General summary

- The modern life style prevailing attributes to a number of health issues. Gastric ulcer is one such problem which holds over 14.5 million people worldwide. The mortality rate in people affected with this problem is 4.08 million. India ranks fifth in the prevalence of peptic ulcer with 12.4 % death rate.

- Gastric ulcer has a cumulative cause. The ulcers are localized erosions of the mucosa of stomach. The cause of ulcer is disputed. The scientific evidence indicates that, H. pylori and NSAIDs are the culprits, however there are other factors causing gastric ulcers such as smoking, excessive consumption of alcohol, cocaine, caffeine, stress and radiations.

- A modest approach to control ulceration is via stimulation of gastric mucin synthesis, enhancement of antioxidant levels in the stomach, scavenging of ROS, inhibition of H⁺- K⁺-ATPase and H. pylori growth by the use of antibiotics, proton pump inhibitors, Histamine (H₂) blockers, antacids, antibiotics and cytoprotective agents.

- There is evidence concerning the participation of ROS in the etiology and pathophysiology of gastric ulcer. Studies have shown alterations in the antioxidant status following ulceration, indicating that free radicals seem to be associated with the stress induced ulceration in rats. Drugs with multiple mechanisms of protective action, including antioxidant properties, may be one way forward in minimizing tissue injury in human disease (Barry, 1991).
The commercial drugs in the market failed to exert multi-step anti-ulcer effect as a single entity and they show to pose adverse side effects. Efforts were made to find a suitable agent for the treatment of gastric ulcer from plants and animal origin. Several herbal remedies have been used for the treatment of ulcers. Generally, anti-ulcer properties have been attributed to phenolics, flavonoids, tannins, alkaloids and occasionally to polysaccharides.

In the current thesis, particular attention has been paid to evaluate potential antioxidant, safety aspects and anti-ulcer property of Mesua ferrea Linn. Phytoconstituents from stem bark of M. ferrea L. were isolated and evaluated free radical scavenging and H⁺- K⁺-ATPase inhibition studies.

The in vitro antioxidant and protective effect of M. ferrea L. against induced oxidative stress in erythrocytes, Hb and DNA was evaluated. The study indicates that, M. ferrea L. possesses significant antioxidant and protective activity. Further HPLC analysis of M. ferrea L. stem bark extracts shows the presence of various antioxidant molecules like gallic acid, acid, ellagic acid, coumaric acid, vanillic acid, rutin, quercetin, myricetin and kaempferol, which rendered the induced oxidative stress by H₂O₂ in erythrocytes, Hb and DNA by acting as potent antioxidant and electro-catalyst. Among the extracts MCE and MEE, MEE showed significant activity; hence, MEE was used for further studies.

MEE at three different doses; 500, 1000 and 2000 mg kg⁻¹ b. w. over a period of 7, 30 and 180 days respectively did not show any toxic effect. Blood clinical parameters, organ-to-body mass index, liver histopathological studies and liver antioxidant enzymes analysis revealed no significant abnormal changes in any of the dose specific group compared to control animals. These data indicate preliminary non-toxicity report in rat model.

The current study unravels the anti-ulcer potential of M. ferrea L. ethanol extract (MEE) against ethanol/swim induced stomach ulcer in rat model. MEE containing
phenolics (1.005 ± 0.005 mg mg⁻¹ GAE) and flavonoids (514.8 ± 0.155 μg mg⁻¹ ECH) prevented the induced stomach ulcer up to an extent of 85.53±0.2 % of ulcer healing index. The possible mechanism involved in gastro protective activity by MEE may involve significant normalization of antioxidant system and oxidative damage, modulation of gastric mucin synthesis, inhibition of H⁺-K⁺ ATPase pump.

- Natural products, such as plant extract, either as pure compounds or as standardized extracts, provide unlimited opportunities for new drug discoveries. Potent significant antioxidant molecules were isolated and characterized. Isolated molecules also showed very good H⁺-K⁺ ATPase pump inhibition.

- Discovery of drugs to control *H. pylori* is a difficult task in view of drug resistance developed by the bacterium against continuous exposure to modern drugs. Virtual screening play an important role in identifying lead drug. In the present study, out of 99 phytocconstituents, nobiletin, silibin and vitexicarpin were identified as possible anti-*H. pylori* drug.

- The study suggests that, *M. ferrea* L. is potent antioxidant, and gastro protective with out any cause of toxicity in animal models. This suggests that further clinical trials are warranted to isolate and find a new drug for the treatment of gastric ulcer.