CHAPTER IV

RESULT AND DISCUSSION
The objective of solid dispersion preparation of insoluble drugs is to enhance the dissolution of insoluble medicament to improve their absorption. To achieve this goal formulations were prepared using four carriers. On the basis of dissolution studies following conclusions were made:

4.1 Increase in the carrier fraction in solid dispersion matrix increases the drug dissolution.

4.2 Impact of polyethylene glycol 6000 is maximum on dissolution enhancement. Out of chosen carrier they exhibited the efficacy order PEG 6000 > PVP mannitol > urea.

4.3 Solvent method was found to be little superior than the melting solvent method.

The above mentioned hypothesis were tested for their authenticity by performing rigorous statistical treatment over the dissolution data. Fischer's F-test have been performed on the dissolution data grouped in three format having null hypothesis for:

4.3.1 Change in the percentage of carrier has no significant effect over drug dissolution.

To prove the validity of the statement "Change in the percentage of carrier has no significant effect over drug dissolution ", F-values were calculated for the solid dispersion having same carrier in different percentages and prepared by same method (table 7.1).

At 5% level tabulated values for 30 degree of freedom
for residual corresponds to 2.92. Using this yardstick statistically significant difference exists among the solid dispersions of ampicillin trihydrate prepared by polyethylene glycol 6000 by both methods and solid dispersion of chlorpropamide prepared by all investigated carrier using both the carrier (F-values were greater than 2.92). F-values for prednisolone carrier system were statistically insignificant.

On the basis of comparison of cal-F values it can be said:

4.3.11: that ampicillin trihydrate dissolution can be significantly altered using various percentages of PEG 6000,

4.3.12: Chlorpropamide dissolution can easily be altered by changing the carrier percentage and

4.3.13: prednisolone dissolution is relatively insensitive to the change in carrier percentage.

4.3.2 Change in the carrier has (table 7.2) no significant effect over drug dissolution.

The influence of the nature of carrier was established by determining F-values among the dissolution data of solid dispersion having the same percentages of different carriers for the similar degree of freedom only chlorpropamide yielded the statistically significant different, which is interpreted as the chlorpropamide dissolution is markedly influenced by the nature of
carrier. (table 7.2).

4.3.3 Change in the method of preparation has no significant effect over dry dissolution (table 7.3).

In an attempt to establish the influence of method of preparation over drug dissolution, similar composition dispersions were prepared by two methods, were subjected to analysis of variance (table 7.3). None of the pair has exhibited the value more than the tabulated value at (5% level for 10 degrees of freedom - 4.17). Which reflects the statistically insignificance between the drug dissolution obtained from matrix prepared by two different methods. A Model calculations for F Value is given in table 7.4.

4.4 Maximum dissolution is encountered in the early dissolution phase than the post dissolution phase.

4.5 On the basis of analysis of variance performed following conclusions can be drawn affirmatively.

4.5.1 Successful dissolution enhancement can be achieved in case of ampicillin trihydrate using PEG 6000.

4.5.2 Chlorpropamide dissolution can be easily increased using solid dispersion having hydrophilic carrier.

4.5.3 Prednisolone is relatively insensitive drug for dissolution modification using carriers under investigation.

4.6 The dissolution improvement of drug, could take place by the combination of following mechanisms:
4.6.1 Generation of very small crystalline particle after dissolving highly water soluble carrier in G.I. fluid.

4.6.2 Solubilization effect by the carrier in the micro environment, immediately surrounding the drug particles in early stages of diffusion.

4.6.3 Absence of agglomeration between fine crystals of hydrophobic drug.

4.6.4 Excellent wettability and dispersibility of a drug generated in situ which is free from non-polar air envelopes.

4.6.5 Formation of metastable crystal form due to sudden solidification from solution.

4.6.6 Formation of amorphous fraction of dispersed drug due to difficulty in drug molecule movement in polymer matrix.

4.6.7 Formation of week complexes having high aqueous solubility.

4.7 The influence of increased dissolution upon bioavailability of drugs is clearly seen by the plasma levels of drug in dogs. The bioavailability improvement after fabricating solid dispersion were quantified. from 13.74 μG-hr/mL to 19.14, from 241.915 to 284.2 & from 4.0785 to 5.0335 μG-hr/mL for ampicillin trihydrate, chlorpropamide and prednisolone respectively.