CONCLUSION

Despite phenomenal advances made in the inhalable, injectable, transdermal, nasal and other routes of administration, oral drug delivery remains preferred delivery route. However, certain conventional oral dosage forms such as tablets, capsules and liquids are difficult to swallow in case of dysphagic patients and thus do not comply with their recommended dose schedule, resulting in ineffective therapy.

To overcome swallowing problem (dysphagia) and improve treatment compliance and safety of such patients, require an appropriate oral dosage form or modification of the dosage form.

There are many dosage forms which are suitable for delivering medications to dysphagia patients of which Fast Disintegrating Films, Fast Disintegrating Tablets and Eatable gels were selected in the present research study. These formulations containing anticancer agents were prepared, optimized and evaluated.

The following conclusions are drawn from the study:

**FAST DISINTEGRATING FILMS (FDF)**

- The fast-disintegrating films of anastrozole, cyclophosphamide, methotrexate and imatinib were successfully prepared using different film-forming materials (HPMC E 5 LV, PVA, Na Alginate, HPC and Na CMC) by the solvent-casting method.

- FT-IR spectral analysis indicated no interaction between the drug and the excipients used for the formulation of films indicating drug-excipient compatibility.

- The film formulations prepared were free from gritty appearance, air bubble, nicks or tears.
The surface pH of all the formulations were in the range of oral pH (6.8), indicating that films have less potential to irritate oral mucosa and hence are acceptable.

All the FDF prepared met the criteria for content uniformity test of dosage units indicating uniform distribution of drug in the films.

Of all the formulations, formulation prepared using HPMC E LV was considered optimized as it showed moderate tensile strength, high % elongation, low elastic modulus and shortest disintegration time.

DSC thermogram of the optimized film confirmed no chemical interaction between the drug and the polymers used indicating drug-excipient compatibility.

TGA curve behaviors confirm the endothermic peak observed in DSC experiments.

XRD diffractograms of the optimized film showed disappearance of the intense sharp peaks which indicated amorphization of drug in the FDF.

SEM studies confirmed smooth surfaced uniform film without any scratches or transverse striations.

Sensory studies reveal that 5.7 mg sucralose with other excipients showed excellent taste property.

The optimized film formulation showed rapid dissolution profile and in vivo studies revealed no statistically significant differences (p < 0.05) in pharmacokinetic parameters between the FDF (test) and solution (control) indicating similarity between test and control group.

Stability studies of the film formulations placed in heat sealed aluminum pouch recommend its storage at refrigerated (for anastrozole, cyclophosphamide, methotrexate and imatinib) or normal temperature (imatinib).
**FAST DISINTEGRATING TABLETS (FDT)**

- The fast-disintegrating tablets of anastrozole, cyclophosphamide, methotrexate, imatinib and capecitabine were successfully prepared.

- FT-IR spectral analysis indicated no interaction between the drug and the excipients used for the formulation of tablets indicating drug-excipient compatibility.

- Anastrozole, methotrexate and cyclophosphamide FDT’s were prepared by direct compression technique whereas imatinib and capecitabine FDT’s were prepared by wet granulation method.

- Preliminary studies showed significant influence of CP (superdisintegrant), neusilin (disintegrant & glidant) and magnesium stearate (lubricant) on disintegration time of FDT.

- The optimized formulations showed satisfactory pre & post compression properties, satisfactory physical resistance and shortest *in vitro* disintegration time.

- Optimized FDT’s prepared, met the criteria for content USP uniformity test of dosage units indicating uniform distribution of drug in the tablets.

- The optimized FDT’s showed smooth surface without any interactions between drug and excipients as confirmed by DSC analysis indicating drug-excipient compatibility.

- TGA curve behaviors confirm the endothermic peak observed in DSC experiments.

- XRD diffractograms of the tablet indicated presence of crystallinity (capecitabine & imatinib) or absence of crystallinity/amorphized (methotrexate, anastrozole & cyclophosphamide) of drug in the optimized FDT.
Conclusions

• Sensory studies reveal that 5.7 mg sucralose with other excipients showed excellent taste property.

• Optimized FDT showed faster rate of *In vitro* drug dissolution due to presence of adequate proportion of excipients which favored faster disintegration followed by dissolution.

• *In vivo* studies revealed that there was no statistically significant difference (p < 0.05) in pharmacokinetic parameters between the FDT (test) and solution (control) indicating similarity in the test and control group.

• Stability studies of the FDT formulation recommends storage at normal temperature (anastrozole, cyclophosphamide, methotrexate, capecitabine and imatinib) or accelerated temperature (imatinib) with proper packing.

**EATABLE GELS**

• Eatable gels of methotrexate were prepared using various natural/semi-synthetic polymers (HPMC, PVA, Na Alginate, HPC, silk fibroin and Na CMC) to obtain desired viscosity as per NDD guidelines.

• Methotrexate was selected for development of eatable dosage form due to its stability in aqueous phase compared to other drugs.

• Silk fibroin only gels at pH 3.2, where methotrexate is not soluble and stable, hence silk fibroin as gelling agent was not considered.

• FT-IR spectral analysis indicated no interaction between the drug and the excipients used for the formulation of gels (physical mixture) indicating drug-excipient compatibility.

• Formulated gels were non-sticky and non-gritty in nature.
• The surface pH of all the formulations were in the range of oral pH, indicating that films have less potential to irritate oral mucosa and hence are acceptable.

• The gels formulated using various polymers showed no sign of syneresis when stored at refrigerated temperature.

• All the gels prepared met the criteria for content uniformity test of dosage units indicating uniform distribution of drug in the gels.

• Viscosity of gels prepared using various polymers meets the viscosity requirements of NDD guidelines [1-50 (thin), 51-350 (nectar-like), 351-1750 (honey-like), > 1750 cps (spoon thick)].

• Of all the gel formulations, gel prepared using HPMC K4M (A, B, C & D of 45 mg and 90 mg doses) was considered optimized as it showed faster In vitro drug release profile compared to other polymers.

• Sensory studies reveal that 5.7 mg sucralose with other excipients showed excellent taste property.

• In vivo studies showed no statistically significant differences (p < 0.05) in pharmacokinetic parameters between the MTX gel (test) and solution (control) indicating similarity between test and control group.

• Stability studies of the gel formulation recommend storage at refrigerated temperature (4 °C – 8 °C).

Thus, the specific study objectives enlisted are achieved, namely formulation, evaluation of eatable dosage form containing anticancer agent for dysphagia patients. These dosage forms not only circumvent the swallowing problem (dysphagia) by providing compliance, safety and improved quality of life but also provide effective therapy for the treatment of cancer by preventing withdrawal of the medication. These formulations may further be scaled up for commercial exploitation.