.

Late-onset AD, the most common form of the disease, develops in people 60 and older and is thought to be less likely to occur in families. Late-onset AD may run in some families, but the role of genes is less direct and definitive. These genes may not cause the problem itself, but simply increase the likelihood of formation of plaques and tangles or other AD related pathologies in the brain.

The number of risk factors and pathophysiologic abnormalities at the anatomical, cellular and molecular levels supports the view that a variety of mechanisms may contribute to AD. There is no compelling evidence that these mechanisms are mutually exclusive. In some patients, a particular mechanism may play a major role, while in others it may not.
In AD, progressive neurodegeneration occurs in multiple areas of the train, including relatively selective involvement of the nucleibasalis, hippocampus, amygdala, entorhinal cortex and eventually the high-order association cortex of the temporal, frontal, and parietal regions. The neuronal damage and the attending loss of synaptic density disable several neural systems essential to learning and retrieval of memories.

The histopathologic hallmarks of AD include the deposition of beta-amyloid in senile plaques and blood vessel walls, as well as the presence of neurofibrillary tangles and loss of neurons. These changes greatly impair the function of neurotransmitter systems.

Decreased levels of acetylcholine and other markers of cholinergic functions are characteristically found and have been associated with the deficits in learning and memory found in AD (Rakel, 2005). Other neurotransmitters, including serotonin, norepinephrine and somatostatin are also decreased and these changes may contribute to the behavioural abnormalities found in AD. Other biochemical evidence suggests that inflammation and / or the deleterious effects of free radicals play a role in the pathogenesis of AD.

A variety of genetic and environmental abnormalities can contribute to Alzheimer’s disease.

2.3.1.1 Comprehensive Theories For Alzheimer’s Disease

2.3.1.1.1. Metabolism of amyloid-βPeptide

AD is characterized by a variety of pathological features, such as extracellular senile plaques, intracellular neurofibrillary tangles, synaptic loss and brain atrophy. The senile plaques are mainly composed of amyloid-β peptide (Aβ) of 40-43 amino acids (Called Aβ1-40, Aβ1-42 or Aβ1-43 according to the number of amino acid residues), and the neurofibrillary tangles consists of twisted filaments of hyperphosphorylated tau. In AD development, a decades-long pathological cascade of Aβ deposition, accumulation of hyperphorylated tau, dysfunction of neurons and neuronal death leads to overt dementia.
Aβ deposition occurs or olisomeric, protofibrillar, amylospheroid, and fibrillar forms. The cause and effect relationship between Aβ deposition and AD development has been strongly supported by the consistent increased Aβ (Particularly Aβ42) production phenotypes of early onset familial AD-causing gene mutations, such as amyloid precursor protein (APP), presenilin (PS)1 and PS2, observed in both in vitro and in vivo experiments. Aβ42 is more hydrophobic and shows a higher potential for aggregation than Aβ40 does and it functions as the primary pathogenic agent. Importantly, Aβ is a physiological peptide, which is constantly anabolized and catabolized in the brain, so that the steady-state Aβ levels are determined by the metabolic balance between anabolic and catabolic activities.

Even subtle alterations in this metabolic balance over a long period of time could result in the appearance of pathogenic forms of Aβ, influencing both the pathological progression and the incidence of the disease.

For instance, just a 1.5-fold increase in Aβ42, caused by most of the above mutations, results in aggressive presenile Aβ pathology. Therefore, in order to overcome AD, it is necessary to lower the Aβ levels in the brain, and several therapeutic strategies (referred to as anti-Aβ strategies), such as inhibition of production, promotion of degradation, inhibition of aggregation and clearance of deposits, have been proposed. In sporadic AD brains, where the elevation of anabolic activity seems to be rarely observed, a reduction in the catabolic activity towards Aβ involving so-called Aβ-degrading enzyme(s) has been a candidate cause for Aβ accumulation associated with late-onset AD development. Either the up-regulation of the catabolic activity or down-regulation of the anabolic activity should prevent or reduce Aβ deposition and thus be applicable to the prevention and therapy of AD.

2.3.1.1.2. Aminergic Disinhibition theory

It includes data-based hypotheses as to the pathoklisis, mechanisms of neuro-degeneration and dementia as well as the aetiology of the disease. Alzheimer’s disease (AD) is regarded as a disorder of neural input modulation caused by the degeneration of four modulatory amine transmitter (MAT)
systems, namely the serotonergic, the noradrenergic, the histaminergic, and the cholinergic systems with ascending projections. MATs modulate cognitive processing including arousal, attention, and synaptic plasticity in learning and memory, not only through direct, mostly inhibitory impact on principal neurons but also partially through interaction with local networks of GABA-ergic inter-neurones.

The distribution and magnitude of the pathology in AD roughly correlate with the distribution and magnitude of MAT modulation. Regions more densely innervated by ascending MAT projections are, as a rule, more severely affected than areas receiving less MAT innervation. Because the global effect of MATs in the forebrain is inhibition, the degeneration of four MAT systems, some related peptidergic systems and a secondary alleviation of the GABA-ergic transmission means a fundamental loss of inhibitory impact in the neuronal circuitry resulting in neuronal (aminergic) disinhibition. Clearly, the basic mechanism promoting neuronal death in AD is thought to be a chronic disturbance of the inhibition-excitation balance to the advantage of excitation. Chronic over-excitation is conceived to result in Ca\(^{\text{2+}}\) dependent cellular excitotoxicity leading to neuro-degeneration including amyloid-\(\beta\) production and Neurofibrillary tangles formation. Disinhibited neurons will degenerate while less excited (relatively over-inhibited) neurons will survive.

Because the decline of aminergic transmission in AD is likely to start at the receptor level, it is hypothesized that early impairment by a molecular ‘hit’ to an MAT receptor (or a group of receptors) initiates a pathogenetic cascade that develops in an avalanche-like manner. Based on experimental evidence from the literature, the ‘hit’ might be the attachment of a targeted pathogen like a small roaming amino acid sequence to the receptor(s), e.g., the serotoninergic 5-HT\(_{2A}\)-R. Referential sequence analysis could be a means to identify such a small pathogen hidden in a large receptor molecule.

2.3.1.1.3. Gene – environment interactions in dementias

The amyloid hypothesis continues to provide the most useful model of AD aetiology. Although the current focus on molecular approaches to AD has
been worthwhile, many clinical scientists believe that AD is best explained by interactions between environmental and genetic factors, this explanation is consistent with a major causal role for non-inherited factors in age-related disease. The ultimate strategy will be to discover interventions to prevent the diseases of old age, including dementia syndromes, by combining genetic and environmental methods of research.

Links are stronger between the first group (cardiovascular disease, Non-insulin-dependent diabetes mellitus (NIDDM) and the metabolic syndrome) and age-related dementia, and weaker between the second group (low average childhood intelligence, education, and socioeconomic status) and late-onset dementia. The main issues are whether there are plausible biological mechanisms that explain how developmental exposure influences brain health towards the end of life and whether one or several pathways are needed to explain these associations.

Crucial experiments are lacking on the effects of altering the early life conditions on the ageing phenotype, although there are tantalizing clues from the effects of life-long caloric restriction. Studies informative to dementia will concentrate on exposures that both modify the development of early neural networks and predict differences in ageing.

Possible pathways from adverse developmental exposures to dementia include a chain of events triggered by fetal malnutrition, leading to low birthweight, low average childhood intelligence, low educational attainments, low occupational status and an unhealthy life style. Acting in combination, the long-term outcome is for these factors to predispose to many age-related diseases including cardiovascular disease, NIDDM, the metabolic syndrome, and dementia. Second, fetal malnutrition may trigger two or more distinct pathways (multiple hits), one affecting neurodevelopment and others perturbing maturation of physiological regulation of blood pressure and glucose metabolism, and thus predisposing to obesity. As yet, there are too few data to distinguish between these pathways, although inflammatory processes may be important. A third possibility, that fetal malnutrition leads to
accelerated ageing, is largely unexplored, but might be sufficient to explain proposed associations between fetal development and age-related diseases.

Therapeutic pessimism greets the many studies that link childhood adversity to late-onset disease. The reality may be more promising than this. Some epigenetic effects, once identified, may be open to later modification. If increased incidence of dementia with age relies on underlying intrinsic ageing processes and these are influenced by fetal development, it is reasonable to assume that some of this developmental contribution is shared with other age-related diseases.

2.3.1.4. Role of Oxidative Stress in dementias

Reactive oxygen species (ROS) are involved in several diseases including ischemic injury, aluminum toxicity, Alzheimer’s disease, Parkinson’s disease and Down’s syndrome all of which affect cognitive processes. Major oxidative free radical scavenging enzymes are superoxide dismuttase (SOD), catalase (CAT) and glutathione peroxidase (GPX). Deficient functioning of these enzymes leads to accumulation of toxic oxidative free radicals and consequent degenerative changes. Therefore several compounds with antioxidative properties are used for the therapy of such neurodegenerative diseases.

