ABSTRACT

Candesartan cilexetil (CC) is a selective angiotensin II receptor antagonist and it is widely used in the treatment of hypertension, heart failure, myocardial infarction and diabetic nephropathy.The solubility of the CC is very poor and its oral bioavailability is only 15%.

Liquisolid compacts of candesartan cilexetil were prepared using a mathematical model to calculate the required quantities of powder and liquid ingredients to produce an acceptably flowable and compressible admixture and compared it with solid dispersions that prepared by solvent evaporation method with different drug to polymer ratios (1:1, 1:3, 1:5, 1:7, 1:9).

Microcrystalline cellulose, colloidal silicon dioxide and croscarmellose sodium were employed as a carrier material, coating material and disintegrant; respectively for preparing of liquisolid compacts. Also polyethylene glycol 400 was used as liquid vehicles.Different ratios of carrier to coating material were used in preparation of liquisolid compact as the followings 10:1, 15:1, 20:1 and 25:1.

The saturated solubility of all the prepared CC solid dispersions and physical mixtures in phosphate buffer solution pH (6.8) were measured. The results showed that the solubility of CC in solid dispersion formula that contain drug and polyvinylpyrrolidon in a ratio of 1:7 (SDPVP-4) was (0.398±0.018)mg/ml ,which was higher than other formulas ,so this formula was formulated into tablet by direct compression method and used for comparative evaluation with CC liquisold tablets.

The physiochemical properties of all prepared tablets as the hardness, drug content uniformity, percentage of friability and disintegration time were evaluated and the results indicated that were within the acceptable limits, also the drug release rates of all prepared liquisolid compacts and solid dispersion (SDPVP-4) were higher as compared to directly compressed tablets, and marketed tablet.

Based on mathematical data revealed from models, it was concluded that the release data of the almost formulas were best fitted with first order kinetics and the diffusion exponent ‘n’ values were found to be above 0.5 for the almost candesartan

cilexetilliquisolid and solid dispersion tablets indicating non Fickian (anomalous) diffusion.

Both Differential scanning calorimetry and X- ray powder diffraction suggested loss of CC crystallinity upon liquisolid and solid dispersion preparation, indicating that drug a morphization was obtained which may be contributed to the enhanced drug dissolution properties.

The Fourier transform infrared spectra showed disappearance of the characteristic absorption bands of candesartan cilexetil (2941.2 cm-1and 1755 cm-1) in both liquisolid and solid dispersion formulations which may be attributed to the formation of hydrogen bonding between the drug and polymer; this resulted in drug dissolution enhancement.

The stability study of the prepared tablet was established through storing at temperatures of 40, 50 and 60°C for four months. The calculated expiration date at 25°C using Arrhenius method was approximately 3.14 years for selected liquisold (LS-4) formula and 3.44years for solid dispersion (SDPVP-4) formula.

The overall results suggest that the liquisolid selected formula (LSF-4) is better than solid dispersion and conventional tablets in term of pharmaceutical properties and could be utilized as a new dosage form for the oral administration.