5. Conclusions

1. The present study was carried out to develop oral mucoadhesive delivery systems for drugs like Furazolidone, Tinidazole, Ornidazole and Metronidazole for an effective and safe therapy of intestinal amoebiasis.

2. Of the various approaches for oral drug delivery, the approach of multiparticulate systems was chosen in the present study to develop mucoadhesive oral drug delivery systems of antiprotozoal drugs.

3. Earlier studies showed that Chitosan, the N-deacylated product of the polysaccharide chitin, Cellulose ether derivative HPMC K4M, Sodium carboxy methyl cellulose and sodium alginate have a potential for oral specific drug carrier to the gastrointestinal tract owing to their good biocompatibility, safety, low cost and biodegradability.

4. In the preparation of Furazolidone microspheres it was observed that increased concentration of HPMC K4M and Chitosan had a positive effect on the encapsulation of Furazolidone. Drug release in basic medium after a lag period of 2 h in acidic medium was controlled by swollen gel.

5. The mucoadhesive microspheres of Tinidazole were prepared by applying $3^2$ factorial designs taking HPMC K4M ($X_1$) and chitosan ($X_2$) as independent variables, while swelling, mucoadhesion and drug release were studied as dependent variables. It was observed that $X_1$ was more dominant than $X_2$. The swelling
behavior in phosphate buffer at 180 minutes was increased with the increase in HPMC K4M concentration due to improved wetting and increased water uptake in to the matrices; while the swelling behavior in phosphate buffer at 300 minutes was influencened by X$_1$, because X$_2$ undergoes minimal swelling in artificial intestinal fluid due to its poor aqueous solubility at neutral pH values. The time taken for 80% of drug release decreased with increase concentration of X$_2$. When drug release data was analyzed according to different models; it was found that TN-1 to TN-6 and TN-9 formulations follow anomalous diffusion transport mechanism while TN-7 and TN-8 follows Case-II transport. The FTIR and DSC study revealed the compatability of drug with different polymers.

6. Ornidazole microspheres were also prepared by using 3$^2$ factorial designs taking chitosan (X$_1$) and HPMC K4M (X$_2$) as independent variables, while particle size, entrapment efficiency and drug release ($T_{80\%}$) were studied as dependent variables. It was observed that X$_1$ was more dominant than X$_2$. The particle size increased with the increased in X$_1$ and X$_2$ concentrations. The entrapment efficiency decreases with the increase in chitosan (X$_1$) concentration. The $T_{80\%}$ drug release increased with increase in X$_1$ concentration.

7. Changing the composition or coating could make formulations of Metronidazole with different drug release profiles and bioadhesive properties. Chitosan dispersed or coated formulations gradually
released the Metronidazole incorporated and showed good mucoadhesion to stomach and intestinal tissues. These properties are applicable to the sustained release of drugs and if present in the human upper gastrointestinal tract, the drug released will penetrate into the gastrointestinal mucosa from both gastric cavity and blood vessels.

8. The in vitro bioadhesion testing studies revealed that the formulations have the ability to adhere to one or both of biological tissues (Stomach and Intestine), but ranking of bioadhesive potential of formulations could not be possible as all the formulations contain more or less same polymer(s) with varying compositions for selected model drugs.

9. Finally, from the results of in vitro evaluation, based on swelling behavior, mucoadhesion potential and drug release profile, Tinidazole formulation (TN-5) and Metronidazole formulation (MTZ-6) were selected for in vivo studies in healthy human volunteers in comparison with marketed products of these drugs.

10. The pharmacokinetic parameters $C_{max}$, $T_{max}$, and AUC$_{0-t}$ of TN-5 and MTZ-6 were calculated and compared with the reference product (i.e., marketed immediate release (IR) product) and showed significant difference ($P<0.05$) between the two formulations. This difference may be due the reason that one product is administered as immediate release tablet and other as gastroretentive controlled release formulation. Hence, it was concluded that developed formulations were able to sustain the
drug release as compared to the marketed product with increase in the extent of absorption.

11. The *in vivo* X-ray studies of TN-5 and MTZ-6 formulation revealed that the microspheres remained in the stomach for about 1h and then passed to lower parts of GIT and were observed for 5 h in GIT.

12. The successful outcome of the *in vitro* and *in vivo* studies on gastrointestinal mucoadhesive microspheres of above anti-protozoal drugs warrants further studies in patient volunteers to establish their credibility in providing an effective and safe therapy of intestinal amoebiasis and other infections.
The Results of the entire investigation have been published in different journals and also presented from time to time in national seminars and scientific conferences:


PAPER / POSTER PRESENTATION:

