SUMMARY AND CONCLUSION

The objective of present investigation was to develop novel bioadhesive controlled release hybrid drug delivery system for the local treatment of candidiasis and cancer. The developed hybrid drug delivery system can be administered by

- Buccal or vaginal route for candidiasis (Miconazole nitrate)
- Buccal or vaginal or rectal route for cancer (5-fluorouracil).

These dosage forms were developed by using four different types of interpolyelectrolyte complex (IPEC).

- Chitosan-carbopol 71G IPEC
- Chitosan-carboxymethyltamarind IPEC
- Chitosan-polycarbophil IPEC
- Chitosan-sodium alginate IPEC

The above mentioned polymers were considered for the study as these polymers are biocompatible, mucoadhesive, non-carcinogenic, extended-release nature and also the interpolyelectrolyte complex of these polymers are not explored completely. The research work consisted of two studies whose significant findings are summarized below.
MN matrix tablets using chitosan-carbopol 71G IPEC and chitosan-CMT IPEC

Chitosan-carbopol 71G IPEC and chitosan-CMT IPEC were prepared by precipitation method and the ratio was optimized by turbidimetric method and viscosity method respectively. The formed complex was characterized by using FT-IR, DSC and XRD studies. The matrix tablets were prepared by direct compression method using various concentrations of chitosan, carbopol, IPEC alone and in combination (similarly chitosan, CMT, IPEC alone and in combination). The preformulation studies like solubility determination of MN in buffer solutions and drug-polymer compatibility studies were carried out prior to compression, yielding satisfactory results. The prepared MN matrix tablets were subjected for pharmaceutical evaluation, swelling studies and in vitro dissolution studies, mucoadhesion studies and in vivo studies.

- FT-IR and DSC studies confirmed the interpolyelectrolyte complex formation of chitosan-carbopol and chitosan-CMT. XRD studies confirmed the crystal lattice changes.

- Turbidimetric study showed 1:4 ratios (% w/v) of chitosan-carbopol is optimum for complex formation. 2:2 ratios (% w/v) of chitosan to CMT were found to be optimum for complex formation by viscosity study.

- The results of evaluation of tablet friability, drug content and weight variation were found to be within standard limits indicating good pharmacotechnical properties.
• Swelling studies for MD1-MD4 exhibited almost similar profile in phosphate buffer pH 6.8 and SVF pH 4.2. MD1-MD4 formulations showed lesser swelling index than ME1-ME4 formulations in phosphate buffer pH 6.8 and SVF pH 4.2.

• Swelling studies for MH1-MH4 showed almost similar swelling profile in phosphate buffer pH 6.8 and SVF pH 4.2. But formulations MI1-MI4 doesn’t show increased swelling in both phosphate buffer pH 6.8 and SVF pH 4.2.

• In vitro dissolution studies showed that increase in IPEC concentration (MD1-MD4) decreased the drug release profile in both phosphate buffer pH 6.8 and SVF pH 4.2. Formulations ME3 and ME4 release more than 90% of MN within 8 h and also showed almost similar drug release profile in both phosphate buffer pH 6.8 and SVF pH 4.2. MI3 and MI4 formulations released 95% of MN within 8 h in both phosphate buffer pH 6.8 and SVF pH 4.2. The dissolution profiles of MI3 and MI4 were almost similar in both phosphate buffer pH 6.8 and SVF pH 4.2.

• Mucoadhesion studies showed highest mucoadhesive strengths for ME4 and MI3 formulations and also in vivo X-ray studies showed ME4 and MI3 formulations were intact and adhered to the buccal and vaginal mucous membrane for over 8 Hrs.

• Kinetic analysis for ME3 and MI3 dissolution data showed zero order which was best fit model indicating non-fickian diffusion mechanism.
MN matrix tablets using chitosan-polycarbophil IPEC and chitosan-sodium alginate IPEC

Chitosan-polycarbophil IPEC and chitosan-sodium alginate IPEC were prepared by normal precipitation method and the ratio was optimized by turbidimetric method and viscosity method respectively. The formed complex was characterized by using FT-IR, DSC and XRD studies. The matrix tablets were prepared by direct compression method using various concentrations of chitosan, polycarbophil, IPEC alone, combination with chitosan, polycarbophil and sodium deoxycholate (similarly chitosan, sodium alginate, IPEC alone, combination with chitosan, sodium alginate and sodium deoxycholate). The preformulation studies like solubility and partition co-efficient studies of 5-fluorouracil in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4 were carried out. The drug-polymer compatibility studies carried out prior to compression, yielded satisfactory results. The prepared 5-FU matrix tablets were subjected for pharmaceutical evaluation, swelling studies and in vitro dissolution studies, mucoadhesion studies, in vivo studies and permeation studies.

- FT-IR and DSC studies confirmed interpolyelectrolyte complex formation of chitosan-polycarbophil and chitosan-sodium alginate. XRD studies confirmed crystal lattice changes.

- Turbidimetric study showed 3:3 ratio is optimum ratio for chitosan-polycarbophil complex formation and by viscosity study 2:2 ratio of chitosan to sodium alginate was found to be optimum for complex formation.
• The results of evaluation of tablet friability, drug content and weight variation were found to be within standard limits indicating good pharmacotechnical properties.

• Swelling studies for FC1-FC4 exhibited highest swelling index and also showed almost similar profile in phosphate buffer pH 6.8 and SVF pH 4.2. FD1 formulation exhibited least swelling index till 8 hrs in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4. FE1 and FE2 formulations exhibited similar swelling profiles as FD2 formulation in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4.

• FH1-FH4 formulations showed lesser swelling index than FC1-FC4 formulations in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4.

• Swelling studies for FH1-FH4 showed almost similar swelling profile in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4. FI2 formulation showed lesser swelling index in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4.

• In vitro dissolution studies showed increase in IPEC concentration in FC1-FC4 and FH1-FH4 formulations decreased the drug release profile in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4. Formulations FD2 and FI2 released above 95% of 5-FU within 8 h and also showed almost similar drug
release profile in phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4.

- FE1, FE2 and FJ1, FJ2 formulations showed similar drug release profile as FD2 and FI2 formulation respectively in both phosphate buffer pH 6.8, SVF pH 4.2 and phosphate buffer pH 7.4.

- Mucoadhesion studies showed highest mucoadhesive strength for FD2 and FI2 formulations and the presence of sodium deoxycholate in FE1, FE2 and FJ1, FJ2 formulations doesn’t increase mucoadhesive strength.

- Ex vivo permeation studies showed highest permeation in FE2 and FJ2 formulations at 3% sodium deoxycholate concentration.

- In vivo X-ray studies showed FD2 and FI2 formulations were intact and adhered to the buccal, vaginal and rectal mucous membrane for over 8 Hrs.

- Kinetic analysis for FD2 and FI2 dissolution data showed zero order is best fit model indicating non-fickian diffusion mechanism.

- Stability studies for FE2 and FJ2 formulations showed no significant change in the tablet properties and drug content.
Conclusion

There is strong prophylactic and clinical need to develop new solid dosage form for candidiasis and cancer with desired characteristics such as better therapeutic efficacy, retention for intended interval, patient flexibility with cost effective medication. The hybrid drug delivery system developed viz., interpolyelectrolyte complexes have demonstrated their superiority and suitability for buccal and vaginal route for candidiasis and buccal, vaginal and rectal route for cancer. Thus the study shows that the developed system have a great appeal for the convenient treatment of candidiasis and cancer that may be explored in improving the limitations of existing drug delivery system.