INTRODUCTION

- Introduction to medicinal plants

- The man has been blessed by the Mother Nature with a rich resources of remedies to cure all ailments of mankind. The knowledge of traditional medicines has accumulated over thousands of years as a result of man’s hunt for acquiring the knowledge from nature so that today he possess many effective means of treatments for various diseases ensuring good health. The history of herbal medicines dates back to human civilization on earth. The available documents, which are of great knowledge since ages and reveals that plants were used as medicines in China, India, Egypt and Greece long before the beginning of the Christian era.

- In India nature is the prominent source for Ayurvedic medicines in the crude form which includes mainly dried herbal products or their extracts or mixtures of products. Other alternative traditional systems of treatment are being practiced for many centuries in most part of the world and apart from these alternative systems there has been a rich heritage of ethno botanical usage of natural sources by various tribal communities in India.

- It is believed that Ayurveda has originated from Vedas which were compiled by Aryans (1500-800 BC) and the Vedas are the informative sources for the systematic usage of medicinal plants for various therapeutic applications. Rigveda, which is believed to be written between 4500 – 1500 BC is one of the oldest document of human knowledge on earth related to the usage of 67 medicinal plants for the therapeutic applications. Yajurveda discusses the applications of 81 medicinal plants and Atharvaveda which was written in 1200 BC provides a list of 290 plants for therapeutic applications.
The medicinal plants have been used as drugs in conventional medicine system for several thousand years and they are time tested. Information about applications of medicinal plants has been accumulated in the course of many centuries. It is reported that more than 2500 plant species serve as sources of medicines. During the few centuries there has been an increasing awareness about medicinal plants utilization in different parts of the world.

In the present modern world, plants have been used as source of medicines for various diseases as an alternative to or in combination with modern medicines. The majority of the population in developing countries today depends on herbal medicines to satisfy their health requirements, due to different reasons like traditional knowledge, economy and skilled practices inherited from their ancestors. The World Health Organization (WHO) estimated that about 70% of the world population depends on plants and plant products for medicinal requirement and they are widely used in Asia, South America and Africa.

Plants continue to be used world-wide for the development of novel lead molecules from their chemical constituents through research and also for the treatment of various diseases. In the developed countries, high-through put screening methods are practiced for bioactivity-guided fractionation and isolation of active constituents that may be developed into new lead molecules either from the natural sources or semi synthetic approach or a totally new synthetic analogue of chemical constituent with enhanced biological activity and/or reduced adverse side effects.

India is considered as golden hub for variety of medicinal plants due to their availability and their extracts were used in Ayurveda, Siddha and Unani for treatment of different types of diseases. Few of the medicinal plants have been reported to be evaluated scientifically for pharmacological potency due to the phytoconstituents.
Introduction present in them. A natural constituent from medicinal plant can act both as preventive and curative drug by boosting up the health and mitigating the ailments.

- **Introduction to medicinal plants in India and western ghats**

  - The Western Ghats of India is reported to be comprising about 4500 plant species out of which 35 percent endemic and among these endemic species, higher plants of nearly 2000 species, fishes of 84 species, amphibians of 87 species, reptiles of 89 species, birds of 15 species, and mammals of 12 species are present.

  - Three major gradients are identified in the distribution of biodiversity in Western Ghats, especially for flowering plants have been recognized in Western Ghats (Gadgil, 1996). The major portion is present along the north-south direction and the species diversity increases along the north-south region of the Western Ghats. There is an increase in the number of rainy area towards Southward direction. The decrease in rainfall, relates to the decrease in diversity from west to east. The third identified gradient is an increase in number of plant species found with an elevated temperature, as one travel from higher elevation of hills to lower coastal plains. This heterogeneous condition is affluent all along the ranges and regions of the Western Ghats. This region is considered to be an ideal ground for the lush growth of plants with medicinal properties. But since the region is being uncontrollably invaded by urban development and human expansion, life of such valuable medicinal wealth is at stake. Hence there is an urgent need to conserve the endemic biodiversity of the medicinal plants before it is wiped out from nature.

