RESEARCH ARTICLE

Solubility and Dissolution Enhancement of Candesartan Cilexetil by Complexation with Cyclodextrin

Ghaith M Aziz[1*], Eman B H Al-Khedairy[2]

[1]*Wassit Health Directorate, Ministry of Health, Baghdad, Iraq.*
[2]*Department of Pharmaceutics, College of Pharmacy, University of Baghdad, Baghdad, Iraq.*

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ABSTRACT

At present, numerous novel chemical compounds face challenges related to their limited solubility in aqueous environments. These compounds are classified under the Biopharmaceutical Classification System (BCS) as either class II or class IV substances. Different carriers were used to increase their solubility. Candesartan cilexetil (CC) is one of the most widely used antihypertensive drugs, which belongs to class II drugs.

The aim of this research was to enhance the solubility and dissolution rate of CC through a complexation approach involving β-cyclodextrin and its derivatives, specifically hydroxypropyl beta cyclodextrin (HP-β-CD), methyl beta cyclodextrin (M-β-CD), and sulfonyl ether beta-cyclodextrin (SBE-β-CD), serving as complexing agents. This complexation process was investigated both with and without the inclusion of poloxamer 407 (PX407) as a hydrophilic polymer. The complex was prepared through a combination of grinding, kneading, and co-evaporation techniques. The resulting complex underwent characterization, including assessments of its percentage yield, drug content, solubility, and dissolution properties, as well as analyses using differential scanning calorimetry (DSC), X-ray diffraction (XRD), and fourier transforms infrared spectroscopy (FTIR). The results revealed that, the complex prepared using 1:1 molar ratio of M -β-CD:CC in the presence of 5% w/w PX407 by co-evaporation method had the highest percentage yield (97%) with drug content of 98.5%, the highest solubility (0.052 mg/mL) and fastest release of drug within 45 minutes compared to the other methods. The FTIR, DSC, and XRD confirmed the development of a partial inclusion complex of an amorphous nature.

Keywords: Solubility, Dissolution, Candesartan cilexetil, Complexation,

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INTRODUCTION

One technical challenge in formulating effective dosage forms for various active pharmaceutical ingredients is their limited solubility. Candesartan cilexetil (CC) is categorized as an angiotensin II receptor blocker and is recognized as one of the most effective antihypertensive medications. From a chemical perspective, it belongs to the tetrazole derivative class and is employed clinically in its ester prodrug form[1] is shown in Figure 1.

It belongs to class II of the Biopharmaceutics Classification System (BCS). It is a highly lipophilic drug (log P = 6.1), practically insoluble in water that causes formulation difficulties and reduces its therapeutic uses and bioavailability, which is around 15%.[2,3]

The solubility and dissolution properties of poorly water-soluble drugs have been improved through the successful use of cyclodextrin complexation.[4]

Cyclodextrins (CDs) are cyclic oligosaccharides composed of α-D-glucopyranose units linked through (α-1, 4) bonds. They possess a hydrophilic outer surface and a relatively hydrophobic central cavity. While the outer surface of CD molecules is water-soluble, their hydrophobic cavity provides a microenvironment suitable for nonpolar molecules of appropriate size. Naturally occurring CDs are found in three distinct forms: α, β, and γ, distinguished by the number of glucose monomers they consist of, which are 6, 7, and 8, respectively. In the pharmaceutical industry, the β form of CD is widely employed. However, due to its limited solubility, various derivatives of β-CD have been developed to enhance their solubility. In this study, we utilized methyl beta cyclodextrin (M-β-CD), sulfonyl ether beta-cyclodextrin (SBE-β-CD), and hydroxypropyl beta cyclodextrin (HP-β-CD).

It's crucial to enhance the complexation of CC with CD. It was stated that the ternary system of drug, CD and the third auxiliary matter can increase the complexation efficiency.[5]

**Author for Correspondence: alghaithpharma@yahoo.com*

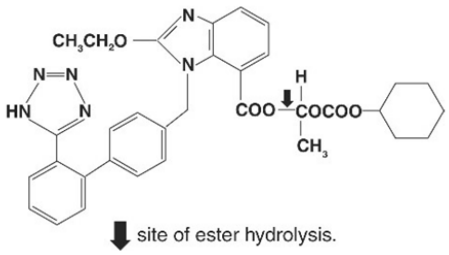

Figure 1: The chemical structure of candesartan cilextil[6]

The objective of this study was to enhance the solubility and dissolution of CC at the same time by using different types of β-CD derivatives as binary or ternary systems by the addition of poloxamer 407 (PX 407) as a third auxiliary hydrophilic substance was investigated.

