ABSTRACT

The objective of the present research was to ensure compliance during oral administration of medications to dysphagia patients, by preparing Fast Disintegrating Films (FDF), Fast Disintegrating Tablets (FDT) and Eatable gels.

Fast disintegrating films (FDF) containing Anastrozole (ANS), Methotrexate (MTX), Cyclophosphamide (CYP) and Imatinib Mesylate (IM) were prepared, optimized and evaluated. Films were prepared by solvent-casting method using various polymers such as Hydroxyl Propyl Methyl Cellulose (HPMC E5 LV), Hydroxy Propyl Cellulose (HPC), Poly Vinyl Alcohol (PVA), Sodium Alginate (Na Alginate). FTIR spectral analysis revealed no incompatibility between drug and excipients used in the formulation. Among the formulations examined, film prepared using HPMC E5LV exhibited shorter disintegration time with satisfactory mechanical properties. Differential Scanning Calorimetry (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. X-Ray diffractograms showed disappearance of the intense sharp peaks in films indicating amorphization of drug. Surface morphology showed even distribution of drug in the film. Sensory studies reveal that sucralose with other excipients showed excellent taste property. The optimized film formulation showed rapid dissolution profile. In vivo studies exhibited no statistically significant differences (p < 0.05) in pharmacokinetic parameters between the FDF (test) and solution (control) indicating similarity between test and control group. The film showed an excellent stability for 24 weeks when stored at refrigerated temperature (2 – 8 °C). Hence it can be concluded that optimized FDF disintegrates rapidly with excellent dissolution profile, thus providing convenience of administration, patient compliance and safety to overcome swallowing problem for dysphagia patients.

Fast Disintegrating Tablets (FDT’s) of MTX, ANS, CYP, IM and Capecitabine (CAP) were prepared incorporating superdisintegrants such as Croscarmellose Sodium (CCS), Crospovidone (CP) and Sodium Starch Glycolate (SSG) and other excipients. Drug-excipient compatibility was confirmed by FT-IR.
Abstract

MTX, ANS and CYP fast disintegrating tablets were successfully prepared by direct compression technique whereas IM and CAP FDT by wet granulation method. The optimized blend mixture (for MTX, ANS & CYP) and granules (for CAP and IM) had good flow and compressible property; hence tablets produced were of uniform drug content with smooth surface. Tablet produced can withstand abrasion during handling, packaging and shipment as FDT’s showed optimum hardness with friability values within the limits. The disintegration time of FDT’s was not more than 30 s. DSC thermogram of the optimized FDT confirmed no chemical interaction between the drug and excipients. X-Ray diffractograms showed disappearance (MTX, ANS & CYP) or retaining of the peaks (CAP & IM) indicating change (amorphosization) or no change in crystalline nature of drug after tableting. FDTs demonstrated excellent in vitro dissolution results. In vivo studies of FDTs (test) compared with drug solution (control) showed no statistically significant difference in pharmacokinetic parameters. Stability studies results were also found to be satisfactory at normal (ANS, CYP, MTX, CAP and IM) or accelerated temperature (IM). The study indicated that FDT’s disintegrates rapidly in seconds and hence is a promising dosage form for dysphagia patients.

Eatable gels were prepared using various natural/semi-synthetic polymers (HPMC, PVA, Na Alginate, HPC, silk fibroin and Na CMC) to obtain desired viscosity. Methotrexate was selected for formulation 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 is not studied further. Drug-excipient compatibility was confirmed by FT-IR studies. Gels were non-sticky and non-gritty in nature with surface pH in the range of oral pH (6.8). Gels showed no sign of syneresis when stored at refrigerated temperature. Viscosity of gels prepared using various polymers meets the viscosity requirements of NDD (National Dysphagia Diet Task Force) guidelines. HPMC K4M gels were considered optimized as it showed faster In vitro drug release profile compared to other polymers. Sensory studies reveal sucralose with other excipients showed excellent taste property. In vivo studies showed no statistically significant differences (p < 0.05) in pharmacokinetic parameters between the gel (test) and solution (control) indicating similarity between test and control group. Stability studies of the gel formulation
recommend storage at refrigerated temperature. The results suggest that the MTX gels having desired viscosity and faster \textit{In vitro} drug release profile have potential to improve compliance and safety for dysphagic patients.