INTRODUCTION

Medicinal plants form the backbone of Traditional Systems of medicine in India. Pharmacological studies have acknowledged the value of medicinal plants as potential source of bioactive compounds (Prusti et al., 2008). Phytochemicals from medicinal plants serve as lead compounds in drug discovery and design. Medicinal plants are rich source of novel drugs that forms the ingredients in Traditional Systems of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediates, bioactive principles and lead compounds in synthetic drugs (Ncube, 2008). WHO pointed out that more than 80% of world’s population depends on plants to meet their primary health care need. However, overexploitation of the selected medicinal plant species lead to the reduction in number of plants in the wild and inclusion of their name in the red data book (Ahmedullah and Nayar, 1999).

Herbal drugs constitute a major share of all the officially recognized systems of health in India viz. Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy, except Allopathy (Vaidya & Devasagayam, 2007). India is one of the 12 mega diversity countries in the world so it has a vital stake in conservation and sustainable utilization of its biodiversity resources. Plant secondary metabolites have been of interest to man for a long time due to their pharmacological relevance (Arora, Kaur & Kaur, 2003).
Indian medicinal plants have been studied for pharmacological activity in recent years. To understand the mechanism of action, the researchers have worked at molecular levels and several significant phytochemicals have been isolated (Singh & Malhotra, 2007).

Every country in the world has list of herbal remedies for the treatment of disease and different other pathological conditions (Satoskar and Bhandarkar, 1983). A large proportion of world population, especially in the developing countries depends on the traditional system of medicine for a variety of diseases. Several hundred plant genera are used medicinally mainly in the form of herbal preparation in indigenous system of medicine in different countries. Plant products are also a source of very potent and powerful drugs that have stood the test of times and modern chemistry has not been able to replace most of them.

Biologically active compounds from natural sources have always been of great interest to scientists working on infectious diseases. Plant kingdom represents a vast emporium of untapped medicinal potential (Sochni et al., 1998).

Medicinal plants are the backbone of Traditional medicine (Farnsworth, 1994). Over the years interest in natural products has acquired a cyclic phenomenon. In many countries, including India and China, thousands of tribal communities still use folklore medicinal plants for the cure of various diseases. The great interest in the use and importance of medicinal plants in many developing countries has led to intensified efforts
on the documentation of ethnomedical data of medicinal plants (Dhar et al., 1968 and Waller, 1993).

It has been confirmed by WHO, that traditional medicines, based largely on different species of plants and animals serve the health needs of large number of people; especially for millions of people in the vast rural areas of developing countries (Chan, 2003; Kong et al., 2003). Two hundred and fifty years ago there were a few or no synthetic medicine and species of higher plants were the main sources of medicines for the world (Duke, 1990). The method of discovery of medicine was probably trial and error that related the cause – and – effect relationship to the use of the plant or animal part and desired result. They used the whole plant or some part of the plant like leaves, bark, root, seeds and fruits, animals, their organs and glands for the therapeutic purpose (http://www.mosby.com).

**Ulcer**

Plants with medicinal properties “The gift of mother nature of mankind” are in use for centuries in the traditional system of medicine like Ayurveda, Unani, Siddha etc., in India and other countries for the treatment of diseases including ulcer. They are considered to be effective and non-toxic (Sadique, 1986).

Peptic ulcer disease (PUD) was recognized through ages and civilization. In fact, gastro – intestinal disease has attracted so much attention from patients and Clinicians as that of peptic ulcer (Naik and Dhiman, 1993). Dyspepsia in its variable form has been Mankind’s companion ever since the advent of bad cooking, over indulgence and
anxiety. Since one “is not altogether fit for the battle of life who is in perpetual contention with his dinner”, considerable energy has gone into relieving the symptoms of gastric upset and peptic ulcer disease (Goodman and Gilman, 1991).

Peptic ulcer may also be defined as pathological lesions as ulcers of any portion of the gastrointestinal tract exposed to acid activated pepsin. It is generally acknowledged that an ulcer results from an imbalance between aggressive gastric factors and resistance factors.

The term “peptic ulcer” is used to refer a group of ulcerative disorders of the upper gastrointestinal tract which appears to have common role to play in the participation of gastro intestinal tract which appears to have common role to play in the participation of acid-pepsin in their pathogenesis (Jain and Santani, 1994).

The causative factors of PUD are many and important among them are hyperacidity, stress, NSAID’s, mucosal barriers and food habits.

Recent information suggest that the prevalence and changing pattern of the disease, is mainly due to a bacterial organism, *Helicobacter pylori* which colonies the gastric mucosa, particularly the anural region. *H. pylori* are often reported in about 100% of patients with gastric ulcers (Jain and Santani, 1994). Until recently the pathogenesis of duodenal ulceration has been attributed to an in balance between aggressive factors such as acid and pepsin that damage the gastric mucosa and protective factors such as prostaglandin’s that prevents the damage. Recent evidence relates *H. pylori* to the pathogenesis of chronic duodenal ulcer, as *H. pylori* infection and
anural gastritis are found together in more than 95% of patients with duodenal ulcers. Thus \textit{H. pylori} infection is now strongly associated with chronic duodenal ulceration (Jain and Santani, 1994). Duodenal ulcer is twice as common and benign gastric ulcer is four times more common in men than in women.