MATERIALS AND METHODS

Materials

Candesartan cilexetil (CC) was obtained as a gift sample from Pioneer Pharmaceutical Company (Iraq). *β*-Cyclodextrin (*β*- CD), methyl-beta-cyclodextrin (Mβ-CD), sulfobutylether β-cyclodextrin (SBEβ-CD) and 2-hydroxypropyl-β-cyclodextrin (HPβ-CD) (Hyper Chem. (China)) poloxamer407 (PX 407) (Shenzhen Nexconn Pharmatechs, Ltd, China). Methanol (RFCL Ltd., New Delhi, India). All other constituents used were of analytical grade.

Phase Solubility Studies

Preparation of binary system

Phase-solubility investigations involving CC and various CDs were conducted. An excess quantity of the drug was introduced into 10 mL of distilled water, with the water containing incrementally rising CD concentrations ranging from 0 to 10 mM/L. The solutions were shaken up in a thermo- control water bath at 25°Cfor 48 hours. After that the solutions were filtered by filter syringe 0.45 µm, and their absorbance was measured at 255 nm against blanks prepared in the same concentration of the used concentration of CD in water.[7]

Phase solubility studies were carried out according to the method reported by Higuchi and Connors.[8] The apparent stability constants were calculated from the slope of the phase-solubility diagrams according to the following equation:-

$$K = \frac{Slope}{S^{\circ}(1-Slope)} \quad \ldots\ldots\ldots (1)$$

Where S0 is the solubility of CC in water in the absence of CD. A slope less than 1 indicates 1:1 molar ratio of Drug:CD.

Preparation of ternary system

Additional amounts of CC were adjoined to 10 mL vials containing aqueous solutions of increasing concentrations of selected CD (0, 2, 4, 6, 8, and 10 mM/L) was prepared. Then (0.25 w/v) of PX407 was added and the samples were placed in the water bath shaker at 25°C for 48 hours. After that, the samples were filtered by filter syringe 0.45 µm and analyzed spectrophotometerically at 255 nm against a suitable blank to determine the concentration of the dissolved CC. The results were compared with those of the binary system.[9]

Preparation of cyclodextrin inclusion complexes

- *Physical mixture*

The pharmaceutical mixture (PM) was prepared through uniform mixing of CC, the chosen CD, and PX407. Subsequently, the resulting powder underwent sieving using a 60-mesh sieve to achieve particles of uniform size.[10]

- *Co-grinding method*

The complex was prepared by mixing selected CD and CC with different concentrations of PX407. The mixture was ground for 45 minutes to ensure a homogeneous blend, and then it was sieved through sieve no 60.[11]

- *Kneading method*

The complex was prepared by mixing CC with selected CD and the different concentrations of PX407 in a mortar and pestle. The mixture was grounded for 1-hour. In order to maintain the desired consistency, the mixture was given an appropriate amount of 50% v/v methanol. The slurry was then air-dried at oven at a temperature of 40ºC for 24 hours, pulverized, and passed through sieve no. 60. The resultant sample was kept in a desiccator till further use.[12]

- *Co-evaporation method*

A transparent solution was achieved by dissolving a specific quantity of the drug in methanol. Subsequently, a precise amount of the selected substance of CD and different concentrations of PX407 were dissolved in water and then added to the drug solution. The resulting suspension was subjected to continuous agitation using a magnetic stirrer for a duration of 1-hour. Following this, it was dried in an oven for a total of 24 hours at a controlled temperature of 40ºC to ensure complete evaporation. The dried material was pulverized and subsequently sifted through a no. 60 sieve. It was then placed in a desiccator for further investigations.[13]

Characterization of complex

- *Saturation solubility study*

In this method, excess amount of the inclusion complex (prepared by grinding (Gr), kneading (Kn), and co-evaporation (Eva) method) was added to 10 mL of distilled water maintained at 25°C and shaken for a period up to 48 hours. The samples were filtered using a filter syringe of 0.45 µm. Then, their absorbance was measured at 255 nm against blanks prepared from distilled water.[14]

- *Percentage yield*

The prepared products were collected and weighed. The measured weight (practical) is divided by the total amount of drug and carrier (theoretical) used for the inclusion of complex preparation. Percentage yield was estimated by using the following equation:[15]

$$percntage\ yield = \frac{actual\ weight}{theoretical\ weight\ of\ drug\ and\ CD} \times 100 \ldots\ldots(2)$$

