SUMMARY & CONCLUSION

Solid dispersions in hydrophilic carriers are regarded as highly effective means of increasing the dissolution rate of poorly soluble drug ACELOFENAC and INDOMETHACIN. Solid dispersions increase the solubility of drug due to the conversion of the drug’s crystal lattice into amorphous form, decrease in the particle size and increase in wettability caused by hydrophilic polymer. Current study investigates the suitability of HPMC AS, Chitosan, HPMC-15cps, PEG 4000 as a carrier for solid dispersions for ACELOFENAC and INDOMETHACIN studies. The purpose of the present investigation is to evaluate the effect of polymer composition, concentration, and solvent characteristics on the dissolution behavior of ACELOFENAC and INDOMETHACIN developed solid dispersion by little modification in solvent evaporation method. Solvent evaporation method was preferred for development of solid dispersion because of their low melting points, the ease in controlling the processing variables such as temperature and shearing rate, and the short duration of preparation (1–2 hr). Solubility of the drug increased in the solid dispersion followed by physical mixture and pure drug.

The increased solubility in solid dispersions is potentially due to the conversion of crystalline drug into amorphous form during the formation of solid dispersion which leads to higher wettability. Phase solubility study showed that the solubility of ACELOFENAC and INDOMETHACIN almost linearly increased as the concentration of HPMC-AS increased ($R^2 = 0.981$ and 0.977) respectively. HPMC AS increases solubility of Acelofenac approximately by 3.61 fold and Indomethacin by 5.79 fold in physical mixture and 24.41 fold in case of Acelofenac as well 18.20 fold in case of INDOMETHACIN loaded solid dispersion and thereby significant increase in dissolution rate.

The solid state studies did not indicate any chemical decomposition or well-defined interactions between the ingredients, showing compatibility between them. It was found that in these carriers the drug dissolution rate was a function of drug loading.

A marked increase in the dissolution rate of drug from the solid dispersions was observed when Chitosan and HPMC 15cps was used as a carrier; however HPMCAS
showed much better results with synergistic effect on the dissolution rate of the drug. Moreover, the incorporation of PEG 4000 yielded dispersions with less tackiness and greater ease of handling. Thus it has shown that HPMC AS used as a best carrier within the solid dispersions as it increase the dissolution rate. The physical mixtures displayed higher dissolution rates in all two drugs as compared to pure drugs which can rightly be attributed to the wettability of drug caused by the presence of HPMC AS. Enhanced solubility and dissolution of drug from physical mixtures could be related to the surface activity, wetting effect that may lead to reduced agglomeration and hence increased surface area and solubilizing effect of HPMCAS. When the mixture came in contact with water, the polymer particles might have hydrated rapidly into polymer solution. This hydration contributed to the increased wettability of the drug particles and to the local enhancement of the drug solubility at the diffusion layer surrounding the particles and subsequently releasing the drug into the medium. These also explain the higher solubility of drug in phase solubility study where the drug particles get dispersed in aqueous polymer solutions.

The kinetics treatment showed that the best formulation $S_2$ and $S_{22}$ follow Korsemeyer Peppas kinetics with ($r^2 = 0.997$) and ($r^2=0.996$) respectively and possess anomalous diffusion as $n= 0.823$ and $0.953$ was obtained by mathematical calculation performed by DD solver. Thus the studies provided better forecasting and understanding of particular systems to be incorporated to develop delivery systems.

In addition, the results were reproducible with relatively higher percentage yields when incorporated to HPMC AS. Drug content analysis indicated that the drug was uniformly distributed in SDs and the higher yield showed relatively lower process loss.

In Anti-inflammatory activity the % inhibition of rat paw oedema was calculated & compare with Control. Acelofenac pure produced 54.44 % inhibition of paw oedema at 3 hrs, whereas Test 1 i.e. Acelofenac physical mixture produced 58.88 % & Test 2 i.e. Acelofenac solid dispersion produced 68.88 % respectively and Indomethacin pure produced 53.33 % % inhibition of paw oedema at 3 hrs, whereas Test 3 i.e. Indomethacin physical mixture produced 58.88 % and Test 4 i.e. Indomethacin solid dispersion produced 70 % respectively when observed after 3 hours of Carrageenan injection.
In Analgesic activity SD significantly reduced the number of abdominal writhing in comparison to the vehicle control. Both PM and SD considerably improved the analgesic activity (35.82 and 44.52\%) respectively in comparison to the Acelofenac pure drug (28.60\%) & (39.02 and 46.34\%) & respectively in comparison to the Indomethacin Pure drug (31.70\%). The increase in analgesic activity with SD was significant in comparison to the same dose of Acelofenac & Indomethacin Pure drug.

The present study was aimed to enhance aqueous solubility of the drug by the use of PM and SD with HPMC AS to get formulations with better analgesic and anti-inflammatory activity than the pure drug. Acelofenac, PM, SD & Indomethacin, PM, It is concluded that solid dispersion of drug Indomethacin & Acelofenac show significant enhancement of anti-inflammatory activity against experimentally induced paw oedema in rats & analgesic activity against experimentally induced abdominal writhing after 1\% v/v acetic acid injection. This may be due to the presence of drug in the amorphous form which enhances the solubility of both drugs & improve the bioavailability of the drugs.