8. CONCLUSION

Colorectal cancer is a disease originating from the epithelial cells, lining the colon or rectum of the gastrointestinal tract. Capecitabine is one of the choices for the treatment of colon cancer. Generally, capecitabine is given in the form of tablet dosage form which has many disadvantages like, delivery of the drug to the healthy cells as well which must not happen, poor patient compliance, larger drug dose etc. Therefore, to target the capecitabine with suitable novel drug delivery system at specific site of action in controlled manner is thought to be beneficial approach.

From research literature, it was found that certain cancer express folate receptors on the cell surface and these receptors are over expressed on colon cancer cells. To support this, preparation and optimization of folic acid-targeted capecitabine loaded nanoparticles as a delivery system for the effective treatment of colon cancer, was the goal of this study. For that purpose, chitosan nanoparticles have been prepared by using ionic gelation method which was, later on, conjugated with folic acid as a targeting carrier.

In chitosan nanoparticle formulation, some parameters such as chitosan concentration and sodium TPP concentration have been studied as they affect the percentage entrapment efficiency. $3^2$ full factorial design was used to statistically optimize parameters and evaluate the main effects of these individual variables on the percentage entrapment, particle size and drug release. The particle size was found to be ~87 nm, spherical in shape. IR spectra have confirmed that there was no any interaction between drug and excipients. From the result, it was concluded that concentration of chitosan, 1.5mg/ml and sodium TPP, 1.5mg/ml were found to be optimum for the preparation of optimized chitosan nanoparticles.

The developed and optimized chitosan nanoparticles were conjugated with folic acid as a targeting tool. This conjugation was carried out using $3^3$ factorial design to statistically optimize three parameters i.e. concentration of folic acid, rpm and reaction time; and evaluate the main effects of these individual variables on the percentage folic acid conjugation. Drug loaded folic acid conjugated chitosan nanoparticles were also evaluated for particle size analysis, compatibility and SEM study. it confirms the conjugation of folic acid as increased particle size ~ 122 nm was observed.
In-vitro cytotoxicity study was carried out using two cancer cell line, folate receptor positive colon cancer cell line HT-29 and folate receptor negative breast cancer cell line MCF-7. From the results of in-vitro cytotoxicity study, it was concluded that capecitabine loaded formulations were highly effective on colon cancer cell line HT-29 and not on the MCF-7 cell line which lacks the folate receptors expression. The FA-CS-NPs formulation were readily taken by HT-29 cell while non-conjugated CS-NPs were not getting internalized with much intensity as compared to folic acid conjugated CS-NPs which indicates that the FA-CS-NPs have good potential as a carrier for the targeting and releases the drug capecitabine in controlled manner.

Finally, capecitabine loaded folic acid-conjugated colon-targeted chitosan nanoparticles, was successfully developed and optimized which can specifically target the colon cancer cells with less side effects and improved efficacy.