- *Drug content*

An exact quantity of inclusion complex powder equivalent to 8 mg of CC was precisely measured and introduced into a 50 mL volumetric flask. Subsequently, 50 mL of methanol was added, and the mixture was subjected to sonication for 15 minutes to achieve thorough homogenization. The resulting solution was appropriately diluted and filtered through a 0.45 µm membrane, and the drug content was determined spectrophotometrically at a specified λ_{max} using the calibration curve equation.[16]

- *In-vitro dissolution*

Accurately weighed samples of selected complex equivalent to 8 mg of CC prepared by different methods were placed in a USP type II dissolution apparatus. This investigation employed a dissolution medium comprising 900 mL of phosphate buffer solution (pH 6.5) with 0.35% Tween 20. The stirring rate was maintained at 50 ± 2 rpm, and the temperature was controlled at 37 ± 0.5°C. At specified time intervals (10, 15, 20, 30, and 45 minutes), 5 mL samples were withdrawn and passed through a 0.45-mm filter syringe. Subsequently, the dissolution medium was replenished with 5 mL of fresh dissolution fluid to maintain a consistent volume. The samples were then subjected to spectrophotometric analysis at 255 nm. The mean value of three determinations was utilized to calculate the drug release for each prepared complex. The drug dissolution profile was depicted as the percentage of drug release versus time.[17]

The resultant dissolution profiles were compared with each other and with that of pure drug and the physical mixture by similarity factor using the following equation:

$$f2 = 50 \times log\ log \left\{\left[1 + \frac{1}{n}\sum_{t=1}^{n} |R_t - T_t|^2\right]^{-0.5}\right\} \times 100 \ldots..(3)$$

Here, 'n' represents the count of sampling points, and 'Rt' and 'Tt' denote the percentage of dissolution for the reference and test profiles, respectively, at the time point 't'. When f2 values are greater than 50 (50–100). The two dissolution profiles are considered similar; otherwise, the profiles are not similar.[18]

Selection of the best complex

The complex with the highest percentage yield, drug content, solubility, and fastest dissolution rate was selected for further study.

Characterization of the best complex

Fourier-transform infrared spectroscopy (FTIR) spectra were acquired using an FTIR instrument, specifically the FTIR Shimadzu 8300 from Japan. Samples of pure CC, PX407, selected CD, physical mixture and the selected complex were compressed with potassium bromide. The spectrum obtained was between the wave numbers 4000 and 400 cm^{-1}.[19]

- *Differential scanning calorimetry*

Differential scanning calorimetry (DSC) is a thermal analysis method employed to investigate the thermotropic characteristics and physical transformations of different substances and assess potential interactions between the drug and excipients. This study conducted DSC analysis on various samples, including pure drug (CC), PX 407, the selected CD, a physical mixture, and the complex. The DSC experiments were carried out using a DSC apparatus manufactured by Shimadzu in Japan. The procedure involved taking approximately 2 to 3 mg of each sample, sealing it in an aluminum pan, and subjecting it to heating at a rate of 10°C/min within a temperature range spanning from 40 to 300°C.[20]

- *Powder X-ray diffraction*

Powder X-ray diffraction (PXRD) is used to study the atomic and molecular structure of crystalline substances such as drugs and excipients. XRD measurement was overlooked on five samples: pure CC powder, selected CD, PX407 physical mixture and the selected complex. The study was done by powder X-ray diffraction (XRD-6000, Shimadzu, Japan 220V/50Hz) at continuous scanning range at 2θ = 10–50°, the operating voltage and current were 40 (kV) and 30 (mA), respectively.[21,22]

- *Statistical analysis*

The results of the experimental work were demonstrated as a mean of triplicate ± standard deviation (SD) and were tested by t-test paired two samples for means to determine if the changes in the applied factors were statistically significant at a level of ($p \leq 0.05$) or non-significant at a level of ($p > 0.05$) using Microsoft Excel 2010.

RESULTS AND DISCUSSION

Phase Solubility Diagram

Binary system

The phase solubility diagram (Figure 2) shows that the aqueous solubility of CC increased linearly (with high R-value) as a function of β-CD, HP β-CD, SBE β-CD and Mβ-CD concentration was increased with slope less than 1, indicating the formation of 1:1 molar ratio of drug:CD. The obtained association constant (K) values were 1063.7, 2839.5, 5153.4 and 6045 M^{-1} for SBE β-CD, HP β-CD, β-CD and M β-CD, respectively, indicating that the most stable complex with highest solubility was obtained by using is Mβ-CD. The low K values in case of SBE β-CD and HP β-CD are most likely due to a small cavity size that reduces the probability of including the bulky groups of CC. Mβ-CD was selected as the host molecule due to its notably higher solubility in aqueous solutions (2000 mg/mL) at room temperature in comparison to unsubstituted β-CD (18.5 mg/mL). The expectation was that the enhanced solubility of Mβ-CD in aqueous solutions would increase the CC-CD complexes' solubility. Consequently, Mβ-CD was chosen for the continuation of this research.[22]