2.3.2 Drug Treatment for memory impairment

Several drugs are available to try to slow the progression of AD and possibly improve the person’s mental capabilities.

These include...

✓ Donepezil
✓ Rivastigmine
✓ Galantamine
✓ Tacrine

All of these drugs affect the level of acetylcholine (a neurotransmitter) in the brain and all have potential side effects, such as nausea and vomiting.
Tacrine also causes an elevation in liver enzymes and must be taken four times a day. It is now seldom used.

Donepezil is taken once a day and may stabilize or even improve the person’s mental capabilities. It is generally well tolerated. Rivastigmine, a new drug, shows a similar effectiveness and is taken twice a day.

Other medications may be required to control aggressive, agitated, or dangerous behaviors. These are usually given in very low doses, with adjustment as needed.

If may be necessary to stop any medications that worsen confusion. These may include pain killers, cimetidine, central nervous system depressants, antihistamines, sleeping pills, and others.

**Supplements**

Folate (vitamin B₉) is critical to the health of the nervous system. Together with some other B vitamins, folate is also responsible for clearing homocysteine (a body chemical that contributes to chronic illnesses) from the blood. High levels of homocysteine and low levels of both folate and vitamin B₁₂ have been found in people with AD. Although the benefits of taking these B Vitamins for AD is not entirely clear, it may be worth considering them, particularly if your homocysteine levels are high.

Antioxidant supplements, like ginkgo biloba and vitamin E, scavange free radicals. These products of metabolism are highly reactive and can damage cells throughout the body.

Vitamin E dissolves in fat, readily enters the brain, and may slow down cell damage. In at least one well-designed study of people with AD who were followed for 2 years, those who took vitamin E supplements had improved symptoms compared to those who took a placebo pill. Patients who take blood-thinning medications like warfarin may should talk to their doctor before taking vitamin E.
Ginkgo biloba is an herb widely used in Europe for treating dementia. It improves blood flow in the brain and contains flavonoids (plant substances) that act as antioxidants. Although many of the studies to date have been somewhat flawed, the idea that ginkgo may improve thinking, learning, and memory in those with AD has been promising. DO NOT use ginkgo if blood-thinning medications like warfarin or a class of antidepressants called monoamine oxidase inhibitors are taken.

**Alternative Options**

The natural alternatives listed below are recommended to help improve cognitive function and memory.

1. **Methylcobalamin** A type of vitamin B₁₂ that may be helpful for nerve fibers and regenerating damaged neurons.

2. **Acetyl-L-Carnitine** This acetylated high energy ester of the amino acid L-carnitine contributes its acetyl group to the production of acetylcholine, the primary neurotransmitter for memory and thought. The enzyme that makes acetylcholine from acetyl groups and choline is choline acetyl transferase.

3. **Phosphatidylserine** By supporting the structure of the brain, phosphatidylserine may be able to improve memory, learning, mood, and concentration in those with decreased cognitive function.

4. **Huperzine A** An extract of the Chinese club moss, Huperzia serrata, huperzine a has been used in Chinese medicine for centuries. It is an effective inhibitor of acetylcholinesterase, the enzyme that degrades acetylcholine, the neurotransmitter important for normal memory and learning function. Huperzine-a may help maintain cognitive function that has been degraded by a reduction in the brain’s functional levels of the neurotransmitter acetylcholine.

5. **Gingko** Can act as a tonic to the circulatory system by increasing blood flow to the brain, which brings more nutrition to the brain.
6. **Choline**  Choline is helpful for making acetylcholine, which is the brain chemical that is involved with memory and thought processes.

7. **Bacopa Ext**  Has been used since the 6th century A.D. by India as a medicine to improve cognitive function and help with the nervous system. It also reported to be effective for enhancing memory, improving brain function, and also improving mental performance.

8. **Vinopextine**  Has been reported to improve brain circulation and oxygenation, helps the brain when there is a lack of oxygen, and slows down clot formation.

9. **Lectithin**  Research suggests that lecithin may improve symptoms of Alzheimer’s.

**Nootropics / Memory Enhancers**

Nootropics / memory enhancers represent a new class of psychotropic agents with selective facilitatory effect on integrative functions of central nervous system, particularly on intellectual performance, learning capacity and memory nootropics such as piracetam and aniracetam are used to ameliorate cognitive deficits.

Nootropic drugs, such as piracetam and aniracetam, improve memory in animal tests, possibly by enhancing glutamate release, but are probably ineffective in Alzheimer’s Disease.
### 2.3.3 PLANTS SHOWING NOOTROPIC ACTIVITY

#### Table 2.3.1 Plants showing Nootropic activity

<table>
<thead>
<tr>
<th>S.No</th>
<th>PLANT NAME</th>
<th>CHEMICAL CONSTITUENTS</th>
<th>OTHER USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Acorus Calamus</em></td>
<td>The main chemical components are acorenone, b-gurjunene, isoshyobunine, b-asarone, calamendiol, a-selinene, a-calacorene, calamusenone, camphone and shyobunone.</td>
<td>Loss of memory, Nervous disorders, Bronchitis, Asthma, Emetic, Epilepsy, Skin diseases.</td>
</tr>
<tr>
<td>2</td>
<td><em>Celastrus Paniculata</em></td>
<td>Seeds contain 52.2% thick, pungent and odorous oil. Alkaloids are also present in it. And about 5% some acids are also present. The oil is extracted from it via two separate methods like one is pressure techniques and other by the instruments of extracting the oil. Oil extracted from the crushing methods yield yellow color oil and the other method yield black colored oil. This oil has a chemical known as criojot. Seeds contain two acids like silestrin and second one is peniculetin.</td>
<td>Brain tonic, Rheumatism, Blood Purifier.</td>
</tr>
<tr>
<td>3</td>
<td><em>Huperiza serrata</em></td>
<td></td>
<td>Improves short-term memory.</td>
</tr>
<tr>
<td>4</td>
<td><em>Ephedra sinensis</em></td>
<td>Ephedra contains alkaloids (inc. ephedrine),</td>
<td>Memory enhancer, Stimulant, Bronchodilator,</td>
</tr>
<tr>
<td></td>
<td><strong>Allium sativum</strong></td>
<td>saponins, volatile oil.</td>
<td>Weight loss aid.</td>
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</tr>
</tbody>
</table>
| **5** | Volatile oil (0.1-0.4%) containing sulfur compounds: including allicin, diallyl disulfide, diallyl trisulfide, ajoene and others.  
• Other sulfur compounds: including allyl cysteine sulfoxide, methyl allyl thiosulfinate and related compounds.  
• Trace minerals: especially selenium, geranium  
• Enzymes: including alliinase, myrosinase, peroxidase.  
• Other: proteins (~16%), vitamins, glucosilinates. | Memory enhancer, Nervous disorders, Leprosy, Worms, Heart diseases, Chronic fever, Intestinal colic. |
<p>| <strong>6</strong> | The main active ingredients in the Panax species are a group of dammarane-type triterpenoid glycosides. They are referred to as saponins. And termed ginsenosides. In Russia they are termed Panaxosides. These are in the ginseng root. There are more than thirty ginsenosides. One of them is an oleanolic acid derivative. | Memory enhancer, Diabetes, Kidney disorders. |
| <strong>7</strong> | Main chemical components are ajmaline, catharanthaine, leurosidine, vincristine, vinblastine, vinorelbine, vindesine, vincamine | Tonic, Astringent. |</p>
<table>
<thead>
<tr>
<th>No.</th>
<th>Species</th>
<th>Chemical Constituents</th>
<th>Medical Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Saussurea lappa(Kuth)</td>
<td>Succinic acid, palmitic acid, alkaloid saussurine,</td>
<td>Tonic, Bronchitis, Dyspnea, Rheumatism.</td>
</tr>
<tr>
<td>9</td>
<td>Embelica officinalis</td>
<td>The major chemical constituents of Amla are Phyllemblin, Ascorbic acid (Vitamin C), Gallic acid, Tannins, and Pectin etc.</td>
<td>Tonic, Diabetes, Eye diseases, Epistaxis, Allergy, Anaemia, Anti-ageing.</td>
</tr>
<tr>
<td>10</td>
<td>Eleuthrococcus</td>
<td>A mixture of phenylpropane derivatives of diverse structure, and various sugar polymers. The principal components of the former group are the lignans, (+)-sesamin (eleutheroside B4), (+)-syringaresinol and its monoglucoside (eleutheroside E1) and diglucoside (eleutherosides D and E); the simple phenylpropanes, syringenin and its monoglucoside (eleutheroside B); and the coumarins isofraxidin and its monoglucoside (eleutheroside B1).</td>
<td>Increases mental output.</td>
</tr>
<tr>
<td>11</td>
<td>Evolvolus alsinoides</td>
<td>The plant contains alkaloids: betaine, shankhapushpine and evolvine. Fresh plant contains volatile oil. It also contains a yellow neutral fat, an organic acid and saline substances. An unidentified compound has been isolated. Scopoletin, scopolin, umbelliferone.</td>
<td>Brain tonic, Memory, Febrifuge, Vermifuge, Dysentery, Chronic bronchitis, Asthma.</td>
</tr>
<tr>
<td>12</td>
<td>Dioscorea bulbifera</td>
<td>Tuber contains steroidal saponins, diosgenin, bitter and non-bitter terpenes, nortriterpene glucosides, diosbulbinside D &amp;</td>
<td>Tonic, Skin diseases, Intestinal parasite, Diabetes.</td>
</tr>
</tbody>
</table>
F, a large number of diosbulbins, diterpene lactones, phenanthrenes, dihydrophenanthrene, furanoid nor-diterpenes and d-sorbitol. Bulbils also contain diosgenin.

