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Studies of Drug-Polymer Interactions of Carvedilol with various Polymers using some Analytical Techniques

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ABSTRACT

The present study aims at investigating the different combinations of polymers with inclusion complex of Carvedilol (CR)-Hydroxypropyl betacyclodextrin (HPβCD) prepared in a ratio of 1:1 by use of various analytical techniques like Fourier Transformation Infrared spectroscopy (FTIR), X-ray diffraction technique (XRD), Digital scanning calorimetry (DSC), Thermo gravimetric analysis (TGA) as a part of preformulation studies. Various polymers used for the present study were Sodium alginate (SA), Hydroxy propyl beta cyclodextrin (HPBCD), Hydroxy propyl methyl cellulose LV E-15(HPMC), Pectin (P), Eudragit NE30D (EU). This study indicated that Carvedilol formed inclusion complex with the HPβCD, but in combination with other polymers, drug did not show any other interactions.

Keywords: Carvedilol, FTIR, TGA, Drug-polymer compatibility

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INTRODUCTION

Carvedilol (CR) is a nonselective β-adrenergic blocking agent with α_1-blocking activity. It is well absorbed from the gastrointestinal tract but subjected to considerable first-pass metabolism in the liver [1] and its oral bioavailability in humans is only 20% [2].

The drug has a short half-life of 2.2 ± 0.3 hrs. The drug is formulated with a series of polymers to improve the absorption and prolong the half life, thereby preventing degradation in gastric region. Since the drug has low bioavailability due to poor water solubility and slow dissolution rates[3] ,several methods are used to improve the solubility profile of CR, of which complexation with cyclodextrins has been widely used to improve the solubility and dissolution rate of poorly soluble drugs [4,5].

The present study deals with the preparation of inclusion complex of Carvedilol (CR) with HPBCD and then preparing physical mixture of this complex with a variety of polymers and analyzed the combinations with the help of some important analytical techniques for detection of any possible interactions.

MATERIALS AND METHODS

Materials

Carvedilol(CR) was kindly gifted by Glenmark Pharmaceuticals (Mumbai, India),Hydroxyl Propyl Beta Cyclodextrin (HPBCD was kindly gifted by Roquette (Lestrem, France), Sodium Alginate(SA) was purchased from Loba Chemicals, India; Hydroxy propyl methyl cellulose LV E-15(HPMC) was generously gifted by Colorcon, Mumbai; Tragacanth (TR) was purchased from Loba Chemicals, India; Gum Acacia(GAC) was purchased from Loba Chemicals, India; Pectin (P) was purchased from Loba Chemicals , India. All chemicals used were of analytical reagent grade purity.

Preparation of CR-HPBCD inclusion complex

Inclusion complex of CR-HPβCD was prepared by Co-grinding technique [3], where mixing of CR with HPβCD was done in a glass mortar for 30minutes in 1:1 ratio and stored in a glass dessicator.

Preparation of physical mixtures of various polymers with CR-HPβCD inclusion complex

The inclusion complex so prepared was triturated for 15 minutes in a glass mortar with series of different polymers until a homogenous mixture was obtained. The different combinations of polymers of with inclusion complex are enlisted in table 1.

Analytical studies of the physical mixtures

The prepared physical mixtures along with individual polymers were studied using various analytical techniques like Fourier Transformation Infrared spectroscopy (FTIR)[6], (Shimadzu, IR Prestige-21), Thermogravimetric analysis (TGA)[7, 8, 9], by using Perkin elmer, SII, Pyris Diamond (With samples weighing about 14mg and a programmed heating of samples were done at a rate of 20^0C/min with temperatures starting from 10^0C to 500^0C).

Table 1: Combinations of Carvedilol-HPβCD inclusion complex with various polymers

Sl No.	Combinations of CR-HPBCD-Polymers	Description of the combination
1	CRHPβCDSA	Carvedilol+Hydroxypropylbetacyclodextrin+ Sodium alginate
2	CRHPβCDTR	Carvedilol+Hydroxypropylbetacyclodextrin+ Tragacanth
3	CRHPβCDP	Carvedilol+Hydroxypropylbetacyclodextrin+ Pectin
4	CRHPβCDGAC	Carvedilol+Hydroxypropylbetacyclodextrin+ Gum Acacia
5	CRHPβCDHPMC	Carvedilol+Hydroxypropylbetacyclodextrin+ Hydroxypropylmethylcellulose LV E-15

RESULTS AND DISCUSSION

Various combinations of CR-HPβCD inclusion complex with polymers were prepared and their interactions were analyzed by using analytical techniques. FTIR analysis of the CR-HPβCD inclusion complex [8] with different polymers was performed for any drug-excipients interactions and as depicted in Figure 1,

