Research Article

Formulation and characterization of the atenolol-β-cyclodextrin-poloxamer 188 ternary inclusion complex with solvent evaporation method

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ABSTRACT

Purpose: The aim of this study was to develop a ternary inclusion complex of atenolol-β-cyclodextrin-poloxamer 188 to enhance the dissolution of atenolol.

Methodology:The ternary inclusion complex of atenolol-β-cyclodextrin-poloxamer 188 in this study was developed into three different ratios (1:1:0.00075; 1:1:0.00015; 1:1:0.00225). The solvent evaporation method was employed to produce these inclusion complexes. The inclusion complexes were characterized using FT-IR, DSC, XRD and SEM. The obtained inclusion complexes were also evaluated to determine the drug content and dissolution parameters.

Results: The results of FT-IR analysis exhibited interaction of atenolol, β-cyclodextrin, and poloxamer 188 through hydrogen bonding in the inclusion complex. Results of DSC and XRD study suggested the conversion of atenolol from a crystalline form to amorphous form. SEM analysis of inclusion complexes revealed that atenolol was entrapped in the β-cyclodextrin cavities and poloxamer 188 attached on the surface of β-cyclodextrin.The dissolution profile of these inclusion complexes showed enhancement of atenolol dissolution compare to pure atenolol. The inclusion complex using 1:1:0,00015 ratio performed the highest dissolution efficiency among three ratios. Therewere a 1.2 fold increases in dissolution efficiency of inclusion complexes compared to the pure drug.

Applications/Originality/Value: In ternary inclusion complex, β-cyclodextrin served as a versatile carrier to entrap the drug inside their cavity via hydrogen bound interaction. The addition of poloxamer 188 is also required to enhance aqueous solubility and fasten the rate of dissolution of atenolol. There was no study to develop a ternary inclusion complex of atenolol using β-cyclodextrin and poloxamer 188.

Keywords: atenolol; β-cyclodextrin; ternary inclusion complex; solvent evaporation.

INTRODUCTION

Atenolol is an antihypertensive drug, belonging to the group of β-blockers. Atenolol works as an antihypertensive drug by slowing down the heart and reducing its workload. Atenolol does not pass through the blood brain barrier, thus avoiding several central nervous system side effects(Bhowmik, Nijhu, Ahmed, & Sultana, 2013). Atenolol has a molecular weight of 266.34. Atenolol water solubility is 26.5 mg/ml in water, categorized as low solubility drugs. The systemic bioavailaibility of atenolol following per oral route is 50%. Regarding these information, atenolol are characterized exhibit poor solubility in gastric fluid, hence the dissolution rate and bioavailability directly influence their efficacy (Borodi et al., 2008). In order to increase the dissolution of atenolol, an inclusion complex of atenolol using β-cyclodextrin can be potentially useful to develop new form which has better dissolution characteristics. This new form is predicted enhance the dissolution of atenolol in dosage forms, aiming to improve its bioavailability (Buha, Baxi, & Shrivastav, 2012).

Cyclodextrins are cyclic oligomers of α-(1,4) -D-glucopyranose units which contribute to the drug-guest phenomena in solution. Its exhibited a downward-like shape, with more hydrophilic character on the outside of cyclodextrin and hydrophobic character within the cavity(Badr-Eldin, Elkheshen, & Ghorab, 2008).The free hydroxyl groups on the outside of the cyclodextrin exhibit hydrophilic character, whereas the oxygen atoms and the hydrogen atoms impart a hydrophobic character within the cavity(Carneiro et al., 2019). β-cyclodextrin is the most commonly used cyclodextrin in pharmaceutical field due to the size of its internal cavity suitable with various substances, the ease of preparation, and low cost. β-cyclodextrin is a cyclic oligosaccharide formed by seven glucose units. Various kinds of

substances or drugs can be incorporated in its cavity as guest molecules, forming an inclusion interaction compound by intermolecular non-covalence force The ability of β-cyclodextrin to form inclusion complex is highly determined by the size, shape, and characteristic of guest molecules. The inclusion complex of drug molecules into cyclodextrin cavity or partial encapsulation of the drug, leads to important enhancement of drug molecules, such as increase the solubility of drugs, improves drug stability, reduce drug toxicity, and increase the bioavailability of drugs(Antony Muthu Prabhu, Subramanian, & Rajendiran, 2012). Generally, the interaction between host and guest molecules occurred in 1:1 host-guest stoichiometry equilibrium.

