Summary and Conclusion
Chapter 5
SUMMARY AND CONCLUSIONS

This dissertation describes studies on design, synthesis and evaluation of gallic acid esters as potential antioxidant compounds. As a result of this study, a total of twenty two compounds were synthesized, characterized and evaluated for antioxidant activity. These compounds were synthesized by conjugating gallic acid (GA) and its intermediate trimethoxybenzoic acid (TMBA) with either phenolic/alcoholic phytophenols or with their potassium salts. The newly synthesized compounds were characterized by using spectroscopic (UV, IR, $^1$H NMR, $^{13}$C NMR, MS, and elemental analysis) and chromatographic (TLC, HPLC) techniques. Physicochemical studies were carried out to assess the partition coefficient, solubility, chemical stability, and enzymatic hydrolysis of the synthesized compounds. *In vitro* (DPPH and ABTS method) antioxidant studies were carried out to ascertain the antioxidant potential of parent compounds GA and TMBA. Anti-inflammatory studies were carried out to assess the antioxidant potential of synthesized compounds. All the synthesized compounds exhibited promising anti-inflammatory activity in carrageenan induced paw edema assay as compare to their physical mixtures and standard drug indomethacin. In particular, compounds 5, 6, 11, 12, 30, 32, 35, and 37 emerged as the most active compounds with more than 70% edema inhibition. Compounds which showed good anti-inflammatory activity were further studied for their gastric ulcer studies. The results of studies indicated these compounds as non-ulcerogenic and gastroprotective. To find out whether the antiulcer activity of said compounds is mediated through its antioxidant action, the levels of various biomarkers of oxidative stress were measured in gastric mucosal cells of pyloric ligated rats both in the presence and absence of test compounds. Biochemical estimations (*ex vivo*) were carried out to assess the potential of newly synthesized compounds on various biomarkers of oxidative stress such as lipid peroxidation, glutathione,
superoxide dismutase, and catalase. The results of the biochemical estimations showed the inhibition of mitochondrial oxidative stress by the test compounds and linked their pharmacological effects to their antioxidant potential. *In silico* docking studies were carried out to postulate the hypothetical binding model for their interaction with cyclooxygenase enzymes (COX-1 and COX-2) to confirm the anti-inflammatory potential of newly synthesized compounds. The results from the docking studies were found to be in good agreement with the results from pharmacological studies. Further, the compounds comply with Lipinski’s rule of five which signifies a good absorption and hence, good bioavailability. The present study suggests these compounds as potent, effective and gastric safe anti-inflammatory agents by virtue of their antioxidant potential, which can be further explored for other therapeutic indications.