SUMMARY AND CONCLUSION

Peptic ulcer (gastric/duodenal) is most prevalent gastrointestinal (GIT) disorders and has affected humans for centuries. A peptic ulcer is condition in which destruction and necrosis of inner surface mucosal cells develops into inflammation, altered normal structure of mucosal tissue of the stomach. The obstruction or erosion in the mucosal layers becomes superficial, moderate and deeply erosive (Sivri, 2004) causes fault in secretary function if they are untreated. It is likely that ulcer severity increased when impairment of mucosal defensive (protective) agents such as mucosal blood flow, ischemic preconditioning, NO and PG generation, growth factors, ghrelin, and aggressive factors such as HCl, pepsin, bile acids and others (Tanigawa, et al.,2005; Noor, et al.,2006). The daily and continuous administration of nonsteroidal anti-inflammatory drugs (NSAIDs), Helicobacter pylori (H. pylori) infection, stress, alcohol and smoking, (Mc Guigan, 1991) are some of the known factors that can cause gastric ulcer (Hsiu-Chi and Bor-Shyang, 2011). The increased rate of acid secretion may increase the parietal cell mass commonly found in duodenal ulcer. The most popular is due to normal or abnormal secretion by an abnormally large number of parietal cells (Marshall, 1994; Wormsley, 1997).

Recently number of treatments are available to cure peptic ulcer includes eliminating the H. pylori bacterium using antibiotics and to use antacids (sodium bicarbonate, aluminum hydroxide, magnesium hydroxide) and/or acid blockers to relieve pain via neutralization of intraluminal acid and promote healing of inflammatory injuries (Hsiu-Chi and Bor-Shyang, 2011), proton pump inhibitors and H₂ receptors antagonists, anticholinergic drugs were concurrently administered to delay emptying of the agents into the duodenum and to inhibit acid secretion (Aihara, et al., 2003; Andersson and Carlsson, 2005). But clinical analysis of such drugs has shown recurrence of ulcer, showed adverse effects, interference of drugs with normal cellular functions and interactions of drugs. This has been the rational for the development of new antiulcer drugs. There is growing focus on the importance
of medicinal plants in the treatment provides additional health care system (viz. Ayurveda, Unani, Homeopathy, Yoga) resolving the health care problems. Because of this awareness plant derived herbal remedies are prominently applied in the therapy of different diseases (Mukherjee, 2003).

Many remedies have been employed during the ages to treat ulcer. Most of the remedies were taken from plants and proved to be useful because plant derived medicines suppresses the relapse of offensive factors. Such medicines are medicinally effective and they are low expensive. Plant derived herbal products are potent source of development of new drugs and they have better quality curing effects against gastric ulcers.

In the indigenous system of medicine, the Aloe vera (A.barbadensis) considered as proficient remedy for ulceration and other gut disorders. Hence, in our present research work, Aloe vera has been selected for analysis of anti-ulcer and antioxidant effect on experimentally induced ulcer in aged mice. Aloe vera is an important, traditional, renowned and medicinal miracle plant belonging to the family Liliaceae.

First chapter contains general introduction about peptic ulcer (gastric and duodenal), histology of duodenum, aging, aging and free radicals, antioxidants, gastrointestinal tract and aging, Oxidative stress in mucosa during aging and ulcer, synthetic drugs and other herbal medicines used to cure peptic ulcer, Aloe vera its medicinal as well as pharmacological use and review of the literature well described in this chapter.

Second chapter regarding with the experimental protocol and methods used for the present experimental research work. Healthy swiss albino mice Mus musculus of both sexes of Young mice 20 ± 2 to 26± 2 gm/bw of 2 month age, Adult mice 35 to 42 ± 2 gm/bw of 5 to 6 month age and old mice 45 to 50 ± 2 gm/bw of 16 to 18 month age were used for present investigation. For the evaluation of antiulcer and an antioxidative property of Aloe vera animals were divided in to 3 mainly into 3 groups. The control group given 0.5 ml of distilled water per day per animal for 15 days, duodenal ulcer induced group mice were given subcutaneous injection of cysteamine-HCl (40mg/100gm/BW) dissolved
in 0.5 ml distilled water (Szabo, 1978) and *Aloe vera* gel treated group mice after 24 hrs of after the dose of cysteamine- HCl administration six mice received orally *Aloe vera* gel 200 mg/kg dissolved in 0.5ml distilled water/ day/ mouse for 15 days (Subramanian, *et al*., 2007). The treatment given one time per day and it was proceed for next 15 days.

After the completion of treatment mice were weighed and sacrificed by cervical dislocation, the duodenum were removed, weighed and were proceed for gross morphological, histological, histochemical and biochemical studies.

**The third chapter** describes the results and discussion about the parameter used for assessment of ulcer protection and antioxidant effects of *Aloe vera* gel in cysteamine- HCl induced ulcer in aged mice. The studied parameters a body weight, ulcer index, histopathological, histochemical and biochemical investigation.

Body weight is significant measure for the evaluation of toxicity of substance, their derivatives and plant derived extracts. It is observed that the weight of cys-HCl ulcerated mice were significantly decreased than control group mice. In *Aloe vera* treated mice body weight becomes increased as compared to Cys-HCl ulcerated mice. The observed weight gain in both sexes of mice after treatment *Aloe vera* gel treatment indicates the recovery of duodenal tissue structure.

