The aim of present study was to develop multiparticulate oral mucoadhesive drug delivery systems of Furazolidone, Tinidazole, Ornidazole and Metronidazole for an effective and safe therapy of intestinal amoebiasis. The microspheres were prepared by orifice-ionic gelation technique using chitosan, HPMC K4M, Sodium alginate and Sodium carboxymethyl cellulose in different concentrations, while Tinidazole and Ornidazole microspheres were prepared by employing $3^2$ factorial designs. The resultant microspheres were evaluated for different in vitro and in-vivo evaluation parameters like swelling studies, entrapment efficiency, bioadhesion test in stomach and intestine, drug release, Scanning Electron Microscopy, bioavailability and X-ray studies. The drug-polymer interaction was also studied by conducting FTIR and DSC tests. To assess the stability of all formulations for two years, the short term stability studies of the selected batches were carried out by keeping them at 40°C ±2°C and 75% ± 5% RH for a period of six months. The preliminary studies were carried out for fixing the needle gauge size, polymer ratio, crosslinking time and the concentration of crosslinking agent. In in-vitro studies, it was observed that increased concentration of HPMC K4M and Chitosan had a positive effect on the encapsulation of all drugs. The particle size increased with increasing of drug-polymer ratio. Bioadhesiveness was influenced with increase in pH and it was more rapid in intestine, rather than in stomach. The swelling studies
in gastric and intestinal mediums were affected by the solubility and concentrations of the polymers. Drug release in basic medium after a lag period of 2 h in acidic medium was controlled by swollen gel. When drug release data was analyzed according to different models; it was found that all formulations tend to fit with different diffusion models, rather than following a single dissolution model. From SEM study, it was concluded that, the leaching out of drugs from calcium alginate microspheres was not only the function of polymer concentration, but also fineness of crystals. The FTIR and DSC study revealed the compatibility of drug with different polymers. When short term stability studies of the ideal batches were carried out, it showed no appreciable difference in the extent of degradation of products, when evaluated for different in vitro parameters. The bioavailability studies of TN-5 containing Tinidazole and MTZ-6 bearing Metronidazole were carried out which exhibited increased pharmacokinetic parameters of $C_{\text{max}}$, $T_{\text{max}}$ and AUC as compared to marketed formulations which indicates improved bioavailability of formulations. The gastrointestinal transit behavior of TN-5 and MTZ-6 in the human stomach was observed in real time using radiographic imaging technique (X-ray), which demonstrated that microspheres remained adhered to stomach for two hours and then passed to lower regions and were detected up to five hours. Thus, the objective of preparation of mucoadhesive microspheres for antiprotozoal drugs using natural and biodegradable polymers with improved bioavailability and gastrointestinal transit time was achieved.