6.0 RESULTS AND DISCUSSION (CARVEDILOL-PREFORMULATION STUDIES)

6.1 Determination of n-octanol: buffer partition coefficient:

Permeation of drug depends on its partition coefficient and in turn depends upon its lipophilicity. The solute requires a certain affinity i.e. lipophilicity to lipid structures in order to enter the cell membrane. Lipophilicity is traditionally expressed as the *n*-octanol–water/buffer partition coefficient: the concentration ratio of the compound between *n*-octanol and an aqueous phase at equilibrium (Kramer et al., 1999). The obtained partition coefficient using n-octanol: buffer (phosphate buffer pH 6.8 ± 0.2) system was 4.10 ± 0.6 indicating the lipophilic nature of Carvedilol implying that, it will easily permeate through the cell membrane. These results can be correlated with the results obtained by Rautio et al. They reported good permeability for prodrug of Naproxen which bears a partition coefficient of 3.9, which is near to obtained partition coefficient of Carvedilol (Rautio et al., 2000).

6.2 Compatibility studies using FT-IR spectroscopy:

The FT-IR spectra of Carvedilol alone and in combination with Carbopol 934P, HPMC K4M and Chitosan were recorded to evaluate any incompatibility between drug and polymers. Fig. 6.1 shows the IR spectra of Carvedilol which shows the principal peaks at wave numbers 1591, 1502, 1454, 1348, 1251 and 1101 cm^{-1}.

Fig. 6.2, 6.3 and 6.4 show the IR spectra of physical mixture of Carvedilol and HPMC K4M, Carvedilol and Carbopol 934P, Carvedilol and Chitosan respectively. All these spectra show principal peaks of Carvedilol with slight shift. This signifies that there is no interaction between Carvedilol and HPMC K4M, Carbopol 934P and Chitosan.

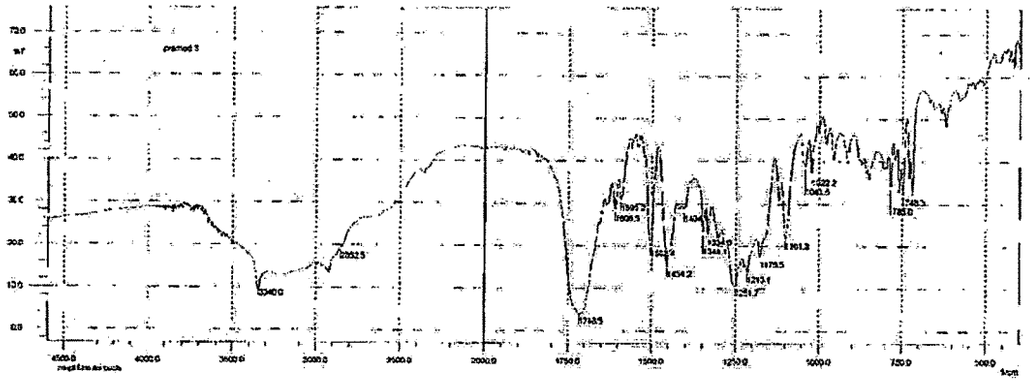


Fig 6.1 IR spectra of Carvedilol.

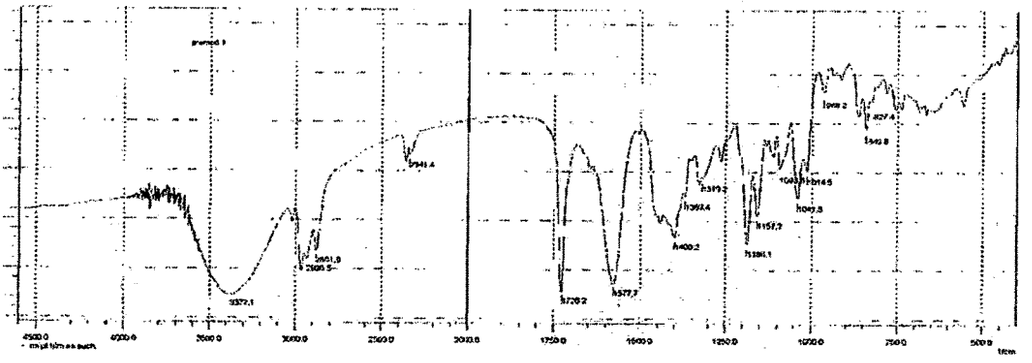


Fig 6.2 - IR spectra of physical mixture of Carvedilol and HPMC K4M.