<table>
<thead>
<tr>
<th></th>
<th><strong>Mucuna pruriens</strong></th>
<th><strong>Adhatoda zeylanica</strong></th>
<th><strong>Santalum album</strong></th>
<th><strong>Punica granatum</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Tonic, Menstrual disorders, Neurological disorders.</strong></td>
<td><strong>Loss of memory, Leprosy, Tumours, Heart problems, Leucoderma.</strong></td>
<td><strong>Brain tonic, Antipyretic, Aphrodisiac, Heart diseases, Bronchitis, Diuretic, Gonorrhoea.</strong></td>
<td><strong>Brain tonic, Cardiac tonic, Rheumatoid arthritis, Peptic ulcer, Intestinal colic.</strong></td>
</tr>
<tr>
<td>13</td>
<td><strong>Mucuna pruriens</strong></td>
<td>important source of phytoconstituents like quinazoline alkaloid vasicine, vasicinone, vasicinol, vasicinine and vasicoline. The alkaloids vasicine and vasicinone</td>
<td>The main constituent of sandalwood oil is santalol. This primary sesquiterpene alcohol forms more than 90 per cent of the oil and is present as a mixture of two isomers, α-santalol and β-santalol, the former predominating. The characteristic odor and medicinal properties of sandalwood oil are mainly due to the santalols. The other constituents reported in sandalwood oil include: the hydrocarbons santene, nortricycloekasantalene and α- and β-santalenes.</td>
<td>Main chemical constitutes are punicalagin, ellagic acid, luteolin, quercetin, kaempferol, ellagitannins, anthocyanins (delphinidin, cyanidin, and pelargonidin) and EA-</td>
</tr>
<tr>
<td>14</td>
<td><strong>Adhatoda zeylanica</strong></td>
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<tr>
<td>15</td>
<td><strong>Santalum album</strong></td>
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<tr>
<td>16</td>
<td><strong>Punica granatum</strong></td>
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<tr>
<td></td>
<td><strong>Poria cocos</strong></td>
<td>Main chemical constituents of <em>Poria cocos</em> includes: beta-pachyman, a polysaccharide beta-pachymarose, several organic acids such as tumulosis acid, eubricoic acid, pinolic acid, and pachymic acid, 3-beta-hydroxylanosta-7,9(11).</td>
<td>Tonic.</td>
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<tr>
<td>17</td>
<td><strong>Linum usitatissimum</strong></td>
<td>Alpha-linolenic acid (ALA), cyanogenic glycosides (linamarin, linustatin, neolinustin), unsaturated fatty acids (linolenic acid, linoleic acid, oleic acid), soluble flaxseed fiber mucilage (d-Xylose, L-Galactose, L-Rhamnose, d-galacturonic acid), lignans (secoisolaricresinol diglycoside (SDG)), monoglycerides, triglycerides, free sterols, sterol esters, hydrocarbons (protein), balast, phenylpropane derivatives.</td>
<td>Brain tonic, Hear tonic.</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td><strong>Gmelina arborea</strong></td>
<td>The roots contain thick yellow colored oil. There is also present resins, alkaloids and benzoic acid. Fruit contains butyric acid and tartaric acid. It also contains alkaloids, sugars, resins and some astringents contents.</td>
<td>Brain tonic, Heart tonic, Piles, Fever, Urinary disorders, Rheumatoid arthritis.</td>
<td></td>
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<tr>
<td>19</td>
<td><strong>Curculigo orchioides</strong></td>
<td>It contains starch 43.48 %, tannins 4.15 %, enzymes 14.18 % and ash 8.6 %. Besides these it also contains glycoside, orcinol-1-O-beta-D-apiofuranosyl-(1--&gt;6)-beta-D-</td>
<td>Tonic, Antipyretic, Aphrodisiac, Carminative, Bronchitis, Lumbago, Gonorrhoea, Diarrhoea, Dyspepsia, Hydrophobia, Ophthalmia.</td>
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<td>20</td>
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<tr>
<td>21</td>
<td><strong>Terminalia chebula</strong></td>
<td>glucopyranoside, curculigoside, syringic acid, curculigoside and curculigoside. The chief constituents of this tannin is Chebulagic acid, Chebulinic acid, Corilagin and gallic acid. Brain tonic, Skin diseases, Eye diseases, Diabetes, Piles, Jaundice, Peptic ulcer, Intestinal parasite, Enlargement of liver and spleen.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td><strong>Citrus medica</strong></td>
<td>main constituents in the distilled lime oil, like the one we sell is a-pinene, b-pinene, myrcene, limonene, terpinolene, 1,8-cineole, linalool, borneol, citral and traces of neral acetate and geranyl acetate. Brain tonic, Cardiac tonic, Asthma, Piles.</td>
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<td></td>
</tr>
<tr>
<td>23</td>
<td><strong>Clitoria ternatea</strong></td>
<td>Brain tonic, Laxative, Diuretic, Alexiteric, Anthelmintic, Corneal ulcer, Elephantiasis, Leucoderma.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td><strong>Rosa centifolia</strong></td>
<td>Main chemical components are citronella, geraniol, neroil, stearopten, farnesol, phenyl ethanol, fatty oil, tannins and organic acids. Brain tonic, Ulcer.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.3.4 Description of plant selected for Nootropic activity

Plate 2.3.4.1 - *Asparagus racemosus*

**Latin name:** *Asparagus racemosus*

**Family:** Liliaceae

**Common names in trade (local and foreign languages)**

Satavari (Sanskrit); Shakakul, Satavari, Chatwal, Satawar (Hindi); Satmuli, Shatarnuli (Bengal); Satavar, Ekalkanto, Satavari, Satawar (Gujarati); Shatavari, Aheruballi, Ashadhi, Satmuli (Kanada); Sejnana (Kashmir); Shatavali, Chatavali, Satavari (Malayalam); Shatavari-mull, Asvel, Shatmuli, Satavari-mull (Marathi); Chhotaru, Mohajolo, Sotabari (Oriya); Tannirvittan-kizhangu, Ammaikodi, Kadumulla, Shimai Shadavari, Kilavari (Tamil); Satavari, Philli-tagga, Challagadda, Pilli-gaddalu (Telugu)

**Chemical Constituents**

*Asparagus* contains steroidal glycosides, bitter glycosides, asparagins and flavonoids. The plant contains four saponins, viz. shatavarin I to IV. Shatavarin IV is a glycoside of sarsasapogenin having two molecules of rhamnose and one molecule of glucose. It also contains mucilage and starch. Recent chemical analyses indicate that the following active constituents are present in Satavari plant: Steroidal saponins, known as
shatavars I-IV. Shatavarin I is the major glycoside with 3 glucose and rhamnose moieties attached to sarsasapogenin Isoflavones including 8-methoxy-5,6,4'- trihydroxyisoflavone 7-O-beta-D-glucopyranoside. Asparagamine, a polycyclic alkaloid Racemosol, a cyclic hydrocarbon (9,10-dihydrophenanthrene) Polysaccharides, mucilage

The Chemical marker is **Shatavarin IV** whose content varies from 0.05%-0.085%.

Uses

The roots are used for its Diuretic Activity, Antitussive Activity, Antibacterial Activity, immunomodulatory activity, Cytoprotective activity, Digestive Activity, Hormonal Activity Antioxytocic Activity, bitter, sweet, emollient, cooling, and nervine Tonic, Constipating,

It is also used traditionally for treating gonorrhea, piles, diabetes, increasing lactation, anathematic (pertaining to a substance capable of destroying or eliminating parasitic worms, esp. human intestinal helminthes), rheumatism, cough, diarrhoea, dysentery, gastric troubles, headache, throat infections, tuberculosis. Generally the root is employed in diarrhoea as well as in chronic colic and dysentery problems. Root boiled with some bland oil, is applied in various skin diseases. Root is boiled in milk and the milk is administered to relieve bilious dyspepsia and diarrhoea
and to promote appetite; root is also used in rheumatism. Tubers are
candied and taken as a sweetmeat. Fresh root juice is given with honey as a
demulcent. Boiled leaves smeared with ghee are applied to boils, smallpox,
etc., in order to prevent their confluence. Juice of this drug taken with milk
is useful in gonorrhoea.

