Summary:

The objective of the present work was to develop and evaluate dosage forms using modified polysaccharide as release modifier. Three formulations were designed, the first formulation was aimed at designing sustained release pellets of Lornoxicam through extrusion/spheronization process using modified polysaccharide i.e. CMTKP, in second part of the study mucoadhesive pellets of miconazole nitrate were designed for vaginal candidiasis through FBP process using Chitosan-Carbopol complex as release modifier and in last part of the study colon targeted microparticles of 5-FU were designed using STMP cross-linked BFG through emulsification method.

**Formulation of Sustained release pellets using Carboxymethyl Tamarind Kernel polysaccharide (CMTKP) through Extrusion/spheronization process:**

- FT-IR and DSC studies confirmed the carboxymethylation of TKP. XRD studies confirmed the crystal lattice change.
- Preformulation studies were carried in order to establish the compatibility between the drug and polymers by FT-IR and DSC studies. The results revealed that, drug and polymers were satisfactory compatible.
- Swelling and viscosity studies revealed that, swelling and viscosity of CMTKP was increased when compared to TKP.
- Pellets were successfully prepared through extrusion/spheronization process.
- In optimization of process parameters it was found that, under the ideal conditions, viz., MCC-drug-CMTKP ratio of 60:20:20, spheronization time of 20 min at 800 rpm speed, maximum yield of spherical particles with narrow size range were obtained.
SUMMARY & CONCLUSION

- Results micromeritic properties of pellets revealed that the obtained pellets were spherical and have good flow properties.
- Drug loading and entrapment efficiency increase with increase in the polymer concentration. From the results it can be inferred that there is a proper distribution of drug in the pellets and the deviation is within the acceptable limits.
- SEM photographs reveal that pellet was spherical in shape with smooth surface and absence of drug particles on the surface of pellets showing uniform distribution of the drug in the pellet.
- The in vitro release studies revealed that there is no significant release of drug at gastric pH from pellets. At the end of 12<sup>th</sup>, in vitro drug release from formulation F1 to F4 was found to be 72.22 to 91.41 in the intestinal environment.
- Formulation F4 gives sustained release of drug when compared to TKP formulation of same ratio.
- Mathematical model fitting data shows that the best fitted model for F4 formulation was found to be zero order with R<sup>2</sup> value of 0.9935.
- In vivo studies confirmed that CMTKP pellets exhibited higher AUC than the TKP formulation. The increase in AUC represents better absorption and bioavailability of drug from the formulated CMTKP pellets. These results can be attributed to the retarded release of drug form CMTKP pellets.
- Stability studies for F4 formulation showed no significant change in the pellet properties and drug content.
Summary & Conclusion

Formulation of Mucoadhesive pellets using Chitosan/Carbopol 71G complex through Fluid Bed Process (FBP)

- The transmittance results clearly show that the complexation unit molar ratio of chitosan with carbopol was 1:4.
- FT-IR and DSC studies confirmed the crosslinking between chitosan and carbopol 71g. XRD studies confirmed the crystal lattice change.
- Preformulation studies were carried in order to establish the compatibility between the drug and polymers by FT-IR and DSC studies. The results revealed that, drug and polymers were compatible.
- Mucoadhesive pellets were successfully prepared through FBP using MCC, tricalcium phosphate, chitosan-carbopol complex and drug.
- Results micromeritic properties of pellets revealed that the obtained pellets were spherical and have good flow properties.
- Drug loading and entrapment efficiency increase with increase in the polymer concentration. From the results it can be inferred that there is a proper distribution of drug in the pellets and the deviation is within the acceptable limits.
- Scanning electron micrographs obtained shows the surface topography of the pellets, where a rough surface can be observed with its optimal, spherical shape. SEM photographs reveal the absence of drug particles on the surface of pellets showing uniform distribution of the drug in the pellet.
- From swelling studies it was found that formulation containing complex exhibited gradual increase in swelling. Formulations containing complex exhibit almost similar
swelling index in both pH 4.5 and pH 7. These findings indicate the presence of complex exhibit slow uniform pH independent swelling degree.

- *In vitro* studies indicated that the presence of complex in pellets exhibited pH independent drug release.

- Similarity and differentiation factor shows that, since the $f_2$ values was higher than 50 (as per USFDA guidelines), these results confirmed that the drug release profiles were almost similar for MP3 formulation for both vaginal pH.