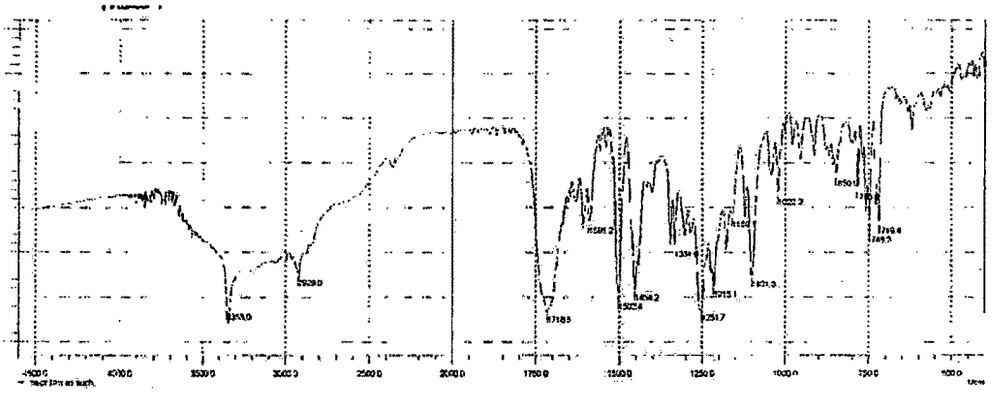


Fig 6.3 - IR spectra of physical mixture of Carvedilol and Carbopol 934P.

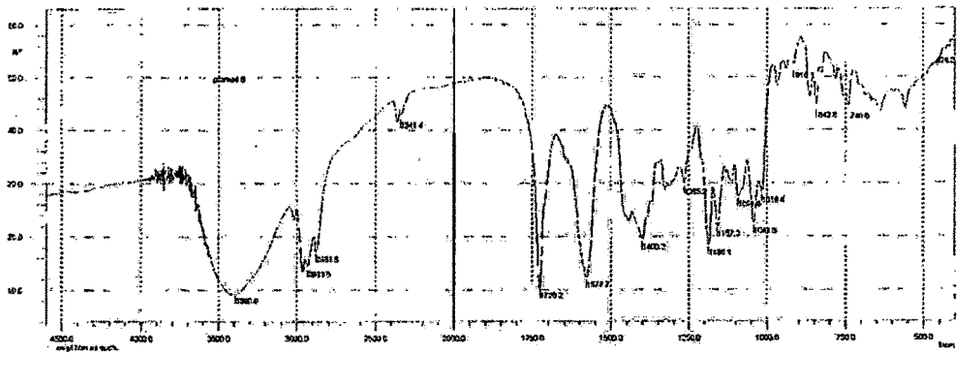


Fig 6.4 IR spectra of physical mixture of Carvedilol and Chitosan.

6.3 Differential Scanning Calorimetry (DSC):

DSC was taken with view to investigate any possible interaction between the polymers with the drug, which may occur at high temperatures during the formulation process. Fig. 6.5 to 6.8 shows the DSC thermograms of Carvedilol, physical mixture of Carvedilol and HPMC K4M, Carvedilol and Carbopol 934P, Carvedilol and Chitosan. Differential Scanning Calorimetry thermograms appeared to be the same for all the polymers and drug mixtures. There was no shift in the melting point of Carvedilol (118^{0}C), which suggested that there may not be any interaction between Carvedilol and HPMC K4M, Carbopol 934P and Chitosan.

Fig 6.5 – DSC Thermogram of Carvedilol

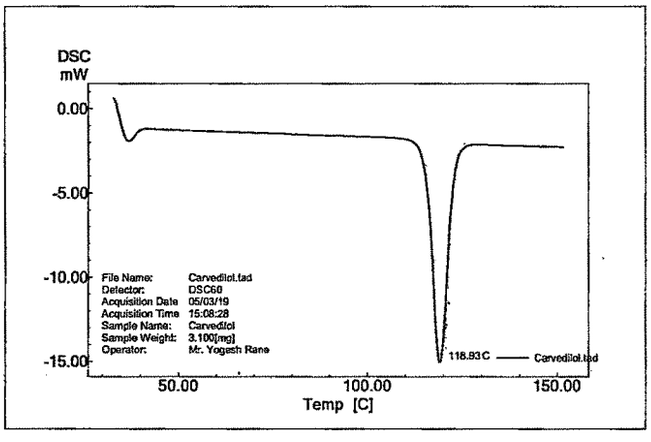


Fig 6.6– DSC Thermogram of physical mixture of Carvedilol and HPMC K4M.