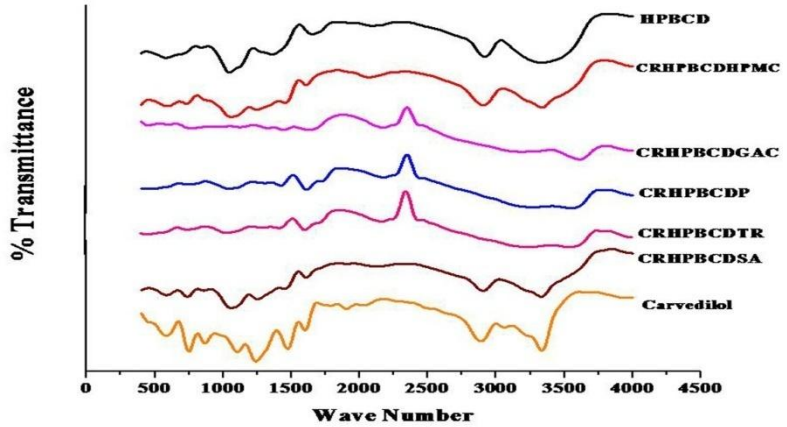

Figure 1: FTIR spectra of Physical mixtures of CR-HPβCD inclusion complex with various polymers compared with pure drug CR and HPβCD

It indicates that there is no characteristic interactions between the drug and polymers except that between drug and HPβCD. FTIR studies indicated in the CR spectra, absorption peaks were observed at 3349.7701cm^{-1}, 2933.55621cm^{-1} due to hydroxyl and amine stretching respectively.

Other peaks were at 1233.5979cm^{-1} due to C-O group (epoxides),1094.86001cm^{-1} due to aryl alkyl ethers and alkyl ether C-O stretching respectively. The FTIR of HPBCD showed prominent absorption bands at 3338cm^{-1}(for O-H stretching), 2926cm^{-1}(for C-H stretching), 1151cm^{-1}(for C-H stretching) and 1035.77cm^{-1} (for C-O stretching).Whereas in the PM, there is an exhibition at 3339.7409cm^{-1}, 2913.4977cm^{-1} due to hydroxyl and amine stretching respectively which matches with pure drug. Also there is an exhibition at 1217.08 cm^{-1}, 1037.32 cm^{-1} indicating no interactions between drug and HPβCD [6].

Thermogravimetric studies of mixtures of CR-HPβCD inclusion complex with different polymers were analyzed for any drug-excipients interactions. Figure 2 depicts the thermograms of blend of Carvedilol (CR) [7] with Sodium alginate (SA), Hydroxypropyl methyl cellulose E-15 LV (HPMC), Pectin (P), Tragacanth (TR), and Gum Acacia (AC) in a ratio of 1:1 physical mixture. The inclusion complex of CR-HPβCD was mixed with polymers separately in a ratio of 1:1 ratio for the study. From Figure 2, TGA studies indicated that carvedilol (CR) has two mass loss event between 210-360 ^{0}C (Δm=52.54%) which confirms with earlier reported data [7] and between 360-500^{0}C (Δm=34.298%), whereas the physical Mixtures of inclusion complex with polymers also has one mass loss event between 215-270 ^{0}C (Δm=28.415%), thus suggesting that the drug CR shows no serious interactions with any polymers.

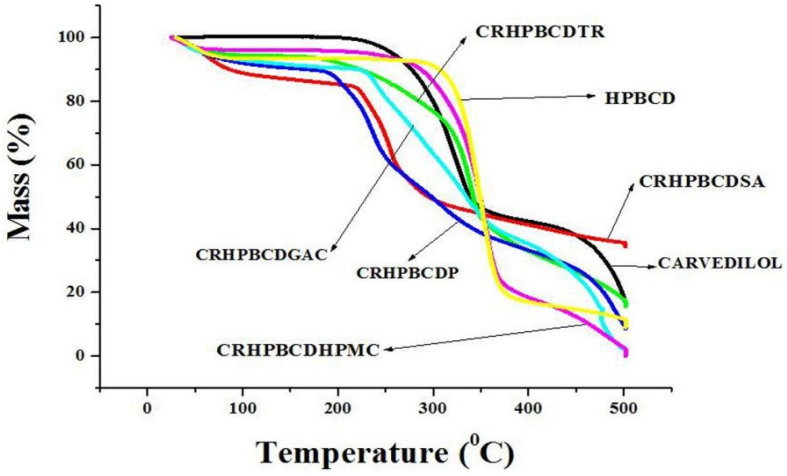

Figure 2: Overlay TGA thermograms of Carvedilol-HPβCD inclusion complexes with various polymers compared with pure drug CR and HPβCD

CONCLUSION

From the above analytical studies, it is confirmed that the drug carvedilol do not show any possible interactions with any of the polymers that are used here for the study, but it forms inclusion complex with HPβCD, thereby increasing the aqueous solubility of the drug. Thus carvedilol can be easily formulated with all the polymers in any drug delivery systems.

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