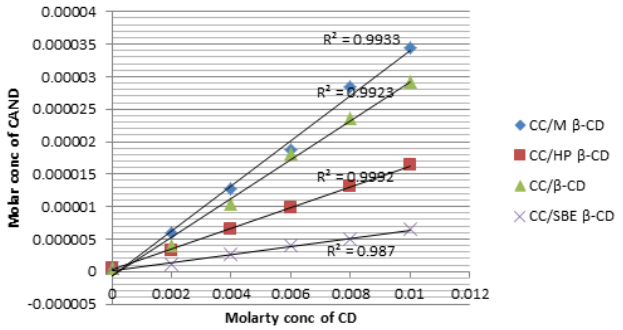

Figure 2: Phase solubility study of CC/β-CD, CC/HP β-CD, CC/SBE β-CD and CC/Mβ-CD complex in DW at 25°C

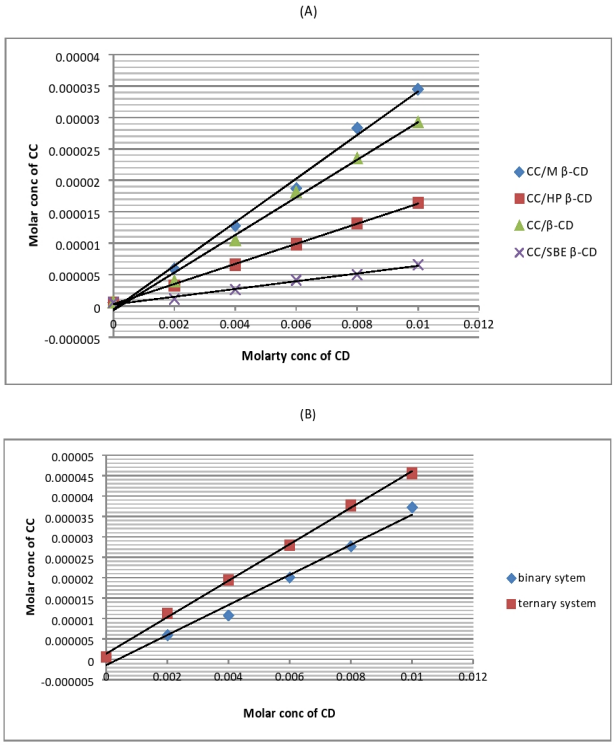

Figure 3: (A) Phase solubility study of CC/β-CD, CC/HP β-CD, CC/SBE β-CD and CC/Mβ-CD complex in DW at 25°C.(B) Phase solubility study of a binary system(CC/M β-CD)and ternary system (CC/M β-CD/PX407) in DW at 25°C

Ternary system

Adding a small amount of water-soluble polymer PX 407 at a percentage (0.25% w/v) to an aqueous complexation medium increased the solubility of CC in the presence of Mβ-CD. The obtained association constant (K) value was 7294 M^{-1} for ternary complex compared to 6223 M^{-1} as shown in Figure 3. The elevated value of K for the ternary complex indicated a stronger interaction between CC and the cavity of Mβ-CD. Additionally, the ternary compound, PX407, established a network involving both the outer surface of Mβ-CD and CC-Mβ-CD, facilitating the formation of the complex. In addition, it is well known that PX407 consists of hydrophilic side chains (ethylene oxide) and hydrophobic core (polypropylene oxide).[23] The further improvement in solubility of inclusion complex obtained with PX407 can be attributed to the interaction of CC with many propylene oxide hydrophobic units, which represents 35% of PX407. that made the lipophilic drug soluble in the aqueous solution.[24]

Characterization of complex

- *Drug content and percentage yield*

Results are shown in Table 1. Drug content of the inclusion complex was between 94 and 98.1%, which met the (USP) requirement for an acceptable range (90–110%), indicating that, there was negligible loss of drug during the preparation. The best percentage yield was obtained by the co-evaporation technique, which can be explained to be due to the nature of the prepared complex, which was freely flowable and easily got out from its container without loss by sticking.

- *Saturation solubility*

As shown in Table 2, all methods increase the solubility of CC significantly ($p < 0.05$), which may be due to the formation of the inclusion of CC within the CD as it will be confirmed. The influential concentration of PX407 was affected by the method of preparation. In the kneading method, 2.5% w/w PX407 was enough to increase the solubility compared to its binary system since there was no significant ($p > 0.05$)increase in solubility by increasing its concentration to 5% w/w. The enhancement in aqueous solubility from the kneading product of CC can be explained in terms of the wetting property of Mβ-CD.

