CHAPTER 7. SUMMARY AND CONCLUSION

7.1 Summary

In the present research work an attempt has been made to optimize, formulate and characterize fast dissolving tablet(s) of anti-emetic drugs (domperidone and ondansetron HCl) to achieve faster drug action in nausea and vomiting. Both drugs are specific anti-emetic action and are prescribed in all cases of nausea and vomiting. The whole research work is presented in different chapters.

Domperidone is practically insoluble in water, so an attempt was made to increase its water solubility. In the present work, Solubility of domperidone was enhanced using solid dispersion technique. Experiments were performed using different carrier system like PVP K30, PEG 4000 and PEG 6000, and PEG 6000 was selected for further studies. Solid dispersions of domperidone: PEG 6000 was prepared in different ratio and by using optimized ratio of domperidone: PEG 6000 solid dispersion, Fast dissolving tablets were prepared.

Fast dissolving tablets were prepared using two different approaches. In one approach FDT were prepared using different superdisintegrants and further optimized by full factorial design. In second approach, FDT were prepared using effervescent material and optimization was carried out using central composite design. The responses were analysed for analysis of variance (ANOVA) using Design Expert version 8.0 software. In full factorial design, effects of formulation parameters like concentration of diluent, concentration and type of superdisintegrant were evaluated and their effect on disintegration time and hardness was determined. In central composite design effects of formulation parameters like concentration of Ac-Di-Sol and effervescent materials (sodium bicarbonate and citric acid) were evaluated. FDT of domperidone prepared using effervescent materials was found to be optimum in relation to disintegration and hardness.

In another study bitter taste of ondansetron HCl was masked by Eudragit® EPO. Drug polymer complex (DPC) in different ratio were prepared using extrusion method and characterized for FTIR, DSC, XRD and in-vitro taste evaluation. The result indicated the ability of Eudragit® EPO for taste masking and improving the dissolution profile. Using
optimized ratio of DPC, FTD’s were prepared by two different methods. In one method different ratio of MCC and lactose as a diluent and different concentration of superdisintegrant was used to develop tablet and further optimized using full factorial design. In another method sublimation technique was used to develop tablets and experiments were performed using full factorial design to evaluate effect of formulation parameters like concentration of subliming material (camphor) and concentration of diluent (mannitol), and their interactions on disintegration time and hardness of dissolving tablet formulation. Tablets prepared using ratio of MCC and lactose (66:34%) and 4.49 % of Ac-Di-Sol were found to be optimum in relation to hardness and disintegration time.

Thus, optimized FDT (s) of both the drugs were compared with market fast dissolving formulations and they were found to be superior in terms of hardness and disintegration. Optimized formulations were selected for stability study for 6 months as per ICH guidelines. No significant change in physical properties, drug content and drug release of the tablets were observed. The dissolution similarity factor ($f_2$) was also calculated to compare before and after storage dissolution profile. The ($f_2$) value was found to be more than 50, indicating a close similarity between both the dissolution profiles.

A single dose bioavailability study was designed in male wistar rats as an animal model. Optimized formulations of both the drugs were administered to rats using gastric intubation method after calculating the animal dose (10 mg/kg). Blood samples were collected at different time interval after dosing. Pharmacokinetic parameters including $C_{\text{max}}$, $T_{\text{max}}$, $AUC_0-t$, $AUC_0-\infty$, $t_{1/2}$ and $K_{el}$ were determined from plasma profile for both drugs. It was found that optimized formulations of domperidone and ondansetron HCl was bioequivalent with market product. Hence, they can be used interchangeably without any prejudice of therapeutic effect. It was also concluded that quick onset of effect was observed with optimized formulations than compare to marked product.

Further to determine in vivo efficacy, conditioned placed aversion study was performed for optimized formulation using swiss albino mice as animal model and it was concluded that optimized fast dissolving tablet (s) of domperidone and ondansetron HCl was superior to market fast dissolving formulations in terms of potency under nauseated condition ($p<0.05$).