Part of plant used: Tuberous root

Earlier work done on this Plant

AntiUlcer

The cytoprotective effect of the powders of dry fruits of *Terminalia
chebula* and root of *A. Racemosus* was studied on the experimentally induced
acute gastric ulcerations. Duodenal ulcers were produced by infusion of
secretagogues and necrotizing agents induced gastric lesions. A mixture of
the two drugs in a dose of 1.5 g/Kg each orally twice a day for 15 days was
effective in preventing formation of duodenal ulcer and diminishing the ulcer
indexing gastric lesions\textsuperscript{117}.

Galactagogue

The effects of intramuscular administration (250mg/Kg) of the crude
alcoholic extract of the root were studied in post partum, estrogen primed
and non primed rats. The extract increased the weight of mammary glands
in post partum and estrogen primed rats and the uterine weight in estrogen
primed group. The increase in the weight of adrenals coupled with the
depletion of ascorbic acid suggested the release of pituitary ACTH\textsuperscript{118}.
Estrogen-primed rats receiving the extract showed well-developed lobulo
alveolar tissue with milk secretion. The mechanism of action of the extract
may be through a direct action on the mammary gland or through the
pituitary or pituitary adrenal axis.

Antioxytocic

The alcoholic extract of the root exhibited antioxytocic activity. The
saponin-glycoside A4,mp 191-95\textdegree C in doses of 20-50 µg/ml produced a
specific and competitive block of the pitocin syntocinon-induced contraction of rat, guinea pig and rabbit uteri in vitro as well as insitu. The saponin also blocked the spontaneous uterine motility. It was also found that the hypotensive action of syntocinon in cat was unaffected by previous administration of saponin A4.

**Anticancer**

The 50% ethanolic extract of the plant excluding root revealed anticancer activity against human epidermoid carcinoma of nasopharynx in tissue culture. The powdered root extract revealed inhibitory action on DMBA-induced mammary tumourigenesis in rats of Holtzman strain. The mammary tumour incidence showed a sharp decline when virgin female rats, normal or primed with 17-estradiol treatment were put on diets containing 0.25%, 0.5%, 1% or 2% root extract powder for 10 days prior to their exposure to DMBA. There was an increase in the latency period.

**Immunomodulatory activity**

The effect of the pretreatment of the decoction of the root 100mg/Kg/day for 15 days orally was evaluated against E.Coli induced peritonitis in mice. The results indicated 50% mortality at 16h as compared to 100% in the control animals, thus suggesting an immunomodulating property. The immunotherapeutic modulation of intraperitoneal adhesions induced by caecal rubbing by the plant 200mg/Kg as total extract administered orally for 15d in experimental rats was studied. The peritoneal macrophages obtained from normal rats exhibited 32 ± 1.77% phagocytosis while, those receiving the plant extract showed a significant increase in phagocytic activity 53 ± 5.78 % of macrophages. Pretreatment of animals with the plant extract in which surgery was used induce intraperitoneal adhesions and their sacrifice after 15d of surgery showed significant decrease in adhesion scores. This was associated with a significant increase in the macrophage activity 70.1 ± 2.52% compared to that in surgical controls 53.77 ± 10.8%. Animals, which received treatment following
induction of adhesions, also exhibited similar response. The peritoneal macrophages increased to 68.5 ± 4.2%.

**Antiinflammatory**

The decoction of the tuber when fed orally at a dose of 1.5ml per 100g, did not prevent the development of swelling of joints in experimental arthritis produced by formaldehyde injection in rats. The methanolic extract of the root at a doses of 20 and 400 mg/Kg showed maximum inhibition of oedema of 18.6% and 33.7% at 3h with carrageenin and 22.2% and 40.5% at 5h with serotonin-induced rat paw oedema, respectively. The anti-inflammatory activity of the extract was comparable to that of phenylbutazone.

**Antidiabetic**

The dried ethanolic extract 250mg/kg body weight and the inorganic parts 90mg pure ash/kg body weight of the root revealed hypoglycaemic activity in a single dose effect on the oral glucose tolerance test GTT in fasting albino rats.

**Enzyme activity**

The aqueous extracts of fresh and dried root were found to have amylase and lipase activities, the activity being higher in the former. The optimum pH at which these activities could be found were 4 to 5 for α-amylase, 6.9 for β-amylase and 7.4 for the lipase activity. The leaves of the seedling as well as the old plants possessed cholinesterase activity in vivo tests while the branch and roots were devoid of the activity.

**CVS activity**

The aqueous solution of the crude alcoholic extract of the root in a dose of 10-20 mg caused initial increase in force and rate of contraction in isolated frog's heart but a higher dose 40mg caused cardiac arrest. The glycosidal fraction 0.5mg of the plant produced bradycardia and reduction in the force of contraction but with 1-5mg dose, complete cardiac arrest was observed for some time after which the force of contraction was restored to
normal. A high dose i.e 15mg/kg of the crude alcoholic extract produced a fall in blood pressure and depression in the respiration of cat. The hypotensive effect could be antagonized by pretreatment with atropine but not with antihistaminic. In mice and rats, mesenteric capillary circulation became static with topical and intravenous administration of crude alcoholic extract.

**CNS activity**

A preliminary study in rats to evaluate the central dopaminergic effect of the plant, revealed that 1g/kg and 2g/kg of the powdered roots administered orally did not produce catalepsy or sedation.

**Anabolic-Action**

The decoction of the root in a dose of 100 mg/kg bw for a varying period of 4 weeks to 8 months showed growth promoting effects in rats. The decoction treated animals also showed a better weight gain 81.19 % as compared to the control animals 67.9 %. It however, had no effect on the progeny of treated animals. The growth promoting effect was indicative of its anabolic effect and ascribed to its adaptogenic substances.

**Antiallergic**

The alcoholic extract of the root at a dose of 50mg/kg p.o. revealed antiallergic activity as evidenced by inhibition of passive cutaneous anaphylaxis in mouse by 57 % and in rat by 53 %.

**Antispasmodic Activity**

The 50 % ethanolic extract of the plant excluding root in a preliminary biological screening revealed antispasmodic activity on isolated guinea pig ileum and effect on guinea pig heart. The MTD of extract was found to be 1000 mg/kg BW i.p in mice. The 50 % ethanolic extract of the root was found devoid of all activities tested viz., effects on isolated guinea
pig ileum, rat uterus and respiration in experimental animals. The LD$_{50}$ of extract was 1000 mg/kg i.p in mice.

**Antibacterial Activity**

The alcoholic extract of the root was found to possess in vitro antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. However, the aqueous extract was found to be inactive.

The hexane, aqueous and alcoholic extracts of the root at concentration of 200 mg/ml were devoid of any *in vitro* antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Proteus vulgaris*, *Salmonella typhimurium*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* using agarwelldiffusion test.

The juice of the root showed fungi toxicity against three-plant fungi viz., *Helminthosporium sativum* (60.7 %) *Colletotrichum falcatum* (58.2 %) and *Fusarium oxysporum* (60.7%).

The root bark showed marked antibacterial, against eight bacteria viz., *Micrococcus pyogenes var. aureus*, *Bacillus subtilis*, *Diplococcus pneumoniae*, *Streptococcus pyogenes*, *Escherichia coli*, *Salmonella typhosa*, *Vibrio comma* and *Shigella dysenteriae*; antitubercular against two mycobacteria *Mycobacterium phlei* and *Mycobacterium 607*; and antifungal actions against four fungi viz., *Microsporum gypseum*, *Trichophyton mentagrophytes*, *Candida albicans* and *Helminthosporium sativum*.

The methanol fraction of the leaves using the disc diffusion test at a concentration of 4000 and 5000 ppm was found to inhibit *Proteus vulgaris* while it was devoid of any activity against *Escherichia coli*, *Klebsiella aerogenes* and *Pseudomonas aerogenes*.

The fresh juice of the plant showed antibacterial activity against *Staphylococcus*. The extract of the plant showed moderate toxicity against *Rhizoctoniasolanil*. 
**Anthelmintic**

The aqueous extract of the root was lethal or inhibitory, in vitro studies to hatching of Meloidogyne javanica and M. arenaria. A one % solution of the active material contained in the nematicide, Nemaphos O-O-diethyl-O-2-pyrazinyl phosphothionate suppressed hatching in dilutions up to 10,000 times and was comparable to activity of 1ml undiluted plant extract 10 g/100 ml.
2.4 UROLITHIASIS

2.4.1 Pathophysiology of Urolithiasis

Urinary stone disease has afflicted humans from antiquity. There is abundant proof from archaeological discoveries and ancient documents to show that the problem of urinary stone or calculi is one of the oldest diseases known. Bladder stone was found in an Egyptian skeleton more than 7000 years old\textsuperscript{119}.