  - Hence, conservation of biodiversity is considered fundamental and urgent need and also millions of people depend on this biodiversity for their livelihood. Medicinal plants play a vital role in the treatment of various diseases and they remains to be the primary source of medicine for majority of people in the region. In India out
of 20,000 species of higher plants, one third being endemic and 500 species is categorized to be of medicinal value. The Western Ghats is one of the major storage of medicinal plants and there is an urgent need to protect this biodiversity of Western Ghats.\textsuperscript{7,8,9}

- Introduction to Urolithiasis and Pashanabheda

Urolithiasis commonly known as kidney stone disease is the condition where the calculi (Calcium oxalate) are formed at any part of urinary tract. It is called as nephrolithiasis if stones are present in nephrons. WHO has reported that 12\% of world population suffers from kidney stone disease and the recurrence rate in male is 70-80\% and in female 47-60\%. It is reported that calculi in urinary tract is the third most common of all the urinary tract diseases which is more severe than the urinary tract infections and prostate diseases. Urinary calculi can be of two types: tissue attached and unattached. Tissue attached calculi mainly contains calcium oxalate monohydrate (COM) and the detectable attachment site is the renal papilla and basically consisting of a core located near to the attachment site like concave zone with radial striations and concentrically laminated having peripheral layers. Unattached calculi with no detectable site of attachment to papilla, are developed in renal cavities with low or reduced urodynamic efficacy and can be of mixed composition and varied structures.\textsuperscript{10-12}

- In Ayurveda ‘Pashana’ means ‘stone’ and ‘bheda’ means ‘to break’. Hence Pashanabheda means the ‘one which breaks the stone’. Stones in this case are stones present in kidney and/or bladder. Traditionally, Pashanabheda is used as antiurolithiatic drug by Indian traditional practitioners\textsuperscript{13-15}. 

The list of some medicinal plants which are categorized as controversial drugs in Indian medicines system that are used traditionally as *Pashanabheda* by Ayurvedic practitioners contains\textsuperscript{16-19}

- *Berginia ligulata*
- *Aerva javanica*
- *Aerva lanata*
- *Coleus aromaticus*
- *Rotula aquatica*
## LIST OF MEDICINAL PLANTS USED FOR THE TREATMENT OF UROLITHIASIS\textsuperscript{20-24}

<table>
<thead>
<tr>
<th>Plant name</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Herniaria hirsute</em></td>
<td>Decrease size of crystal &amp; increase COD, diuretic action</td>
</tr>
<tr>
<td><em>Amni visnaga</em></td>
<td>Potent diuretic, prevent renal epithelial cell damage caused by oxalate &amp; COM</td>
</tr>
<tr>
<td><em>Tribulus terrestris</em></td>
<td>COM, Decrease oxalate formation</td>
</tr>
<tr>
<td><em>Bergenia ligulata</em></td>
<td>COM, Decreases calcium oxalate crystals</td>
</tr>
<tr>
<td><em>Dolichos biflorus</em></td>
<td>Oxalate crystals</td>
</tr>
<tr>
<td><em>Aerva lanata</em></td>
<td>Decrease crystal ppt</td>
</tr>
<tr>
<td><em>Vediuppu chunnam</em></td>
<td>Decrease urinary calcium oxalate, uric acid &amp; Diuretic</td>
</tr>
<tr>
<td><em>Raphanus sativus</em></td>
<td>Diuretic</td>
</tr>
<tr>
<td><em>Achyranthus Aspera</em></td>
<td>Prevent renal epithelial damage, Diuretic</td>
</tr>
<tr>
<td><em>Quercus salicina</em></td>
<td>Reduction in oxalate induced renal epithelial cell injury</td>
</tr>
<tr>
<td><em>Phyllanthus niruri</em></td>
<td>Antispasmodic &amp; relaxant</td>
</tr>
<tr>
<td><em>Cranberry juice</em></td>
<td>Decrease calcium oxalates</td>
</tr>
<tr>
<td><em>Cynodon dactylon</em></td>
<td>Increase COD as compare to COM</td>
</tr>
<tr>
<td><em>Grapefruit juice</em></td>
<td>Diuretic</td>
</tr>
<tr>
<td><em>Paronychia argentea</em></td>
<td>Antioxidant activity</td>
</tr>
<tr>
<td><em>Lemonade juice</em></td>
<td>Increases urinary excretion</td>
</tr>
<tr>
<td><em>Pyracantha crenulated</em></td>
<td>Increase diuresis and lowering of urinary</td>
</tr>
<tr>
<td>Plant Name</td>
<td>Effect</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Concentration of stone forming constituents</td>
<td>Maintains renal functioning; Reduce renal injury and decrease crystal excretion in urine and retention in renal tissues</td>
</tr>
<tr>
<td><em>Trachyspermum ammi</em></td>
<td>Diuretic, improved renal function</td>
</tr>
<tr>
<td><em>Moringa oleifera</em></td>
<td>Decrease stone size</td>
</tr>
<tr>
<td><em>Costus spiralis</em></td>
<td></td>
</tr>
</tbody>
</table>
Proposed Mechanism of action \textsuperscript{24}
Introduction

- **Types of stones**
  - Calcium oxalate crystals- These are commonly occurring kidney stone and mainly composed of calcium oxalate, occurring in about 80% of cases.
  - Urate crystals –These are composed of uric acid, about 5-10% of all stones.
  - Struvite crystals-These are mainly composed of ammonium and phosphate crystals.
  - Calcium phosphate-These are composed of calcium and phosphate
  - Cystine crystals-less common

It is reported that the level of contribution by different risk factors to stones formation varies among different populations. Many patients reportedly had more than one risk factor.