Ulcer scoring is used as a one of the most reliable, accurate factor and relevant parameter to assess ulcer severity (Minaiyan, *et al*., 2005). In our present investigation the number of mucosal lesions significantly increased in mucosa of the cys-HCl induced duodenal ulcer. But, after the treatment of *Aloe vera* gel significantly decrease in the number of lesions in the duodenal mucosa of all three aged mice of both sexes.

Study of morphological, structural and histochemical secretary changes in the cellular organization of tissue during cysteamine- HCl induced duodenal ulceration and after the treatment of *Aloe vera* gel evaluated by histological, histopathological and histochemical methods. The progression of ulcer in cys-HCl induced ulcer group mice of both sexes showed dilation of lumen, altered
epithelial cells structure these findings similar with the histological changes occurred might be due to shortening of villi results into the devoid of villus at mucosal surface area and necrosis, inflammation and erosion seen at epithelial cell region Thus, balanced gastric acid secretion may indirectly responsible for cure the ulcer lesions in *Aloe vera* treated young, adult and old mice. After the *Aloe vera* gel treatment acid reducing effects lowered and the mucosal lining recovered towards the normal structure.

Histochemical results showed that cysteamine – HCl induces constant and precisely located duodenal ulcer in young, adult and old mice. The result of present study there was highly decrease in staining intensity of glycoprotein in old mice by the administration of cys –HCl during ulcer which was restored significantly due to treatment of *Aloe vera* gel by its antiulcer anti antioxidant cytoprotective activity. In our present study there was highly weak staining intensity of glycoprotein in old mice by the administration of cys –HCl during ulcer which was restored significantly due to treatment of *Aloe vera* gel by its antiulcer, antioxidant and cytoprotective activity.

Mucus is the viscous glycoproteins, the important component of gastric mucus are sialic acid, neutral substances such hexose, fucose and hexoamine. All these components are readily involved in the formation of viscosity and gel nature of mucus. Their qualitative determination has been used as a measure of thickness and turnover rate of mucus formation (Lukie and Frostner, 1972). Hence, we have included these parameter such as qualitative determination of total protein, glycoproteins (sialic acid, fucose and Hexose). In the present study the protein and glycoproteins such sialic acid, fucose and Hexose content decreased by the administration of Cys –HCl induced ulcer which was restored significantly due to treatment of *Aloe vera* gel treatment. Recovered structural integrity of duodenum by *Aloe vera* gel increases the level of protein and glycoprotein content, this indicates that the *Aloe vera* heals ulcer erosion due to flavonoids protects the stomach of rat from peptic ulcer occurred by oxidative stress (Roa, et al., 2003).
In our present study cysteamine induces alterations in the antioxidants enzyme activities which were recovered at normal level by the treatment of Aloe vera gel. In the Cys-HCl induced ulcerated group of mice free radical scavenger enzymes such as reduced glutathione, catalase (CAT), Super Oxide Dismutase (SOD) decreased LPO highly increased. All these effects were significantly reversed by treatment after the treatment of Aloe vera gel that supporting a close relationship between free radical scavenging activity of some enzymes reflecting the development of ulcer due to oxidative stress these indicates that Aloe vera possesses both antiulcer and antioxidant activity.

**The chapter fourth** deals with Summary and conclusion. The chapter contains summary of the entire work incorporated in thesis and conclusion of the research work followed by references in which lists of the references cited in the text of the thesis.

**CONCLUSION**

From the present study, it can be concluded that the oral administration of Aloe vera displayed a significant antiulcer activity and antioxidant mechanism without any apparent toxicological effects, which supports the use of Aloe vera for ulcer therapy. Cys-HCl induced ulcer not showed any significant difference between male and female in aged mice. The period required to cure ulcer in aged mice similar to the young and adult after the Aloe vera gel treatment.

Aloe vera possess significant anti-ulcer activity. This may be due to their antioxidants and cytoprotective activity. It is conceivable that the cytoprotective activity of Aloe vera may relate primarily enhancing cellular detoxification mechanisms, repair damaged non-proliferating cells, inducing cell proliferation. Proliferation of small intestinal epithelial cells occurs in the crypt cells. Crypt cells which rapidly regenerate and migrate to the villus tip lead to replacement of intestinal epithelium and self-renewal of damaged proliferating tissues, and replenishing them by eliminating damaged or cells.

The antioxidant activity of Aloe vera associated with the inhibition of the oxidative modification of certain proteins whose free radical mediated
structural modification and loss of functions is particularly relevant to the
development of cell injury also it could be due to quenching free radicals,
presence of vitamin-C and E.

*Aloe vera* showed anti-ulcer activity through significant decrease in acid-pepsin secretion and increase in mucosal protective factors like mucus secretion, cellular mucus and life span of mucosal cells (Sairam, *et al.*, 2003), by scavenging free radicals and restoring the antioxidant level. Hence, it’s concluded that *Aloe vera* exhibited both antiulcer meanwhile strong and potent antioxidant property.