ABSTRACT

Fast dissolving tablet (FDT) is a dosage form which can disintegrate in smaller granules, or melt in mouth, from a hard structure to gel like structures within a minute allowing easy swallowing by the patients. A comprehensive review of current technologies in making fast dissolving tablet was conducted. FDT can be formulated using various methods. Some of them involve increasing the porosity of the tablet and decreasing the disintegration time (DT). Superdisintegrants are used that swell or absorb water rapidly to disintegrate the tablet. Technologies like Zydis based on lyophilization yield tablets that dissolve in a few seconds. Most of the techniques aim at lowering the DT, but doing this always compromises the mechanical strength. Zydis tablets need special packaging and patient counselling for removing the tablets from the strip. The disintegration time for fast dissolving tablet is less than one minute and it should have adequate mechanical strength. Hence, the objective of present investigation was to develop and optimize fast dissolving tablet of domperidone and ondansetron HCl for better patient compliance with improved mechanical properties, rapid disintegration and pleasant taste.

Solubility of domperidone was enhanced using solid dispersion technique. Experiments were performed using different carrier system, and PEG 6000 was selected for further studies. Solid dispersions of domperidone: PEG 6000 was prepared in different ratio and by using optimized ratio of domperidone: PEG 6000 solid dispersion, fast dissolving tablets were prepared. Fast dissolving tablets were prepared using two different approaches. In one approach FDT were prepared using different superdisintegrants and further optimized by full factorial design. In second approach, FDT were prepared using effervescent material and optimization was carried out using central composite design. The responses were analysed for analysis of variance (ANOVA) using Design Expert version 8.0 software. In full factorial design, effects of formulation parameters like concentration of diluent, concentration and type of superdisintegrant were evaluated and their effect on disintegration time and hardness was determined. In central composite design effects of formulation parameters like concentration of Ac-Di-Sol and effervescent materials (sodium bicarbonate and citric acid) were evaluated. FDT of domperidone prepared using effervescent materials was found to be optimum in relation to disintegration (31.08 seconds) and hardness (4.1 kg/cm²).

Pharmacokinetic studies were performed using male wistar rats as animal model and it was
found that optimized FDT of domperidone was bioequivalent with reference product (Domel MT). Hence, it can be used interchangeably without any prejudice of therapeutic effect. From pharmacokinetic study it was also concluded that quick onset of effect was observed with optimized FDT as compared to marked product (Domel MT). Results from conditioned placed aversion study, which was performed on swiss albino mice showed that optimized FDT of domperidone was superior to market fast dissolving formulations in terms of potency under nauseated conditions (p<0.05).

In another study bitter taste of ondansetron HCl was masked by Eudragit® EPO. Drug polymer complex (DPC) in different ratio were prepared using extrusion method and characterized for FTIR, DSC, XRD and in-vitro taste evaluation. The result indicated the ability of Eudragit® EPO for taste masking and improving the dissolution profile. Using optimized ratio of DPC, FTD’s were prepared by two different methods. In one method different ratio of MCC and lactose as a diluent and different concentration of superdisintegrant was used to develop tablet and further optimized using full factorial design. In another method sublimation technique was used to develop tablets and experiments were performed using full factorial design to evaluate effect of formulation parameters like concentration of subliming material (camphor) and concentration of diluent (mannitol), and their interactions on disintegration time and hardness of fast dissolving tablet formulation. Tablets prepared using ratio of MCC and lactose (66:34%) and 4.49 % of Ac-Di-Sol were found to be optimum in relation to hardness (4.4 kg/cm²) and disintegration time (24 seconds). Pharmacokinetic studies was performed using male wistar rats as animal model and it was found that optimized FDT of ondansetron HCl was bioequivalent with reference product (Ondem MD). Hence, can be used interchangeably without any prejudice of therapeutic effect and it was also concluded that quick onset of effect was observed with optimized FDT than compare to marked product (Ondem MD). Further, from conditioned placed aversion study it was concluded that optimized FDT of ondansetron HCl was superior to market fast dissolving formulations in terms of potency under nauseated condition (p<0.05). Thus, optimized FDTs of both the drugs were found to be superior in terms of hardness and disintegration time compare to market fast dissolving formulations. Optimized FDT of both the drugs were submitted to short term stability study as per ICH guidelines and no substantial change in the quality of tablet during storage is to be observed.
**Key words**: Ondansetron HCl, domperidone, full factorial design, central composite design, solid dispersion.