In other methods (grinding, co-evaporation) the 5% w/w PX407 caused a significant increase the solubility ($p < 0.05$) compared to their binary system with no significant increase ($p > 0.05$) by further increasing its concentration to 10% w/w. From the above results,it is obvious that the ternary complex (1mole Drug:1 mole Mβ-CD:5% w/w PX 407) prepared by co-evaporation had significant highest solubility ($p < 0.05$) compared to other complexes. This result may be attributed to the involvement of stirring in the preparation of the complex that caused the best homogenization of CC with CD and led to uniform distribution of the drug and included into CD. Furthermore, decreasing surface tension between CC particles and the solvent had a role in increasing the solubility of the drug. The presence of PX407 increased Mβ-CD solubilizing and complexing effect by synergistic multi-component complex formulation and by its wetting and solubilizing properties.[25]

- *In-vitro dissolution studies*

The release profiles of CC by co-evaporation, kneading and grinding methods are shown in Figure 4, which reveals that, the presence of PX407 enhances the dissolution rate mainly due to its solubility-enhancing effect, as it was mentioned previously. Figure 5 demonstrates that the dissolution was affected by the method and the concentration of PX407 used in the preparation of the inclusion complexes, Kn2.5 and Eva5. The complex exhibited an improved dissolution rate in a phosphate buffer (pH 6.5) when compared to the pure drug, ($f2 = 10.18$) and ($f2 = 6.29$) respectively, while grind 5 and PM gave similar

Table 1: Drug content and percentage yield of ternary complex prepared by different methods

Formula code	*Method*	*Conc of polymer*	*Drug content*	*Percentage yield*
Gr 0	Grinding	Zero	98.1	95
Gr 2.5	Grinding	2.5	97	92
Gr 5	Grinding	5	98.3	94
Gr10	Grinding	10	98.3	93
Kn 0	Kneading	0	94	91
Kn2.5	Kneading	2.5	96.8	93.4
Kn5	Kneading	5	95.5	92.3
Kn10	Kneading	10	95.8	89.8
Eva 0	Co evaporation	0	99	95.4
Eva 2.5	Co evaporation	2.5	97.3	96.2
Eva 5	Co evaporation	5	98.5	97
Eva 10	Co evaporation	10	96.7	95.6

Table 2: Saturation solubility of ternary complex prepared by different methods

Formula code	*Method*	*Conc of polymer*	*Solubility mg/mL (mean ± SD)*
Candesartan	-	-	0.000345 ± 0
Gr 0	Grinding	Zero	0.023 ± 0.0018
Gr 2.5	Grinding	2.5	0.031 ± 0.0019
Gr 5	Grinding	5	0.037 ± 0.0018
Gr 10	Grinding	10	0.037 ± 0.002
Kn 0	Kneading	Zero	0.023 ± 0.002
Kn 2.5	Kneading	2.5	0.027 ± 0.0014
Kn 5	Kneading	5	0.033 ± 0.0024
Eva 0	Evaporation	Zero	0.027 ± 0.0026
Eva2.5	Evaporation	2.5	0.030 ± 0.0041
Eva5	Evaporation	5	0.052 ± 0.0059
Eva1o	Evaporation	10	0.049 ± 0.0056

