Chapter 3

DRUG-POLYMER COMPATIBILITY STUDIES

3.1. DRUG-POLYMER COMPATIBILITY STUDIES

Drug polymer compatibility studies were carried out by differential scanning calorimetry (DSC) and fourier transmission infrared (FTIR) spectroscopy.

Differential scanning calorimetry:

DSC thermograms of nebivolol, felodipine, individual polymers [Ethyl cellulose, PLGA (50:50), Eudragit® RS 100 and chitosan] and 1:1 ratio of physical mixtures of both drug and polymers were recorded using Differential Scanning Calorimeter (DSC-60, Shimadzu, Japan). The physical mixtures of pure drug, polymer and drug-polymer (1:1) were sealed in DSC aluminum pan and scanned between 25 to 300 °C with heating rate of 10 °C /minute under nitrogen atmosphere. An empty aluminium pan served as reference. The thermograms obtained were observed for any interaction.

Fourier transmission infrared spectroscopy:

FTIR spectra were recorded for nebivolol, felodipine, ethyl cellulose, PLGA (50:50), Eudragit® RS 100 and chitosan and 1:1 physical mixtures of drug and the individual polymers. Samples were prepared separately with potassium bromide (200-400 mg) and compressed by applying the pressure of 200 kg/cm$^2$ for 2 min in hydraulic press to prepare the pellets. The samples were scanned in the range of 4000 to 400 cm$^{-1}$ with resolution of 2 cm$^{-1}$.

3.2. Results and Discussion:

Differential scanning calorimetry

The DSC thermograms of pure drug nebivolol, felodipine, pure polymers [Ethyl cellulose, PLGA (50:50), Eudragit RS 100 and chitosan] and physical mixtures of drug and individual polymers are shown (Fig. 3.1.1 to Fig. 3.1.8). The characteristics endothermic peak values of pure drug, polymer and drug-polymer mixtures are shown in the figures. The characteristics peak of the nebivolol (Fig. 3.1.1) at ~192 °C, which provides the endothermic melting value of the pure drug. Similarly the endothermic peak at ~147 °C for pure felodipine (Fig. 3.1.2) is due to the melting of the drug. The
polymers are characterized by using the differential scanning calorimetry. The characteristic peaks appear at the melting point of the polymers (Fig. 3.1.3 to Fig. 3.1.7). The physical mixture of the pure nebivolol and the individual polymers, i.e. ethyl cellulose, PLGA (50:50), Eudragit® RS 100 or chitosan in the ratio of 1:1 are used to determine the drug- polymer compatibility study. The melting endothermic peak of nebivolol is shifted to ~187 °C and ~183 °C in the physical mixture with chitosan and ethyl cellulose. However, the endothermic peak of nebivolol does not show any shift in the physical mixture with PLGA (50:50) and Eudragit® RS 100 polymers. The presence of polymer affects the peak shape, and intensity of the drugs leads to lowering of purity. Hence, the minor changes observed in peak values of drugs are not indication of any potential incompatibility.

The endothermic peak of felodipine is shifted to ~141 °C and ~143 °C in the physical mixture with chitosan and ethyl cellulose. But, no shifting of endothermic peak of felodipine is observed with the physical mixture with PLGA (50:50) and Eudragit® RS 100 polymer. The minor changes in the peak values revealed no interaction.

Literature reports (Adibkia et al., 2011, Ajit et al., 2007, Devarajan et al., 2007, Dongming et al., 2007, McNeely and Goa, 1999, Troost et al., 2000) corroborates well with the present study report.
Figure 3.1.2. DSC thermogram of pure felodipine

Figure 3.1.3. DSC thermogram of PLGA 50:50
Figure 3.1.4. DSC thermogram of Eudragit® RS100

Figure 3.1.5. DSC thermogram of ethyl cellulose
Figure 3.1.6. DSC thermogram of chitosan

Figure 3.1.7. DSC thermogram of physical mixture of (a) nebivolol-PLGA (50:50), (b) nebivolol-Eudragit® RS100, (c) nebivolol-ethyl cellulose and (d) nebivolol-chitosan.
Figure 3.1.8. DSC thermogram of physical mixture of (a) felodipine-PLGA (50:50), (b) felodipine-Eudragit® RS100, (c) felodipine-ethyl cellulose and (d) felodipine-chitosan.