Symptoms of urinary stone disease vary according to the location and size of the calculi. Kidney stones often move through the urinary tract and leave the body without any symptoms at all. Such stones are referred to as “silent” stones and are usually very small (< 4mm). Larger calculi can not be excreted and even small ones can cause problems by becoming lodged in the ureter, the long narrow tube that carries urine from the kidney to the bladder.

When calculi become lodged in the urinary tract they can cause irritation or blockages. The calculi cause the urinary tract to go into spasm, a condition known as renal colic causing severe cramping pain felt in the back and the side and sometimes in the lower abdomen. Eventually, pain may spread to the groin.

Irritation of the urinary tract often causes frequent urination. Blockages may result painful micturition. Hematuria is also common indicating that a stone is trying to move through the narrow ureter.

In addition to renal colic, hematuria and frequent urination symptoms like nausea, vomiting, burning sensation while urinating, fever and chills are seen\textsuperscript{120}.

EPIDEMIOLOGY:

Andersen (1973) classified the epidemiological factors involved in the genesis of urinary calculi into two factors
1. Extrinsic factors

2. Intrinsic factors

1. **Extrinsic Factors:**

These are also called environmental factors. The factors responsible for stone formation are

- Geography
- Climatic and seasonal factors
- Water intake
- Diet /Nutrition
- Occupation

**Geography:**

Geographical variations has significant impact in the incidence and type of calculi. Urolithiasis is a common disorder affecting 1-5% of the population in industrialized countries\textsuperscript{121}. Many scientists and their co-workers agreed that the areas of highest incidence of urolithiasis in the United States are the North-West the South East and the arid South West\textsuperscript{122}. Other areas of high incidence are the British Isles and Scandinavian Countries. Mediterranean countries, Northern India, Pakistan, Northern Australia, Central Europe, portions of the Malayan Peninsula and China\textsuperscript{123}.

In addition to the variations in the incidence of urinary calculi, differences are also noted in the types of urinary stone disease in various regions of the world. Stones from Great Britain, Scotland and Sudan are mainly composed of mixed calcium oxalate and calcium phosphate. In India, a high incidence of urolithiasis is predominant in North and North-Western regions\textsuperscript{124}.

**Climatic and seasonal factors:**

Several studies show a relationship between higher environmental temperature and higher seasonal incidence of urinary stone disease. Increased mean environmental temperature seems to be related to increased
incidence of urinary calculi. Similarly, a decrease in the number of calculi was noted during cool periods of climate\textsuperscript{125}.

**Water intake:**

Increased water intake and increased urinary output decrease the incidence of urinary calculi in population liable to the formation of stones. Mineral content of water may also contribute to the formation of stones. Excessive water hardness for example calcium sulphate in some states contributes to calculi, whereas in other states excessive softness for example sodium carbonate also causes a greater incidence of stone disease\textsuperscript{126}.

**Diet / Nutrition:**

Nutritional factors play a strong role in the incidence and recurrence of renal stones. Higher intake of animal protein\textsuperscript{127} ketogenic diet, fat, sugar, oxalates, Vitamin D, calcium, phosphorous\textsuperscript{128} and salt increases the incidence of stone formation. Deficient intake of fluids, Vitamin B\textsubscript{6}, Vitamin C, Vitamin A, potassium and L-glutamic acid leads to the formation of calculi\textsuperscript{129}.

**Occupation:**

Occupation was also found to have an important role in kidney stone formation. Urinary calculi are much more likely to be found in individuals who have sedentary occupation. Weightlessness contributes to increased risk for renal stone formation in astronauts involved in a space flight. Coppersmiths and workers in cadmium battery industries have shown significant dose-related risk of renal stone formation\textsuperscript{130}.

2. **Intrinsic Factors:**

Intrinsic factors are related to the inherited bio-chemical or anatomic make up of an individual. These include
• Genetic factors
• Age
• Sex
• Diseases
• Drugs Intake

Genetic Factors:

Genetic factors appear to be more prominent in whites as opposed to African Americans. Stone formers report more frequent episodes of stone formation in their family members, particularly father and brothers than do non-stone formers\textsuperscript{131}.

Age:

Risk of stone formation increases with age. The incidence of stone formation in India is rare below the age of 18 years. Urolithiasis in the pediatric age group, although occurring less often than in adults causes considerable morbidity\textsuperscript{132}. 

Sex:

Urinary stones occur more often in males with a males to female ratio of 3:1. Pure calcium oxalate stones were more frequent in male than in females. Some studies have suggested that this difference is due to variation in citrate excretion, because the 24 hours urinary citrate excretion was found to be, higher in women than men\textsuperscript{133}. It has been reported that men have higher urinary excretion of oxalate than women. The lower serum testosterone levels may contribute to some of the protection in women and children against oxalate stone disease.

Disease Conditions:

Renal stone formation appears to be higher than normal in children and adults with Cushing’s syndrome, elevated levels of parathyroid hormone increases the incidence of stone formation. Sarcoidosis and other granulomatous diseases, osteoporosis, inflammatory bowel disease, gout and
hyperuricemia increases the incidence of kidney stones. Persons with recurrent urinary tract infections are more susceptible for kidney stones\textsuperscript{134}. 

**Drugs Intake:**

Excessive antacid use has been reported to induce hypophosphatemia, hypercalciuria and elevated plasma 1, 25-dihydroxy Vitamin D, all contributing to the increased incidence of renal stones. Long term ingestion of oral contraceptives reduce Vitamin B\textsubscript{6} levels, Protease inhibitors for HIV induce renal stone formation. Long term use of some diuretics like triamterene has also been known to contribute to urolithiasis. Sulfonamides and carbonic anhydrase inhibitors cause urolithiasis up to 1.6\%\textsuperscript{135}.

**TYPES OF STONES AND INCIDENCE:**

Urinary stones are polycrystalline aggregates composed of varying amounts of crystalloid and organic matrix. 80-85\% of all urinary stones are calcium based.

**Table 2.4.1- Types of Stones and Incidence**

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>% of Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure calcium oxalate stones</td>
<td>33%</td>
</tr>
<tr>
<td>Mixed calcium oxalate and phosphate</td>
<td>34%</td>
</tr>
<tr>
<td>Struvite</td>
<td>15%</td>
</tr>
<tr>
<td>Uric acid</td>
<td>8%</td>
</tr>
<tr>
<td>Pure calcium phosphate stones</td>
<td>6%</td>
</tr>
<tr>
<td>Cystine</td>
<td>3%</td>
</tr>
<tr>
<td>Artifacts and others</td>
<td>1%</td>
</tr>
</tbody>
</table>

Other less commonly found stones are xanthine and silica stones.

**Calcium stones:**
Calcium urinary lithiasis is associated with hypercalciuria or hyperoxaluria. Urinary calcium stones occur in the form of calcium oxalate, calcium phosphate or as mixed calcium oxalate and calcium phosphate stones\textsuperscript{136}.

**Hypercalciuria:**

Absorptive hypercalciuria is present in 50-60\% of patients with calcium oxalate stones. These patients exhibit elevated levels of urinary calcium. These patients are believed to have an altered intestinal response to Vitamin D that causes increased absorption of calcium a condition known as absorptive hypercalciuria and elevated serum calcium levels and depression of parathyroid function with the result that increased amounts of calcium are delivered to the kidney and excreted in the urine \textsuperscript{137}.

**Renal hypercalciuria:**

It occurs when the kidney is unable to conserve calcium\textsuperscript{137}.

**Resorptive hypercalciuria:**

It is found primarily is patients with hyperparathyroidism and excessive parathormone secretion, which stimulates bone resorption and increases intestinal absorption of calcium, both of which contribute to hypercalciuria \textsuperscript{138}.

**Hyperoxaluria:**

In humans, oxalate appears in urine from two sources. One is endogenous production by means of glycolic acid oxidase. By the action of this enzyme glyoxylate get converted to oxalic acid\textsuperscript{139}. Second source is absorption of excess oxalate via gut from foods like almonds, plums, raspberries, spinach etc., and liquids like apple juice, beer, coffee, cola, grape fruit juice, cocoa, tea etc.,\textsuperscript{140}.

**Struvite Stones:**

Struvite stones contain a crystalline substance composed of Magnesium ammonium phosphate. These stones are produced in urine with
a pH greater than 7.2 and ammonia in urine, produced by urease producing bacteria, such as *Proteus* species\(^{141}\). Infection with this bacteria capable of producing the enzyme urease raises urinary pH.

\[
\text{NH}_2\text{CONH}_2 \rightarrow 2\text{NH}_3 + \text{H}_2\text{CO}_3
\]

Thus the concentration of OH\(^-\), NH\(_4^+\), CO\(_3^-\) and urinary pH are elevated to a degree that induces crystallization for struvite stones\(^{142}\).

