1 INTRODUCTION

For more than a century, peptic ulcer disease (PUD) has been a major health problem throughout the world. Peptic ulcer disease (PUD) occurs due to the disruption of gastric mucosa leading to a local defect or excavation due to active inflammation. Clinically it is defined as the disruption of the mucosal integrity frequently occurring along the lesser curvature of the antral end of the stomach and in the duodenum. The major forms of peptic ulcer include gastric and duodenal ulcer both of which are chronic in nature (Valle, 2005). The basic cause of peptic ulcer has not been understood until the recent times. Important advances have occurred in the last two decades that improved our understanding for the disease and as well improved our therapeutic strategies. PUD occurs basically due to an imbalance between the rate of secretion of gastric juice and the degree of protection afforded by the gastro duodenal mucosal barrier as well as the neutralization of the gastric acid by duodenal juices (Mossner et al., 2005).

Peptic Ulcer can occur due to normal/ hypersecretion of hydrochloric acid. Hypersecretion of gastric acid is a pathological condition, which occurs due to uncontrolled secretion of hydrochloric acid from the parietal cells of the gastric mucosa through the proton pump, H⁺K⁺-ATPase (Jainu et al., 2006). Even the normal rate of secretion of acid secretion may cause ulceration in the breached mucosa when some gastroprotective factors are lost (Bandhopadyay et al., 2002). Hence inhibition of gastric acid secretion acts as an important target for the treatment of ulcer. The modern approach to control gastric ulceration focuses on the inhibition of gastric acid secretion (Forte, 1986). Most of the antisecretory drugs such as proton pump inhibitors and histamine H₂ receptor blocker are extensively used to control increased acid secretion and acid related disorders. Proton pump inhibitors (PPIs) inhibit the final step of acid secretion, and are currently the most potent acid inhibitors.

Gastric acid is secreted by the gastric parietal cell, also known as the oxyntic cell. The gastric H⁺-K⁺-ATPase enzyme, which is located in the parietal cells, mediates the electroneuronal exchange of intracellular H⁺ and extracellular K⁺ to achieve acid secretion when parietal cells are under stimulation. The gastric H⁺-K⁺-ATPase is the molecular base of gastric acid production and the final common pathway mediating secretion of hydrochloric acid by gastric parietal cells. The capability of gastric acid secretion is thus dependent on the gastric H⁺-K⁺-ATPase activity (Jainu et
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al., 2006). Therefore, regulation of H⁺-K⁺-ATPase activity can serve as an accurate indicator for evaluating the ability a drug in controlling secretion of gastric acid from parietal cells.

Gastric mucosal layers are continuously exposed to a wide variety of injurious agents originating either endogenously or exogenously. These include hydrochloric acid, pepsin, H. pylori, alcohol, non steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. When these aggressive factors exceed the ability of the mucosa to resist, multiple pathologies such as peptic ulcers, gastritis and even gastric cancer can develop. One of the main pharmacotherapeutic options for these pathological conditions is the suppression of acid secretion by Proton Pump Inhibitors (PPIs) or Histamine type 2 receptor antagonists (H2RAs) as well as the eradication of H. pylori by antibiotics. The other very promising approach for treating gastric mucosal damage is to augment the defensive factors such as the mucus-bicarbonate layer, prostaglandin (PG), and growth factor. A gastric mucus bicarbonate barrier protects the mucosa from damage caused by acid and pepsin by acting as a blanket over the mucosal layer which protects the epithelium from bacteria by trapping and excreting them in the feces.

Today's available drug therapies are aimed primarily at reducing acidity, either through direct neutralization by antacids or administration of acid-suppressing agents such as H2RAs and PPIs. PPIs such as omeprazole block the final common pathway of gastric acid production, provide significantly higher healing rates than H2RAs and are now the drugs of choice for healing of peptic ulcer. Despite the rapid and clear efficacy of these antisecretory drugs, there are a number of shortcomings that need to be addressed. For example, H2RAs and PPIs induce rapid tolerance during therapy and rebound hyper secretion following drug withdrawal which leads to high ulcer relapse rate. In addition, H. pylori negative patients are being encountered in increasing numbers and gastric ulcers recur even after the successful eradication of the bacteria. Such acid-reducing agents such as H2RAs and PPIs are available to treat ulcer, however, there are no safe, effective and durable therapies available today for improving ulcer healing. These patients often continue to experience symptoms because PPIs do not augment any cytoprotective defects. Moreover these drugs showed incidence of relapses and side effects that make their efficacy arguable. Thus in order to overcome these drawbacks investigation has been extended for the search of new and novel molecules from plant sources which can show better protection and lesser rate of incidence of relapse.
Drugs from indigenous sources of natural products are thus now a target for development, refinement and pharmacological modification for anti-ulcer treatment. The need of new chemical entities (NCEs) for health care is explored and served through the plant sources. The World Health Organization (WHO) estimates that about 80% of the population living in the developing countries relies on traditional medicine for their primary health care needs. Roughly 50% of the NCEs introduced during the last two decades are from natural products. In almost all the traditional systems of medicine, the medicinal plants play a major role and constitute their backbone. Indian medicinal plants possess enormous healing power and only a part of this potential is known to mankind. Evolution of Ayurveda and plant-based remedies for health care through day-to-day life experiences is a part of cultural heritage of India. Ayurveda, which literally means the science of life, is one of the oldest systems of medicines in India. This system of using natural resources for betterment of health was developed through the experimentation and experiences of day-to-day life style of Indian people. Besides Ayurveda, there are several other complementary and alternative systems of medicine like Homeopathy, Siddha and Unani systems of medicine, which are also practiced and developed with the course of time in India, where plants and plant-based formulations are employed for health care and disease treatments. These systems are based on experience and interaction with nature and natural resources. Around 70% of population in India relies on these systems for primary health care. Scientific evidence to prove the rationale of using these formulations in health care is essential to develop.

Treatment of symptomatologies related to peptic ulcers or gastritis with medicinal plants are quite common in traditional medicine worldwide. Indian medicinal plants and their derivatives have been an invaluable source of therapeutic agents to treat various disorders including peptic ulcer disease (PUD). Several studies on the gastroprotective effect of crude plant extracts have been undertaken. Of these Indian medicinal plants are of prime significance. Various Indian medicinal plants like *Allophylus serratus* (Dharmani et al., 2005b), *Desmodium gangeticum* (Dharmani et al., 2005a), *Ocimum sanctum* (Dharmani et al., 2004), *Xylocarpus granatum* (Lakshmi et al., 2010), *Tectona grandis* (Singh et al., 2010), *Annona Squamosa* (Singh et al., 2011), *Dysoxylum binecteriferum* (Singh et al., 2012) etc. have been reported to possess anti-ulcer activity. Several studies on the gastroprotective effect of crude drugs extracts, herbal mixtures and pure active compounds isolated from the crude drugs and their
derivatives suggest that traditional Indian systems of medicine gained considerable momentum in treatment of gastric ulcer.