Fourier transmission infrared spectroscopy (FTIR):

The fourier transmission infrared (FTIR) spectroscopy of pure drug nebivolol, felodipine, pure polymers [Ethyl cellulose, PLGA (50:50), Eudragit RS 100 and chitosan] and physical mixtures of drug and individual polymers are shown in (Fig. 3.1.9 to Fig. 3.1.16).

The FTIR spectrum of pure nebivolol showed the characteristic peaks at 3304.71 cm\(^{-1}\) (O-H stretching), 2963.28 cm\(^{-1}\) (C-H stretching), 1863.05 cm\(^{-1}\) (C=O stretching), 1303.88 (C-N stretching) and 1138.35 (C-O stretching Cyclic ether). The FTIR spectra of felodipine shows peaks at 3422.25 cm\(^{-1}\) (N-H stretching, secondary), 2998.71 cm\(^{-1}\) (C-H stretching, -CH3), 2950.05 cm\(^{-1}\) (C-H stretching, aromatic), 1722.25 cm\(^{-1}\) (C=O stretching), 1457.57 cm\(^{-1}\) (C-Cl stretching). The IR spectra of Ethyl cellulose, PLGA (50:50), Eudragit RS 100 and chitosan had characteristic peaks of the respective polymers (Fig. 3.1.11 to Fig. 3.1.14).

The FTIR spectra of the physical mixtures of drug and polymers had all the characteristic peak and band values of pure nebivolol or felodipine confirming that all
the functional groups of nebivolol or felodipine are well preserved (Fig. 3.1.15 to Fig. 3.1.16). This study clearly indicate absence of any chemical interaction between the drug (nebivolol/ felodipine) and the polymers [Ethyl cellulose, PLGA (50:50), Eudragit RS 100 and chitosan] and thus confirming that the drug (nebivolol/ felodipine) is compatible with all the polymers used in the present investigation. However, the intensity of the some peaks were slightly decreased in the FTIR spectrum of the physical mixture due to the intermolecular hydrogen bonding between drug and polymer, indicating the chemical stability of the drug with the polymer.

Literature reports (Shah et al., 2014, Dunselman et al., 1991, Lobenberg et al., 2000, Meng et al., 2013, Pagar and Vavia, 2012, Li et al., 2014, Verma et al., 2014) corroborates well with the present study report.

![Figure 3.1.9. FTIR spectrum of nebivolol](image)

Figure 3.1.9. FTIR spectrum of nebivolol
Figure 3.1.10. FTIR spectrum of felodipine

Figure 3.1.11. FTIR spectrum of PLGA 50:50
Figure 3.1.12. FTIR spectrum of Eudragit® RS100

Figure 3.1.13. FTIR spectrum of ethyl cellulose
Figure 3.1.14. FTIR spectrum of chitosan

Figure 3.1.15. FTIR spectra of physical mixture of (a) nebivolol-PLGA (50:50), (b) nebivolol-Eudragit® RS100, (c) nebivolol-ethyl cellulose and (d) nebivolol-chitosan.
Figure 3.1.16. FTIR spectra of physical mixture of (a) felodipine-PLGA (50:50), (b) felodipine-Eudragit® RS100, (c) felodipine-ethyl cellulose and (d) felodipine-chitosan.

The drug and polymer compatibility studies were carried out with DSC and FTIR. The DSC and FTIR study of the individual drug and polymer and their physical mixture (1:1) were carried out separately. The results reveal that, nebivolol and felodipine have interaction with chitosan and ethyl cellulose as evident from DSC study. However, compatibility study showed no interaction of both the drugs with PLGA (50:50) and Eudragit® RS 100 polymers. Therefore, PLGA (50:50) and Eudragit® RS 100 are selected for development of nanoparticles.