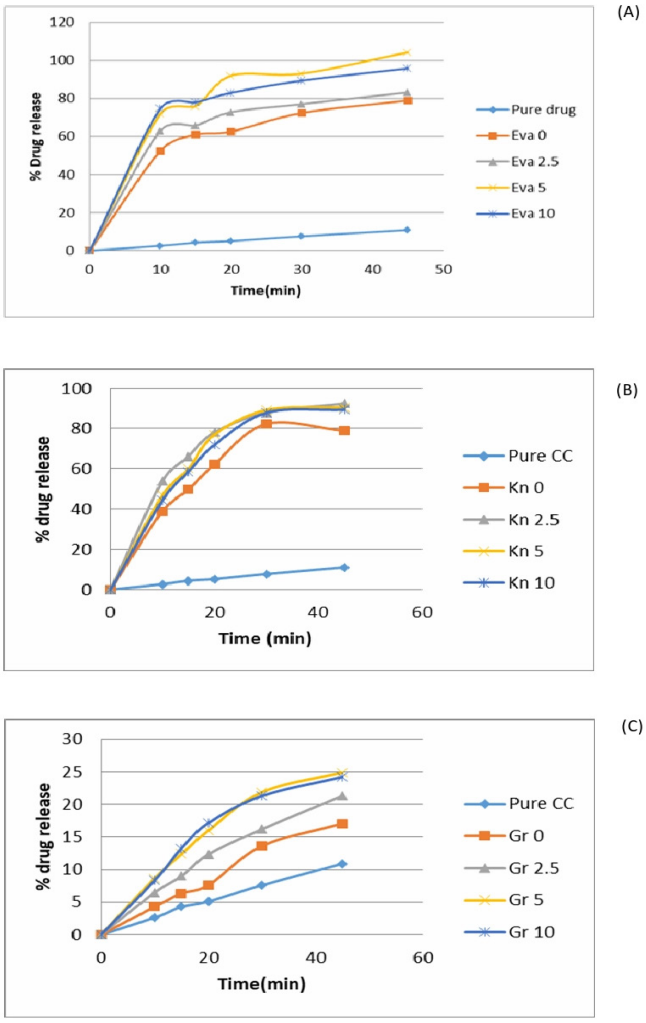

Figure 4: Dissolution profile of CC/Mβ-CD complex with different percentage of PX407 in phosphate buffer (pH=6.5) with 0.35%Tween 20 at 37 ºC prepared by:(A) Co evaporation method.(B) Kneading method.(C) Grinding method

release profiles (f2 = 56.09) and (f2 = 62.91), respectively, in comparison to pure drug. The efficiency of co-grinding method was low as it was performed under dry conditions. It was thought that the molecular interaction between CC and CD might not occur, so an inclusion complex might not be formed under such conditions. Furthermore, the CC particles seemed to aggregate rigidly and cover the whole surface of the amorphous CD, resulting in the sample with a hydrophobic surface, which could explain the poor wettability of the ground and the anhydrous CD:CC mixture. The increase in the percentage of drug release from the complex prepared by the kneading method (presence of solvent 50% v/v methanol) proved that the presence of water played a crucial role in the *in-vitro* release of the drug from the mixture. Water helps form a strong drug inclusion complex with CDs at the optimum solvent concentration. Conversely, the significant enhancement in dissolution rate observed in the co-evaporation method may be attributed to several factors, including the thorough blending of the drug with hydrophilic excipients, mitigation of aggregation and agglomeration, and enhanced wetting and solubilization of the drug within the diffusion layer.[26]

- *Selection of the best complex*

Inclusion complex with high drug content, high percentage yield, high solubility study and high *in-vitro* dissolution profile was considered as best complex. Therefore, the best complex was selected as 1 mole Drug: 1 mole Mβ-CD:5% w/w PX407 prepared by co-evaporation method.

Characterization of the best complex

- *Fourier transforms infrared spectroscopy*

The FTIR spectrum gives some information about the functional groups that may interact with excipients during formulation. The FTIR spectrum of CC (Figure 6) shows a characteristic broad peak in the region of 3400 to 3500 (N-H stretching), 2939.95 cm^{-1} (aromatic C-H group stretching), 2860 cm^{-1}

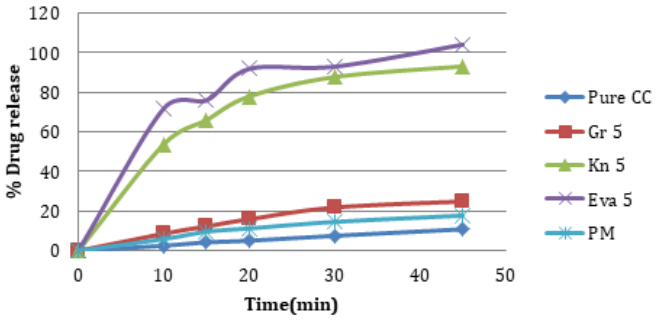

Figure 5: Effect of method on the dissolution profile of CC/Mβ-CD complex with different percentage of PX407 in phosphate buffer (pH = 6.5) with 0.35%Tween 20 at 37ºC