Different stone diseases-

- Hypercalciuria: 61%, (including some patients with primary hyperparathyroidism)
- Hyperuricosuric calcium stones: 36%
- Gouty diathesis: 10% (patients had normal uric acid excretion but a low urine)
- pH and developed either calcium or uric acid stones.
- Hypocitraturia: 28% idiopathic and 3.3% due to distal renal tubular acidosis
- Chronic diarrhoea
- Hyperoxaluria: 8%, including enteric and primary forms and markedly increased
- Oxalate intake (food and other sources)
- Low urine volume (1 lit/day): 15% (less water consumption)
SIGNS AND SYMPTOMS OF UROLITHIASIS

It is reported that the Urolithiasis may produce one or the other following symptoms:

- Colic pain,
- Nausea/vomiting
- Hematuria,
- Pyuria,
- Dysuria,
- Oliguria
- UTI

The urinary tract consists of organs like kidneys, ureter, bladder and urethra, the main function of which is to filter blood to remove liquid waste (urine) that is excreted from the body. Urinary calculi are composed of mineral masses deposited at any part of the urinary tract. The stone (bladder stone, ureteric stone and kidney stone) initially forms in the kidney and then it travels down to other parts of the urinary tract where it may become trapped in smaller tubes and the condition may become extremely painful.

On the basis of the chemistry (composition) of the stone formed and the severity of the disease, different types of ‘stone formers can be identified.

1. **Calcium stones**: Calcium is the most common constituent of calculi. Such stones are radio-opaque, the types include:
   - Calcium oxalate
   - Calcium phosphate

2. **Non-calcium stones**-These are other than calcium oxalate stones
   - Struvite (Magnesium ammonium phosphate)
   - Cystine
**Calcium oxalate:** Calculi also called as Whewellite or Mulberries. These stones are dark brown/black in colour, with a dense, smooth appearance as seen under electron microscope. Calcium oxalate monohydrate crystals appear like dumbbell-shaped when viewed under light microscope.

- **Calcium phosphate:** These are chemically Calcium hydroxyl phosphate stones which commonly comprise of significant proportion of carbonate to form apatite stones. These apatite stones are normally white in colour and are relatively poorly crystallized compared to hydrated acid calcium phosphate stones.

- **Struvite** (\(\text{NH}_4\text{MgPO}_4\cdot6\text{H}_2\text{O}\)): These are also called triple phosphate, named after Heinrich von Struve who first explained their composition. They are usually formed in the presence of chronic urinary infection. Urea splitting organisms within the urine (e.g. *Proteus* species) cause the urine to become more alkaline (pH rising above 7.0) which causes precipitation and hence stone formation.

- **Uric acid:** Uric acid is the end product of purine metabolism. It is very insoluble in water and thus uric acid becomes insoluble in urine and as urine becomes more acidic this leads to deposition of stone.

- **Cystine:** Cystinuria formation occurs due to an inherited defect in the transport of amino acids like cystine, lysine, arginine and ornithine. Cystine is insoluble in water and hence excessive deposition in urine lead to cystine stone formation.
Introduction

The rationale behind the investigation of the urinary stone composition in the patients originate from the assumption that derangement of urine biochemistry may play a vital role in the pathogenesis of Urolithiasis. Also other parameters like anatomical abnormalities of kidneys and urinary tract, genetic, environmental and dietary factors may also contribute in the pathophysiology of renal stone disease.

The urinary excretions of many substances (i.e., water, electrolytes, nitrogen, acid and alkali) depend on their glomerular filtration and the subsequent tubular reabsorption, which in turn is usually modulated so that their external balance is maintained in equilibrium.

In other cases (for example, fasting hypercalciuria syndromes, renal tubular acidosis and cystinuria) it is observed that the tubular reabsorption of stone promoters and stone inhibitors, as well as their urinary pattern, can be strongly influenced by genetic factors.

Eventually, despite urolithiasis/nephrolithiasis is a multiple reasons, the study of the propensity towards the crystallization of different salts in urine still remains the...
easiest strategy to estimate the possibility of the relapses of stone disease in individual patients.