**Uric acid stones:**

Chemically uric acid stones are uric acid anhydrate and uric acid dehydrates. The principle cause of uric acid crystallization is the supersaturation of urine with respect to undissociated uric acid\(^{143}\). Stone formers maintain a constant urinary pH in the acidic range (5-5.5). A low urine volume also can lead to over saturation with uric acid and can increase the incidence of uric acid stone formation\(^{144}\).

**Cystine Stones:**

Cystine stones occur in patients with cystinuria. It is an inherited defect in renal tubular and intestinal transport of dibasic aminoacids resulting in elevated urinary excretion of cystine and other amino acids and leading to development of urinary tract cystine calculi.

**Xanthine Stones:**

Xanthine stones are rare and occur only in disorders like hereditary xanthinuria and also in patients treated with allopurinol, a xanthine oxidase inhibitor which blocks conversion of xanthine to uric acid.

**Miscellaneous stones:**

Stones that occur rarely include dihydroxy adenine, matrix calculi and ammonium uric acid calculi\(^{145}\).
THEORIES OF STONE FORMATION:

Urinary calculous disease may be separated conveniently into four major theories\textsuperscript{146}.

a. Supersaturation / Crystallization theory

b. Matrix nucleation theory

c. Inhibitor absence theory

d. Epitaxy

Urolithiasis is a consequence of complex physical processes and it appears to be multifactorial. The major factors are supersaturation and crystallization, inhibitors, complexors, promoters, and matrix. No single theory can explain the stone formation satisfactorily. A combined approach can be postulated to explain the pathogenesis of urolithiasis\textsuperscript{147}.

Urinary Saturation:

Stones form in urine that is supersaturated with respect to the ionic components of the specific stone and saturation is dependent on chemical free ion activities. The chemical free ion activities of the components of a stone, in a solution in which the stone will neither grow nor dissolve, is at the “equilibrium solubility product”. A decrease in the free ion activity will not grow and may even dissolve. An increase in the free ion activity will cause the urine to become supersaturated, a state that would favour a stone to form or increase in size\textsuperscript{148}.

The chemical free ion activities of the components of the stone are influenced by many factors including the concentration of the relevant ions, urine pH and complexation with substances in the urine. The chemical free ion activity is directly related to ion concentration. Ion concentration is a function of how much of the particular ion is excreted in the volume of urine. Increased urinary ion excretion and decreased urine volume will both increase free ion activity and favour stone formation and growth. Urine pH is
particularly important with respect to uric acid supersaturation. Citrate forms soluble complexes with calcium and will thus reduce its free ion activity.

Kidney stones, consists of approximately 98% crystalline material. The formation of kidney stones is a result of a complex biologic process that involves crystallization. Kidney stones do not consist of crystal alone, since biomineralization requires an organic material on which the mineral is deposited. Infact, loosely clustered crystals would not become a dense stone if they were not tightly glued together by some organic material. This matrix accounts for about 2% of the weight of a stone and is found is concentric layers throughout the stone\textsuperscript{149}.

Chemical analysis of the matrix has proved to be unrewarding, because the dissolution of the stone for analysis requires aggressive procedures, such as acid hydrolysis. Thus, most of what is known about the composition is based on the substances found soluble in urine. The matrix is believed to be composed predominantly of protein, with small amounts of non amino sugars, glucosamine, water and organic ash.

The formation of crystals in urine is largely a function of supersaturation. A solution that contains any salt at a concentration above the salt’s solubility is said to be supersaturated. Supersaturation often is expressed as the ratio of a dissolved materials to it’s solubility concentration it’s solubility concentration has a super- saturation of 1. In tubular fluid and urine, the supersaturation may rise to between 2 and 8 without new solid phase formation. Such a solution is called metastably supersaturated. If a solid phase is placed is to metastable solution, crystalline growth of the particle occurs.

At supersaturation values above the metastable upperlimit, crystals will form spontaneously, a process called nucleation. Once nucleation occurs, the kinetic phase, characterized by growth and aggregation, proceeds. If the supersaturated solution is the tubular fluid or urine, the result is the spectrum of crystalluria, gravel, stones and nephrocalcinosis\textsuperscript{149}. 
Stone formation and growth:

Kidney stones can form and increase in size through either homogenous or heterogeneous nucleation\textsuperscript{150}. During homogenous nucleation, increasing chemical free ion activity leads to supersaturation with respect to a solid phase. Once this supersaturation reaches the “formation product”, the ions form clusters that can increase in size to form a permanent solid phase. With heterogeneous nucleation, crystal growth occurs on the surface of a dissimilar but complementary crystal or on another, generally foreign substance. \textit{In vivo}, heterogeneous nucleation predominates over homogenous nucleation because the presence of a solid phase allows for crystal growth at a lower level of supersaturation, a so-called “metastable solution”. Microscopic crystals take longer to grow into clinically significant stones than the calculated passage time for fluid through the renal tubule. Crystals appear to adhere to tubular cells allowing time for further growth.

Urine from stone formers generally is more supersaturated than urine from non-stone formers\textsuperscript{151}. However, despite similar degrees of supersaturation, some people form stones, whereas others do not this may be due to the presence of inhibitors of crystallization. Citrate, uropontin, nephrocalcin and pyrophosphate inhibit the formation of calcium-containing crystals\textsuperscript{152}. Although some studies have shown a decrease in inhibitor activity when the urine of stone forming patients is compared with that of control subjects, the influence of abnormalities in the composition or amount of inhibitors in the occurrence or frequency of stone formation has not been determined.

Clinicians generally determine a patient’s potential for stone formation by measuring the rates of urine solute excretion in mass per unit time, of the principal components of stones. However, it is clear that the critical determinant for crystallization is urine-supersaturation and not the absolute quantity of ions excreted over period of time. Computer programs are now available, such as EQUIL, that calculate saturation from measured
concentrations and should be used for a more accurate determination of the lithiasis risk\textsuperscript{153}. Even with sophisticated calculations of saturation, variations in hourly urine output of both water and solute dictate that any mean collection will be an underestimation of the maximum supersaturation\textsuperscript{154}.

### 2.4.2 Drug treatment for Urolithiasis

Management of Urolithiasis is of 3 types

1. Diet
2. Surgical
3. Medical

**1. Management with Diet:**

With intake of ten grams of rice bran b.i.d reduced recurrence up to 84% and stone free up to 61% was observed.

Daily ingestion of 2 litres of lemonade which included 120ml of reconstituted lemon juice has been shown to double citrate excretion in nephrolithiasis\textsuperscript{155}.

Incidence of stone formation was 32% in those ingesting 1.5gm or more daily dose of Vitamin C compared to those with intakes of less than 250mg daily \textsuperscript{156}.

The decreased risk of stone formation was observed in women taking vitaminB\textsubscript{6} upto 25mg daily, which may be attributed to decreased oxalate production.

Preincubation of erythrocytes with eicosapentanoic acid dose dependently decreased the phosphorylation level of band 3 protein, which mediates erythrocyte oxalate flux and decreases transmembrane oxalate self-exchange. This has indicated that nutritional changes in membrane
phospholipids fatty acid composition play a crucial role in modulating cellular oxalate transport in idiopathic calcium oxalate stone formation\textsuperscript{157}.

Nephrolithiasis induced by calcium injections in animals is prevented by concomitant treatment with fish oil (omega-3-oils). Urinary calcium and oxalate excretion in hypercalciuric and hyperoxaluric stone forming men treated with fish oil for 8 weeks was reduced by 40\% and 50\% respectively\textsuperscript{158}.

Administration of glycosaminoglycans 30mg for 15 days in 40 idiopathic calcium oxalate stone formers had significantly reduced, urinary oxalate concentrations as well as improved erythrocyte oxalate self-exchange. These changes reverted to their baseline levels in 15 days after treatment\textsuperscript{159}.

Anthraquinones at levels less than those which produce laxative effects had shown to bind calcium and reduce formation of calcium crystals\textsuperscript{160}.

2. Surgical management:

Surgery should be reserved as an option for cases when other approaches have failed. Surgery may be needed to remove a kidney stone if it

- Does not pass after a reasonable period of time and causes constant pain.
- Is too large to pass on its own or is caught in a difficult place.
- Blocks the flow of urine.
- Causes ongoing urinary tract infection.
- Damages kidney tissue or causes constant bleeding.
- Has grown larger. (as seen on follow up X ray studies).

Until 20 years ago, surgery was necessary to remove a stone. It was very painful and required a recovery time of 4 - 6 weeks. Today treatment for these stones is greatly improved and many options do not require major surgery.
**Extracorporeal Shock Wave Lithotripsy (ESWL):**

ESWL is the most frequently used procedure for the treatment of kidney stones. In ESWL shock waves that are created outside the body travel through the skin and body tissues until they hit the denser stones. The stones breakdown into sand like particles and are passed through the urinary tract in the urine. There are several types of ESWL devices. In one device, the patient reclines in a water bath while the shockwaves are transmitted. Other devices have a soft cushion on which the patient lies. Most devices use either x-rays or ultrasound to help the surgeon to pinpoint the stone during treatment. For most types of ESWL procedures, anesthesia is needed.