Marshall and Warren (Marshall and Warren, 1984; Warren, 1983) were the first to describe the association of the presence of \textit{Campylobacter} like organism in the central mucosa with histological evidence of antral gastritis as well as peptic ulcer, especially duodenal ulcers.

Autoimmune phenomena are absent in type $\beta$- gastritis and it has been contributed as idiopathic. There is now evidence that the gram negative bacterium \textit{H. pylori} may be important in the etiology of type $\beta$- gastritis (Mc Nulley \textit{et al.}, 1986).

Treatment of PUD in modern medicine has undergone remarkable degree of transformation. The therapeutic management of PUD includes antacids, anti cholinergic and antispasmodic drugs, H2 receptor antagonists such as cimetidine, ranitidine, famotidine and proton pump inhibitors viz. Omeprazole, Lansprazole, Patoprazole etc. In the recent past, with the acknowledgement of the etiological association of \textit{H. pylori} in PUD, a range of anti bacterial such as Metronidazole, Tididazole, Ampicillin, Amoxycillin, Clarithyromycin, Tetracycline, etc., are being used in a combined regimen to provide both bacteriological and histological remedy (Goodman and Gilman, 1991).
Plant extracts are some of the most attractive sources of new drugs and have been shown to produce promising results for the treatment of gastric ulcer (Alkofahi and Atta, 1999; Schmeda–Hirschmann and Yesilada, 2005).

During the past 40 years, the frequency of duodenal ulcer now appears to be approximately as common in males as in females (Takeuchi, 1983).

**History of Ulcer**

John Lykoudis, a general practitioner in Greece, treated patients for peptic ulcer disease with antibiotics, beginning in 1958, long before it was commonly recognized that bacteria were a dominant cause for the disease. (Marshall B.J., 2002)

*Helicobacter pylori* were discovered in 1982 by two Australian scientists, J.Robin Warren and Barry J.Marshall as a causative factor for ulcers (Marshall B.J. 1983). In their original paper, Warren and Marshall contended that most stomach ulcers and gastritis were caused by colonization with this bacterium, not by stress or spicy food as had been assumed before (Warren J.R, 1984)

In 1994, a National Institutes of Health Consensus Development Conference concludes that there is a strong association between *H. pylori* and ulcer disease, and recommends that ulcer patients with *H. pylori* infection be treated with antibiotics.
In 1995, data showed that about 75 percent of ulcer patients are still treated primarily with anti-secretory medications, and only 5 percent receive antibiotic therapy. Consumer research by the American Digestive Health Foundation finds that nearly 90 percent of ulcer sufferers are unaware that *H. pylori* cause ulcers. In fact, nearly 90 percent of those with ulcers blame their ulcers on stress or worry, and 60 percent point to diet.

In 1996, the Food and Drug Administration approves the first antibiotic treatment of ulcer disease.

In 1997, the Centers for Disease Control and Prevention, with other government agencies, academic institutions, and industry, launched a national education campaign to inform health care providers and consumers about the link between *Helicobacter pylori* and ulcers. This campaign reinforced the news that ulcers are a curable infection, and that health can be greatly improved and money saved by disseminating information about *H. pylori*. (Marshall, 1983).

In 2005, the Karolinska Institute in Stockholm awarded the Nobel Prize in Physiology or Medicine to Dr. Marshall and his long-time collaborator Dr. Warren "for their discovery of the bacterium *Helicobacter pylori* and its role in gastritis and peptic ulcer disease". Professor Marshall continues research related to *H. pylori* and runs a molecular biology lab at UWA in Perth, Western Australia.

It was a previously widely accepted misunderstanding that the use of chewing gum resulted in gastric ulcers. The medical profession believed that this was because the action of masticating on gum caused the over-
stimulation of the production of hydrochloric acid in the stomach. The low (acidic) pH (pH 2), or Hyperchlorohydria was then believed to cause erosion of the stomach lining in the absence of food, thus causing the development of the gastric ulcers. (Toohey, 1974).

On the other hand, in the recent past, some believed that natural tree resin extract, mastic gum, actively eliminates the H. pylori bacteria (Huwez FU, 1998). However, multiple subsequent studies have found no effect of using mastic gum on reducing H. pylori levels (Loughlin et al., 2003, Bebb JR et al., 2003).

