CHAPTER 8
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- The present investigation is an in depth study about formulation and characterization of solid dispersions to improve dissolution characteristics of some poorly water soluble drugs.
- Different methods for preparation of solid dispersions were reviewed. Kneading and solvent evaporation methods were used for the preparation of solid dispersions due to their advantages over other methods.
- Different polymers like PEGs (PEG 600, PEG 1000, PEG 2000, PEG 3000, PEG 4000 and PEG 6000), PVPs (PVPK25, PVPK30, PVPK35 and PVPK40) and β-cyclodextrin were used for the preparation of solid dispersions. Among various polymers used, PEG4000, PVPK30 and β-cyclodextrin gave best results with respect to solubility and dissolution behavior.
- Etoricoxib and cilostazol were taken as poorly water soluble drugs for preparation of solid dispersions.
- For preparation of solid dispersions of etoricoxib, PEG4000, PVPK30 and β-cyclodextrin, when used alone, did not give satisfactory results (less than 80% dissolution in 30 min). This prompted us to use combination of the polymers. As expected, solid dispersions prepared by using both PEG4000 and PVPK30 displayed good dissolution behavior (more than 80% dissolution in 45 minutes).
- Also, for preparation of solid dispersions of cilostazol, PEG4000, PVPK30 and β-cyclodextrin, when used alone, did not give satisfactory results (less than 80% dissolution in 30 min). On the other hand, solid dispersions prepared by using both β-cyclodextrin and PVPK30 showed good dissolution behavior (more than 80% dissolution in 45 minutes).

Prepared solid dispersions were characterized by different analytical techniques. Preliminary characterization was done by solubility study, dissolution study and wettability study. Based on the results, it was thought of interest to confirm the solid dispersions using following analytical techniques.

- FTIR spectra gave information about possible chemical interaction.
DSC thermograms and X-ray diffractograms gave information about conversion of the drug from crystalline to amorphous state.

HPTLC study gave information about presence of drug in solid dispersions.

Microscopic analysis reflected shape and surface morphology of drug present in solid dispersions.

Different batches of solid dispersions were prepared by using different ratio of drug and polymer. Solubility, dissolution and wettability studies were performed for all batches.

The batch which displayed best results (etoricoxib: PEG4000: PVP, 1:2:2; cilostazol: β-cyclodextrin: PVPK30, 1:1:5) with respect to solubility, dissolution and wettability studies was further characterized by previously mentioned techniques.

Stability studies were carried out at ambient temperature for selected batches. Solid dispersion of ET: PEG4000: PVP (1:2:2) was stable for 1 year while that of cilostazol: β-cyclodextrin: PVPK30 (1:1:5) was stable for 6 months.

Physical mixtures of drug and polymer in the selected ratio was prepared and characterized in a similar manner.

Two spectrophotometric methods, UV method (method A) and first derivative UV method (method B) were developed, validated and applied for determination of etoricoxib in bulk and four marketed tablet dosage form. The linearity was found to be 5 to 25 μg/ml and 5 to 30μg/ml for method A and method B, respectively.

Method A was applied for determination of etoricoxib in formulated solid dispersions, solubility study and dissolution study.

HPLC method was developed, validated and applied for determination of etoricoxib in bulk and three marketed tablet dosage forms. The linearity was found to be in the range of 1.25 to 20.00μg/ml.

The proposed HPLC method was applied for determination of etoricoxib in formulated solid dispersions.
The proposed spectrophotometric and HPLC methods were found to be simple, sensitive, accurate and rapid for estimation of etoricoxib in bulk, tablet dosage form and solid dispersions.

HPLC method was developed, validated and applied for determination of cilostazol in bulk and three marketed tablet dosage forms. The linearity was found to be in the range of 1.00 to 50.00μg/ml.

The proposed HPLC method was applied for determination of cilostazol in formulated solid dispersions.

The proposed HPLC method was found to be simple, sensitive, accurate and rapid for estimation of cilostazol in bulk, tablet dosage form and solid dispersions.