**Complications:**

1) Blood in urine for few days after treatment.
2) Bruising and minor discomfort in the back or abdomen.

**Percutaneous Nephrolithotomy:**

This treatment is often used when the stone is quite large or in a location that does not allow effective use of ESWL. In this procedure, the surgeon makes a tiny incision in the back and creates a funnel directly into kidney using an instrument called a nephroscope. The surgeon locates and removes the stone. For large stones, some type of energy probe (ultrasonic or electrohydraulic) may be needed to break the stone into small pieces. Generally patients stay in the hospital for several days and may have a small tube called a nephrostomy tube left in the kidney during the healing process^161^.

One advantage of percutaneous nephrolithotomy over ESWL is that the surgeon removes the stone fragments instead of relying on their natural passage from the kidney.
**Ureteroscopic stone removal:**

Although some kidney stones in the ureters can be treated with ESWL. Ureteroscopy may be needed for mid and lower ureter stones. No incision is made in this procedures, instead, the surgeon passes a small fiberoptic instrument called a ureteroscope through the urethra and bladder into ureter. The surgeon then locates the stone and either removes it with cage-like device or shatters it with a special instrument that produces a form of shock wave. A small tube or stent may be left in the ureter for a few days to help the lining of the ureter heal. Before fiberoptics made ureteroscopy possible, physicians used a similar “blind basket” extraction method. But this is outdated technique should not be used because it may damage the ureters\(^1\).

3. **Medical management:**

The drug selection depends mainly upon the associated metabolic disorder and the type of urinary calculi.

First step in the management of acute renal colic is to alleviate the patient's pain with analgesics such as oxycodone, morphine derivatives and NSAIDS.

**Treatment for calcium oxalate stones:**

Thiazide diuretics like Hydrochlorothiazide 50mg twice a day has been effective in preventing stone formation in patients with hypercalciuria and type-I absorptive hypercalciuria\(^2\).

Orthophosphates 2gm, three times a day have been effective in preventing reabsorptive hypercalciuria. The mechanism of action is by decreased intestinal absorption of calcium, increased pyrophosphate excretion and urinary acidification\(^3\).
Cellulose sodium phosphate is useful in the treatment of type-I absorptive hypercalciuria. This binds with calcium and decreases calcium absorption\textsuperscript{164}.

Ingestion of 300-600mg magnesium daily were reported to be stone free in 89\% of patients after 6 years of the study. Mg acts by increasing the solubility of calcium oxalate in urine\textsuperscript{165}.

Magnesium citrate equivalent to 480mg of elementary Mg and potassium citrate of 500-1000mg appears to reduce urinary saturation of calcium oxalate and calcium phosphate and retards calcium crystal development by chelation\textsuperscript{166}.

Potassium citrate is used to prevent hypocitraturia, hyperuricosuria and enteric hyperoxaluria. It is also recommended for the treatment of homozygous cystinuria. It acts as alkalinizing agent.

**Treatment for struvite stones:**

Acetohydroxamic acids with antibiotics are preferred as they inhibit urease splitting organisms and prevent breakdown of urea into ammonia.

Renacidin, a buffer consisting of citrate and gluconate was effective in dissolving struvite stones\textsuperscript{167}.

**Treatment for uric acid stones:**

Alkalization of urine with bicarbonate or a bicarbonate precursor such as citrate should be used\textsuperscript{167}. If nocturnal urinary pH falls, then acetazolamide may be administered. Allopurinol can be added if these measures in combination are not successful in reducing super saturation and stone formation.

**Treatment for cystine stones:**

Tiopronin or d-pencillamine will both bind cystine and reduce urinary supersaturation.
### 2.4.3 PLANTS SHOWING ANTIUROLITHIATIC ACTIVITY

Table 2.4.3.1- Plants showing Antiurolithiatic activity

<table>
<thead>
<tr>
<th>S.No</th>
<th>PLANT NAME</th>
<th>CHEMICAL CONSTITUENTS</th>
<th>OTHER USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Bergenia ligulata</em></td>
<td>Bergenin, leucocyanidin, gallic acid, methyl gallate, catechin, sterols, sitosterol,</td>
<td>Antiinflammatory, antiurolithiatic, antiviral, diuretic, analgesic, antibacterial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><em>Crataeva nurvala</em></td>
<td>Triterpenoids lupeol and varunol have been isolated from the roots and stem bark. Leaves</td>
<td>Hepatoprotective, Antibacterial, Anticomplement, Antiurolithiatic, Antifertility, Antiinflammatory.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>yield flavonoids including rutin, quercetin and isoquercetin.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><em>Tribulus terrestris</em></td>
<td>Steroidal saponins viz., terrestrosins A, B, C, D and E, desgalactotigonin, F-gitonin,</td>
<td>Cytoprotective, Steroidal, Diuretic, Antiurolithiatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydrolysed products include diosgenin, hccogenin, neotigogenin, Alkaloids, β-sitosterol,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>stigmasterol.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><em>Cicer arietinum</em></td>
<td>Gama galactine, para-galactoaraban, betaine, biochaninA, B, and C.</td>
<td>Purgative, Abortifacient, Bronchitis, indigestible, tonic, Aphrodisiac, Expectorant, Hyperdipsia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Burning sensation, Splenohepatomegaly, Leprosy, Inflammation, Skin diseases.</td>
</tr>
<tr>
<td>5</td>
<td><em>Aerva lanata</em></td>
<td>Canthin-6-one, aervine, methyl</td>
<td>Astringent, Bitter, Cooling, Emollient,</td>
</tr>
<tr>
<td>No.</td>
<td>Species</td>
<td>Active Constituents</td>
<td>Medicinal Uses</td>
</tr>
<tr>
<td>-----</td>
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<td>-----------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>6</td>
<td><em>Alternanthera sessilis</em></td>
<td>aervine, aervoside, aervolanine.</td>
<td>Vermifuge, Suppurative, Diuretic and lithontriptic, cephalalgia, cough, strangury.</td>
</tr>
<tr>
<td>7</td>
<td><em>Cyclea peltata</em></td>
<td>Carotene, B-carotene, ricinoleic acid, myristic, palmitic, stearic, oleic and linoleic acids, a-spiraterol, uronic acid, and B-sitosterol, phenolic acid and flavonoids.</td>
<td>Bitter, Astringent, Constipating, Depurative, Digestive, Galactogogue, Febrifuge, Diarrhoea, Leprosy, Skin disease, Haemorrhoids, Agalactia, Splenomegaly and fever.</td>
</tr>
<tr>
<td>8</td>
<td><em>Coleus aromaticus</em></td>
<td>Carotene, B-carotene, ricinoleic acid, myristic, palmitic, stearic, oleic and linoleic acids, a-spiraterol, uronic acid, and B-sitosterol, phenolic acid and flavonoids.</td>
<td>Thermogenic, Digestive, Carminative, Antihelminthic, Constipating, Antiinflammatory, Depurative, diuretic, Bronchitis, Painful swellings, leprosy, ulcers, wounds, Cardiac disorders.</td>
</tr>
<tr>
<td>9</td>
<td><em>Trigonella foenum-graecum</em></td>
<td>Carotene, B-carotene, ricinoleic acid, myristic, palmitic, stearic, oleic and linoleic acids, a-spiraterol, uronic acid, and B-sitosterol, phenolic acid and flavonoids.</td>
<td>Aromatic, carminative, emmenagogue, diaphoretic, tonic, stimulant, dyspepsia, asthma, chronic coughs, bronchitis, colic, flatulence, rheumatism.</td>
</tr>
<tr>
<td>10</td>
<td><em>Anacardium occidentale</em></td>
<td>Galactomannans, trigonellin, mucilage, coumarins, tannic acid, diosgenin, trigocoumarin.</td>
<td>Swellings, Burns, mucilaginous, aromatic, carminative, Thermogenic, galactogogue, Astringent, Emollient, anaphrodisiac, ulcers, veterinary medicine, Antibacterial.</td>
</tr>
<tr>
<td>11</td>
<td><em>Ananas comosus</em></td>
<td>Galactomannans, trigonellin, mucilage, coumarins, tannic acid, diosgenin, trigocoumarin.</td>
<td>Purgative, treatment of snakebite, ulitis, leprosy, ulcers, thermogenic, aphrodisiac, antihelminthic, haemorrhoids, anorexia.</td>
</tr>
<tr>
<td></td>
<td><strong>Basella alba</strong></td>
<td>Iodine, fluorine, carotenoids, organic acids, vitamin K</td>
<td>Sedative, appetizer, urolithiasis, diuretic, aphrodisiac, ulcers.</td>
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<td></td>
<td><strong>Anethem graveolens</strong></td>
<td>The main chemical components of dill oil are d-carvone, dillapiol, dhc, eugenol, limonene, terpinene and myristicin.</td>
<td>Digestive, carminative, stomachic, antihelminthic, anodyne, anti-inflammatory, diuretic, expectorant, cardiotonic, amenorrhoea, hiccoughs, asthma, bronchitis</td>
</tr>
<tr>
<td></td>
<td><strong>Bambusa aruninacea</strong></td>
<td>Silica 90%, silacum, potash, lime, alumina, cholin, betain, hydrate of silicic acid, nuclease, urease, proteolytic enzyme, cyanogentic glucoside and an alkaloid.</td>
<td>Astringent, laxative, depurative, diuretic, leprosy, skin diseases, burning sensation, discolorations, strangury, ring worm, ulorrhoea, arthralgia, general debility, emmenagogue, ophthalmic, febrifuge, vulnerary, constipation, gonorrhoea, amenorrhoea, dysmenorrhoea, wounds, skin diseases, fever, carminative, anthelmintic, flatulence, alexeteric, aphrodisiac &amp; tonic.</td>
</tr>
<tr>
<td></td>
<td><strong>Benincasa lispida</strong></td>
<td>B-sitosterol, amino acids, mucin, cucurbitine, acid resins.</td>
<td>Anti ulcer, bronchodilator, hypoglycemic, urolithiasis, antioxidant.</td>
</tr>
<tr>
<td></td>
<td><strong>Blumea lacera</strong></td>
<td>Scineol, fenchone, blumea camphor, campesterol, flavones</td>
<td>Anti-inflammatory, urolithiatic, antispasmodic, diuretic, astringent.</td>
</tr>
<tr>
<td></td>
<td><strong>Boerhaavia diffusa</strong></td>
<td>B-sitosterol, palmitic acid, urosilic acid, arachidic acid</td>
<td>Antiasthmatic, astringent, appetizer, Anti-inflammatory.</td>
</tr>
<tr>
<td></td>
<td><strong>Boswellia serrata</strong></td>
<td>Boswellic acid, essential oils, gums, resins, B-sitosterol, lignin and terpinoids.</td>
<td>Urolithiatic, diarrhea, diuretic, Anti-inflammatory, urinary tract infections, Anti ulcer, aphrodisiac.</td>
</tr>
<tr>
<td></td>
<td><strong>Caesalpinia sappan</strong></td>
<td>Gallic and tannic acid, haematein, phellandrene</td>
<td>Anti-tuberculosis, atonic, dysentery, skin infections, antiulcers, anaemia</td>
</tr>
</tbody>
</table>
2.4.4 Description of plants selected for Antiulcer activity:

1. *Macrotyloma uniflorum*

   Plate 2.4.4.1 - *Macrotyloma uniflorum*

   Botanical name: *Macrotyloma uniflorum*

   Family : Fabaceae

   **Vernacular names**

<table>
<thead>
<tr>
<th>Language</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>horsegram, Madrasgram</td>
</tr>
<tr>
<td>Transcribed Chinese</td>
<td>yingpidou</td>
</tr>
<tr>
<td>French</td>
<td>dolicbiflore</td>
</tr>
<tr>
<td>German</td>
<td>Pferdebohne</td>
</tr>
<tr>
<td>India</td>
<td>kulthi</td>
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<tr>
<td>Portuguese</td>
<td>faveira</td>
</tr>
<tr>
<td>Tamil</td>
<td>Kollu</td>
</tr>
<tr>
<td>Kerala</td>
<td>kuthira</td>
</tr>
<tr>
<td>Andhra pradhesh</td>
<td>Ulavalu</td>
</tr>
</tbody>
</table>
**Geographical distribution:**

_Africa:_ Angola, Botswana, Democratic Republic of Congo (Zaire), Ethiopia, Kenya, Mozambique, Namibia, Rwanda, Somalia, South Africa (Transvaal), Sudan, Tanzania, Uganda, Zimbabwe. _Asia:_ Bhutan, China, India, Indonesia (Java), Nepal, Pakistan, Philippines, Sri Lanka, Taiwan. _Australasia:_ Australia.

**Chemical constituents:**

Natural phenols are mostly phenolic acids, namely, 3, 4-dihydroxy benzoic, p-hydroxy benzoic, vanillic, caffeic, p-coumaric, ferulic, syringic and sinapic acids, high protein.

**Medicinal uses:**

To treat renal stones, piles, edema, astringent, treating and controlling skin rashes and boils, to regulate fever, reducing weight, lowering cholesterol levels, peptic ulcer, reducing flatulence.

**Earlier work done on this Plant:**

1) Total phenolics and the antioxidative properties of two varieties of horse gram (_Macrotyloma uniflorum_) were studied. The raw and dry-heated seed samples were extracted successively with methanol and 70% acetone separately. After removing the solvents, the extracts were freeze-dried. The black seeds contained relatively high levels of total phenolics and tannins than the brown seeds with respect to the treatments and solvents extraction\(^1\). The DPPH radical and ABTS cation radical-scavenging activities were well proved and related with the ferric-reducing/antioxidant capacity of the extracts.

2) Investigation was done on _Macrotyloma uniflorum_ (Lam.) Verdc. against _Aedes aegypti_ (L.) larvae. _Macrotyloma uniflorum_ α-amylase inhibitor (MUAI) was partially purified using ion exchange chromatography on a carboxymethyl cellulose column. MUAI at concentrations of 20, 60, 100 and 200 ppm was tested against different instar larvae, pupae and adults of _A._
aegypti to establish its bioefficacy\textsuperscript{169}. MUAI showed a strong larvicidal and a moderate adulticidal effect at a concentration of 200 ppm but did not exhibit pupicidal and ovicidal activities. MUAI-treated larvae showed lower α-amylase activity. MUAI also exhibited ovipositional deterrence activity. Dose-dependent mortality was observed, being highest in the first and second instar larvae.

3) \textit{M. uniflorum} cv. VZM1 seedlings grown in Petri dishes were unstressed or stressed by adding 5, 10 or 20% polyethylene glycol 6000. After 7 d, root and shoot activities of nitrate reductase and glutamine synthetase were decreased by stress, whereas activities of NAD and NADP dependent glutamate dehydrogenase, alanine aminotransferase and aspartate aminotransferase were increased\textsuperscript{170}. Ammonia concentration increased, and glutamine concentration decreased, in stressed plants.

\subsection*{2. \textit{Melia azadirachta}}

Plate 2.4.4.2 - \textit{Melia azadirachta}

Botanical Name: \textit{Melia azadirachta}

Family : Meliaceae
Vernacular names

Bengali : bakarjan, ghora nim, mahanim, mahnim
Cantonese : mindi kechil
English : azedarach, bead tree, China berry, China tree, Persian lilac, India, syringa
Filipino : bagaluña, balagañgo, paraiso
Hindi : bakain, bakarja, betain, deikna, dek, drek, mallan nim
Indonesian : gringging, marambung, mindi
Nepali : bakaina, bakaino, bakena
Sanskrit : mahanimba
Spanish : Alilaila, Arbol enano, Lila, Lilayo, mal kohomba, Paraíso, Violeta
Swahili : mmelia, mwarubaini nusu
Tamil : malai vembu, mallay vembu, puvempu
Thai : khian, lian, lian-baiyai
Tigrigna : melia

Geographical Distribution:

Catechin, p-coumaric acid, ferulic acid, quercetin, epicatechin, kaempferol, gallic acid, (-) epicatechin, and the respective calibration straight lines (absorbency 280 nm).

Chemical Constituents:

Branched chain paraffin alcohol, C_{26}H_{54}O, nimbosterol, sugiol and a new ketophenol, nimbiol, β-sitosterol, catechin, p-coumaric acid, ferulic acid, quercetin, epicatechin, kaempferol, gallic acid, (-) epicatechin

Medicinal uses:

Pesticidal, nematicidal, fungicidal, bactericidal, anti inflammatory, anti-tumor and other properties.
Earlier work done on this Plant:

1) The effect of the water extract of *Melia azedarach* L. (Meliaceae) leaves on human complement and polymorphonuclear leukocytes was investigated. This extract showed a strong anticomplementary activity, which was more pronounced in the classical pathway assay. The extract did not affect the phagocytic activity of polymorphonuclear leukocytes, nor the respiratory burst of these cells as measured by the nitro blue tetrazolium reduction assay.

2) The antifungal activity of *Melia azedarach* L. leaves was investigated against *Ascochyta rabiei* (Pass.) Lab., the cause of destructive blight disease of chickpea (*Cicer arietinum* L.). Bioassay guided fractionation revealed that the chloroform fraction of the methanolic extract of *M. azedarach* leaves was highly effective against *A. rabiei*. Six compounds, namely β-sitosterol (1), β-amyrin (2), ursolic acid (3), benzoic acid (4), 3,5 dimethoxybenzoic acid (5) and maesol (6) were isolated from the chloroform fraction through column chromatography. The *in vitro* antifungal activity of compounds 2–5 was evaluated against *A. rabiei*. A commercial fungicide, mancozeb, was used as a positive control.