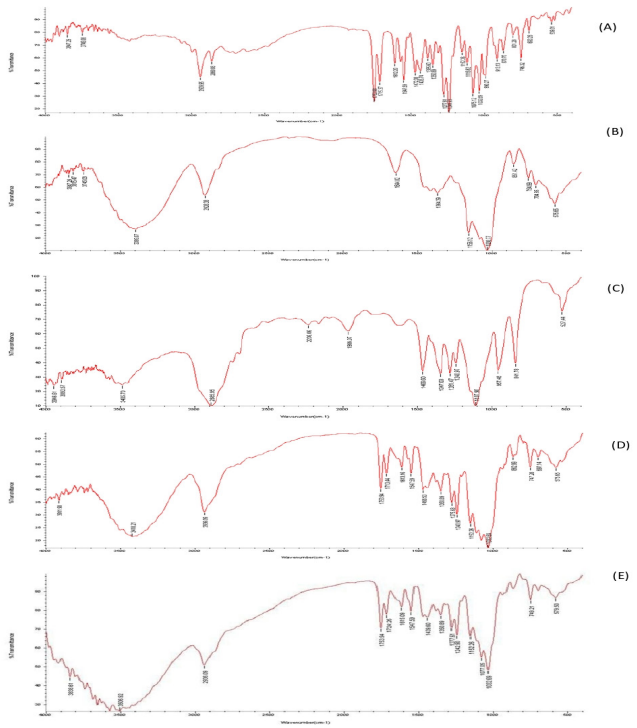

Figure 6: FT IR of : (A) CC.(B) Mβ-CD. (C)PX407 .(D) Physical mixture.(E) Inclusion complex (Eva 5)

(aliphatic C-H group stretching), 1752.08 and 1715.37 cm^{-1} (−C=O stretching vibration), 1612 cm^{-1} (Amine bending of tetrazole) 1435 cm^{-1} (C-H bending), 1355 cm^{-1} (aromatic C-N stretching) and 1277 cm^{-1} due to (-C-O) stretching of the carbonyl group of aromatic ester, 1115 cm^{-1} (C-OH group bond) and 746 cm^{-1} due to (-O-) substitution. These results were in agreement with previous studies.[27] The FTIR spectrum of Mβ-CD (Figure 6) shows characteristic peaks 3000 to 3600 cm^{-1} (-O-H stretching), 2928 cm^{-1} (CH- CH2 asymmetric and symmetric bond), 1644 cm^{-1} (-C = O bond), 1364 cm^{-1} (CH bending, CH stretching in CH3) and 1156 cm^{-1} (C-O-C ether bond). Same results were obtained by Lu *et al.*[28]

The FTIR spectrum of PX407 (Figure 6) shows the characteristic peak of 3485 cm^{-1} (OH stretching), 2885 cm^{-1} (aliphatic C-H stretching) and 1466 cm^{-1} (OH alcoholic bending vibration). These results were in accordance with the previously documented results.[29] The FTIR spectrum of the physical mixture (Figure 6) shows the disappearance of N-H stretching band of the drug, which may be masked by -O-H stretching of Mβ-CD. Furthermore, the mixing process resulted in other CC peaks with decreased intensity due to dilution. The FTIR spectrum of the selected complex (Eva5) (Figure 6) revealed the possibility of inter-molecular hydrogen bonding between the N-H group of CC and the OH groups of PX407 and Mβ-CD indicated by a broad highly intense peak at region of 3200 to 3700 cm^{-1}. On the other hand, there was a shift in the ester (-C=O) stretching vibration from 1715.37 to 1724 cm^{-1}, which may be attributed to the conversion of CC from crystal form to an amorphous form as it would be confirmed.[30] The absent of minor peaks of CC may indicate the trapping of CC inside the inner core of Mβ-CD.[30]

- *Differential scanning calorimetry*

Pure CC in Figure 7 showed a sharp characteristic endothermic peak at (171.1°C) corresponding to its melting point.[31] The thermogram of Mβ-CD as shown in Figure 7, reveals an endothermic event at 97.7°C, corresponding to the water molecules' loss. It was found that M β-CD decomposed at temp above 300°C. Therefore, the scan was done till 300.[32]

Figure 7 shows the DSC thermogram of PX407. An endothermic peak was found at about 59.33°C, representing its melting point.

The DSC curve of physical mixtures (Figure 7) shows that the endothermic peak of the drug was slightly broader with a slight decrease in their intensity without a change in its position. These changes may be attributed to the mixing process that resulted in the dilution effect and denied the formation of the complex. Furthermore, the DSC thermograms of Eva 5, Figure 7 showed a decrease in the characteristic endothermic peak of CC to 164.27°C with broadening, indicating the partial change in the crystalline nature, which might be the reason for the enhanced solubility in addition to complex formation. Thus, the DSC confirmed the FTIR results.