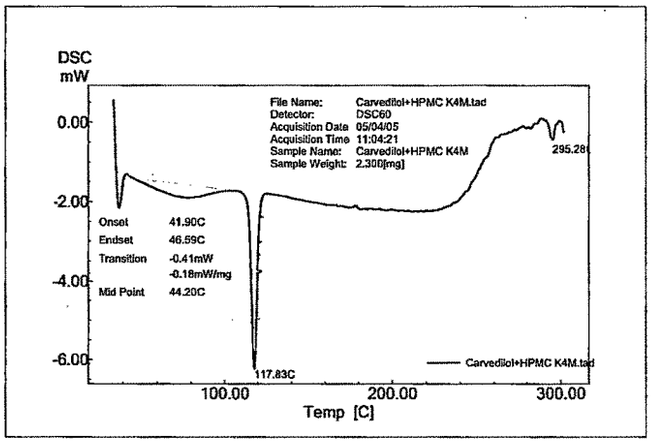


Fig 6.7 – DSC Thermogram of physical mixture of Carvedilol and Carbopol 934P.

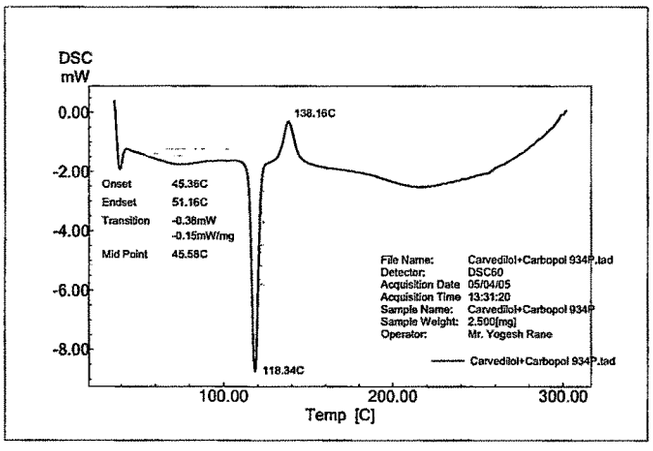
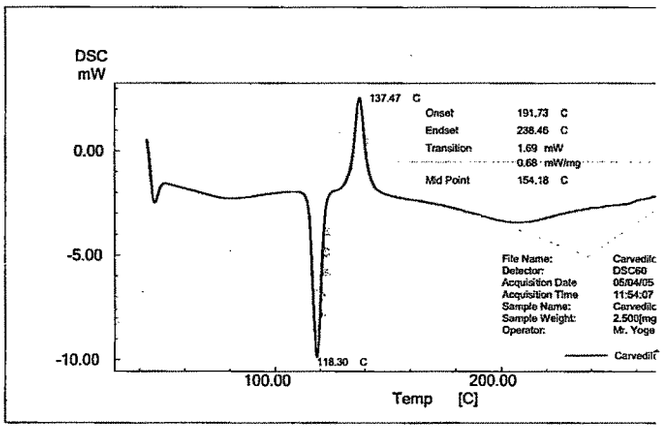


Fig 6.8 – DSC Thermograms of physical mixture of Carvedilol and Chitosan.



6.4 *In vitro* permeation studies:

The in vitro permeation of Carvedilol was investigated through sheep buccal mucosa by using Franz diffusion cell. The study was conducted for 8 hr at pH 6.8 ± 0.2 at RT. The flux of Carvedilol was found to be 6.09 ± 0.43 x 10^{-6} µg cm^{-2} min^{-1} at pH 6.8 ± 0.2. Obtained flux value indicates good permeability of Carvedilol through sheep buccal mucosa. Thiocolchicoside which showed high flux value of 3.8 µg cm^{-2} min^{-1} in 3 hr has shown good permeability (Artusi et al., 2003).

Carvedilol is biopharmaceutical classification system – class II drug having low solubility and high permeability. High flux value through sheep buccal mucosa coupled with higher

partition coefficient signifies good transmucosal permeability of Carvedilol. Yamsani et al reported $8.35 \pm 0.29 \times 10^{-6}$ μg cm^{-2} min^{-1} flux of Carvedilol and concluded good permeability of Carvedilol (Yamsini et al., 2007).

6.5 References:

1. Artusi, M., Santi, P., Colombo, P., Junginger, H., 2003. Buccal delivery of thiocolchicoside: *in vitro* and *in vivo* permeation studies, Int. J. Pharm. 250, 203-213.
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3. Rautio, J., Nevalainen, T., Taipale, H.,Vepsalainen, J., Gynther, J., Laine, K., Jarvinen, T., 2000. Piperazinylalkyl prodrugs of naproxen improve in vitro skin permeation. Eur. J. Pharm. Sci. 11, 157–163.
4. Yamsini, V. V., Gannu, R., Kolli, C., Bhanoji Rao, M. E., Yamsani M.R., 2007, Development and in vitro evaluation of buccoadhesive Carvedilol tablets. Acta Pharm., 57, 185–197.