- *In vitro* mucoadhesive tests showed that 98% of mucoadhesive pellets adhered strongly to the vaginal mucosa and could be retained for period of 8h.

- In *in vivo* X-ray studies it was evident that from the pictures the pellets showed swelling, remained intact and adhered to the vaginal mucous membrane for over 8 h.

- Results Model fitting of formulation MP3 in both pH was found to be following zero order kinetics with regression co-efficient value of 0.9902 and 0.9953 for 4.5 and 7 pH respectively. The $n$ (0.8142) value in peppas is between 0.5 to 1 indicating non-fickian diffusion as the release mechanism.

- Stability studies for MP3 formulation showed no significant change in the pellet properties and drug content.
Formulation of STMP (Tri sodium tri meta phosphate) Cross-linked BFG (Bael Fruit Gum) microparticles as biodegradable carrier:

- FT-IR and DSC studies confirmed the crosslinking between STMP and bael fruit gum. XRD studies confirmed the crystal lattice change.

- Preformulation studies were carried in order to establish the compatibility between the drug and polymers by FT-IR and DSC studies. The results revealed that, drug and polymers were compatible.

- Microparticles were successfully prepared from emulsification method and it was found that a speed of 1000 rpm, time of about 5h and emulsifier concentration of 2%, reproducible microparticles with better yield and flow property were obtained.

- Results micromeritic properties of microparticles revealed that the obtained microparticles have good flow properties.

- Relatively high encapsulation efficiency was observed for all microsphere formulations. The encapsulation efficiency ranged between 48.78±0.81% and 83.53±1.21%. B5, B7, showed relatively higher encapsulation efficiency as these formulations composed of high concentration of polymer. Among all formulations, B5 and B7 showed maximum percentage yield and drug loading.

- Swelling studies shows that, as a result of cross-linking with STMP the overall swelling of polymer decreased significantly thereby enhancing the release of drug at specific site. Cross-linking interferes with free access of water to the BFG hydroxyl group, which in turn reduced the swelling properties of cross-linked polymer.

- From the in vitro release studies it was found that, the release of drug coincides with swelling properties of the polysaccharide. Formulation B6 which has swelling of
more than 2 degree, the drug release at the end of 8\textsuperscript{th} h was found to be 72\%, which is mainly due to diffusion of drug from the swollen polymeric gel formed around microparticle. Formulation B3 which has least swelling property compared to other formulations, the drug release at the end of 8\textsuperscript{th} h was found to be 38\%. This can be attributed to the cross-linking of BFG with STMP completely interferes with the free access of water to the hydroxyl group of BFG, thus swelling of the BFG is reduced and thus preventing the drug release through diffusion.

- \textit{In vitro} release data of B3 formulation in presence of rat cecal medium shows that, only 27.37±0.19 \% of drug released in SGF and SIF of pH 1.2 and 4.5. After 6 h the percentage drug released in rat cecal content medium was 43.81 ±0.14\% and release was further increased to 96.20±0.18\% at 8 h because of the digestion of the polysaccharide by the enzymes induced by colonic microbial flora in the enzyme induced rat cecal medium.

- The \textit{in vitro} release studies data was fitted into various mathematical models to determine the best-fit model. The results indicated that, the best-fit model was found to be Zero-order model.

- The results of \textit{in vivo} studies indicate that after oral administration of plain drug suspension of 5-FU. 9.74\% absorption of 5-FU was observed after 2 h, and 41.33 \% absorption was observed at 8\textsuperscript{th} h was observed. The cross-linked microparticles of formulation (B3) were observed to be relatively intact in the upper part of the GIT with absorption of 17.77\% during transit through the upper GIT (0-5 h). 53.52\% of the drug was absorbed during 8\textsuperscript{th} h of administration.
SUMMARY & CONCLUSION

- Stability studies for B3 formulation showed no significant change in the microparticle appearance and drug content.

**Conclusion:**

In the present study an attempt was made in designing various formulations using modified polysaccharides of natural polymers. The designed formulations like Sustained release pellets of CMTKP, mucoadhesive pellets of chitosan-carbopol 71g and colon targeted microparticles of STMP cross-linked BFG containing a model drug achieved the required study objectives. The dosage forms containing modified polysaccharides proved to be release modifiers in the form of sustained, mucoadhesive and colon targeted release. Further these modifications of polysaccharides can be explored in designing various drug delivery systems.