- *Powder X-ray diffraction*

The X-ray diffractograms of pure CC, Mβ-CD, PX407, the physical mixture and inclusion complex (Eva 5) are shown in Figure 8. The X-ray diffraction analysis of pure CC powder indicated the crystalline nature of the drug, as evidenced by well-defined and sharp peaks, particularly at 2θ diffraction angles of 17.2137°, 18.6489°, 19.8632°, 21.5225°, 23.8034°, 25.5001°, 27.7464°, and 29.1848° similar to the evident values.[33] The X-ray diffraction patterns of the Mβ-CD show broad hallow peaks confirming its amorphous form. PX407 is crystalline in nature and gives two characteristic peaks: one at 19° and the other broader one 24°. For the physical mixture, the typical peaks of CC were presented with lower intensity, mainly due to the dilution effect, and no new peaks were observed, suggesting the absence of interaction among drug, Mβ-CD and PX407 in their physical mixture.

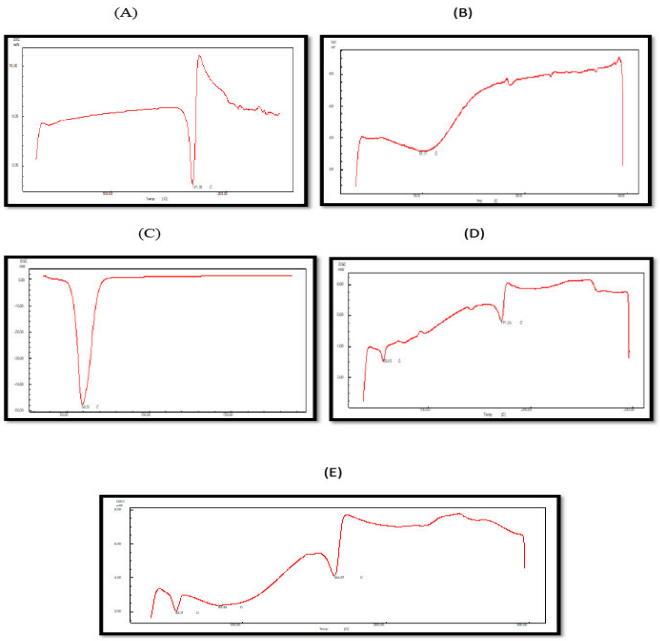

Figure 7: DSC of (A) Pure CC (B) Mβ-CD (C)PX407 (D) Physical mixture (E) Inclusion complex (Eva 5)

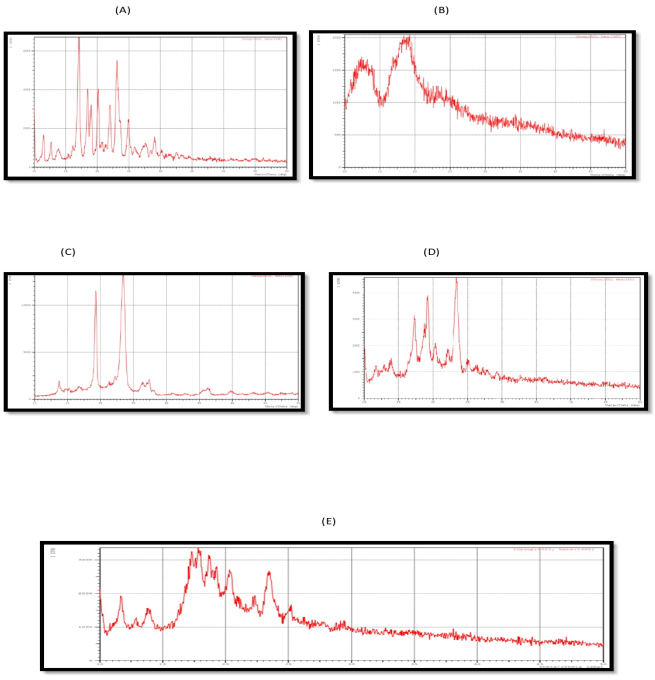

Figure 8: Powder X-ray difractogram of:(A) pure CC (B) Mβ-CD (C) PX407 (D) Physical mixture (E) Inclusion complex (Eva 5)

On the other hand, the X-ray diffraction pattern of Eva5 Figure 8 showed a broadening of the existing peaks with reduced intensity, Suggesting that during the complexation process, the drug transitioned into a partially amorphous or disordered crystalline phase.[10] These results gave further confirmation about the nature of the complex formation, similar to those obtained from FTIR, DSC, and dissolution studies.

CONCLUSION

Based on the results obtained from the present study, it can be concluded that the poor solubility of CC (class II drug) was successfully enhanced using a complexation technique. The best complex was obtained by preparing 1:1 CC: MBCD molar ratio in the presence of PX407 (5% w/w) by co-evaporation method due to the partial inclusion of CC within the MβCD cavity with an amorphous nature.

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