ROLE OF PLANTS IN THE TREATMENT OF AILMENTS

Data from 1991, Indicate that more than half of the world’s 25 best selling pharmaceuticals either themselves natural product or derived from Natural products (O’Neill and Lewis, 1993). Within the developed countries 25% of medicines contain active principle derived from plants, and the majority of drugs in current use were developed following studies of traditional herbal treatments (Day and Bailey, 1988). Aspirin, Quinine, Theophiline, PencillinG, Morphine, Palcitaxel, Digoxin, Vincristine, Doxorubicin, Cyclosporin and Vitamin A all share two important characteristics: They are in the cornerstones of modern pharmaceutical care and they are all natural products. So natural products, so called secondary metabolites from plants continue to be an important segment of modern drugs in clinical use in spite of all substantial advances that have been made in synthetic drug-design chemistry. There is still a great thirst for novel compounds with unique mechanisms of action in the field on Medicine.
The medications used in PUD management include acid suppressants (antacids, histamine-2 receptor blockers, and proton pump inhibitors) and gastric mucosal protectants, for relief of symptoms and to promote ulcer healing, and antibiotics to eradicate *H. pylori* when it is present. All are found to produce side effects such as constipation, diarrhea and toxic effects on chronic administration.

**SELECTION OF PLANTS FOR STUDIES**

Nearly 240 medicinal plants and 21 plants based compounds were identified as anti ulcer worldwide so far (Duke 2009). In Siddha literature, many medicinal plants are indicated for anti ulcer and among them *Aegle marmelos* is indicated for anti ulcer (Murugesh Mudaliar, 1988).

*Aegle marmelos* (L.) (Tamil Name: Vilvam) is important medicinal plant available in TamilNadu, India and are reported to have various medicinal property in Traditional medical systems.

*Aegle marmelos* is common medicinal plant available in South India and is used as medicine in Siddha and Ayurveda. The plants are distributed throughout India, cultivated as well as grow in wild. In TamilNadu it is located in the river belt of Vattaru and Cauvary and it is also present in most of the Shiva temple of TamilNadu.

The unripe and ripe fruits of *A.marmelos* are bitter, acrid, sour, astringent, digestive and stomachic and are useful in diarrhoea, dysentery and stomachalgia (Warrier *et al*., 1998, Khanna *et al*., 1991). Stem bark is
used in fever (Kurup et al., 1979). In bacillary dysentery Bael is useful adjuvant (Prosad Benerjee, 1977).

The leaves are astringent, laxative, febrifuge and expectorant and are useful in ophthalmic, deafness, inflammations, catarrh diabetes and asthmatic complaints (Varma, 1981). The ripe fruits are astringent, sweet, aromatic, cooling, febrifuge, laxative and tonic and are used for heart and brain and in dyspepsia (Warrier et al., 1998)

Various pharmacological studies are carried on Aegle marmelos plant. However, comparative pharmacological and Biochemical studies on leaves of variants of Aegle marmelos was not carried out. It is essential in standardsation of traditional medicine and to know their therapeutic potential.

Even though, medicinal plants are used increasingly throughout the world in healthcare, scientific validation and strandardsation of herbs and herbal drugs need to be carried out for most of the medicinal plants used in Traditional Systems of medicine. Therapeutic potentials of medicinal plants depend upon the quality and quantity of biological active compounds they possess. Medicinal plants show variation in their biological compounds due to various factors like season, growth stage, climate, and soil type and genetic. There are varieties of variants within a single species of medicinal plant which tend to show difference in the quality and quantity of biological active compounds.
Ghosh et al., (2002) reported 13 variants among A. marmelos in West Bengal. Amarnath Pandian (2009) evaluated pharmcognostical, phytochemical and pharmacological profiles of fruits of three variants of A. marmelos. Leaves of variants of A. marmelos have not been studied and compared for their pharmacological and phytochemical profiles.

Hence, the present work was undertaken with a view to compare phytochemical, biochemical and pharmacological profiles of leaves of two variant of A. marmelos variant-I and variant-III are commonly available in and around Thanjavur and hence these two variants are selected for the present study. And the objectives of the present work are as follow:


2. To evaluate toxicological profile of leaf of two variants of Aegle marmelos.

3. To establish phytochemical profile of two variants of Aegle marmelos.

Plan of work

- Collection of plant materials- leaves of var. I and var. III of Aegle marmelos
- Drying and powdering.
• Behavior of powder to different chemical reagents.
• Fluorescence characteristics of powder.
• Percentage of loss on drying.
• Ash values.
• Extractive value of the leaves of medicinal plant (Aegle marmelos).
• Preliminary Phytochemical analysis of leaf extracts.
• Quantitative Phytochemical screening of leaf extracts.
• TLC and HPLC profiles.
• GC- MS studies.
• Toxicological screening.
• Pharmacological and Biochemical evaluation.
  ➢ Anti-ulcer activity.
  ➢ Anti-inflammatory activity.
  ➢ Anti-pyretic activity.
  ➢ Anti-oxidant activity.
  ➢ Anti-microbial activity.

2. REVIEW OF LITERATURE

MORPHOLOGY

Syn. : Crataeva marmelos Linn.