The previous study revealed that the stoichiometry of atenolol-β-cyclodextrin inclusion complex was exhibited in 1:1 equimolar (Borodi et al., 2008).

In this study, the preparation of inclusion complex was conducted in 1:1 molar ratio to reach the optimum entrapment. The enhancement of drug molecules solubility via inclusion complex using β-cyclodextrin can be achieved by adding small amounts of surfactants(Szafraniec *et al*., 2019). The effect of a surfactant on the solubility of poorly water soluble drugs can be performed by three mechanisms: (i) aid the dispersability of drugs through increase in contact with aqueous medium; (ii) increased solubility of drugs through micelle formation; (iii) facilitated transport of the drugs to the aqueous phase through interaction with solid interface*(Li et al*., 2010). Design to increase the dissolution of atenolol using complexation with cyclodextrin and surfactants have not been developed yet. Therefore, this study investigated the effect of complexation using β-cyclodextrin and the addition of poloxamer 188. Poloxamer 188is a non-ionic triblock copolymer composed of two hydrophilic polyoxyethylene chains connected by a hydrophobic polyopxypropylene chain(Qiu, Chen, Zhang, Liu, & Porter, 2009). Poloxamer 188 has been widely used by researchers to increase the aqueous solubility of low water solubility drugs. In this study, the ternary inclusion complexes of atenolol-β-cyclodextrin-poloxamer 188 developed in three different molar ratios (1:1:0,00075; 1:1:0,00015; 1:1:0,00225). The solvent evaporation method was employed to produce these inclusion complexes. The inclusion complexes were characterized using FT-IR, DSC, XRD and SEM. The obtained inclusion complexes were also evaluated to determine the drug content and dissolution parameters.

MATERIALS AND METHODS

Materials

Atenolol was obtained fromRefarmed Chemicals ; Lugono Switzerland. β-cyclodextrin was gifted from Roquette, France, and Poloxamer 188 was obtained from BASF corporation. All other chemicals materials and reagents which used in this study were of analytical grade.

Methods

Preparation of ternary inclusion complexes of atenolol-β-cyclodextrin-poloxamer 188

In this study, inclusion complex of atenolol-β-cyclodextrin-poloxamer 188 were prepared in three different molar ratios. The ratio of atenolol:β-cyclodextrin:poloxamer 188 for formula 1 was (1:1:0.00075), formula 2 was (1:1:0.0015), formula 3 was (1:1:0.00225). The ternary inclusion complexes were prepared by solvent evaporation method. Required quantities of atenolol, β-cyclodextrin, and poloxamer 188 according to the ratio were weighed. The composition of each formula was tabulated in Table 1.

Table 1: Composition of ternary inclusion complex of atenolol-β-cyclodextrin-poloxamer 188

Materials	Molecular weight	Formula 1		Formula Formula 2		Formula 3	
		1 part	500 part	1 part	500 part	1 part	500 part
Atenolol	266	50 mg	25 g	50 mg	25 g	50 mg	25 g
β-siklodekstrin	1153	216.8 mg	108.4 g	216.8 mg	108.4 g	216.8 mg	108.4 g
Poloxamer 188 (1:1:0.00075)	8525	1.2 mg	0.6 g	-	-	-	-
Poloxamer 188 (1:1:0.0015)	8525	-	-	2.4 mg	1.2 g	-	-
Poloxamer 188 (1:1:0.00225)	8525	-	-	-	-	3.6 mg	1.8 g
Ethanol		3 ml	800 ml	3 ml	800 ml	3 ml	800 ml
Purified water		9.34 ml	2173 ml	9.34 ml	2173 ml	9.34 ml	2173 ml

Accurately weigh quantities of atenolol was dissolved in ethanol and stirred until dissolved. The solution of poloxamer 188 then was added slowly to the solution of atenolol. This mixture was

stirred using magnetic stirrer and heated on 50ºC for 15 minutes. β-cyclodextrin was dissolved in purified water, then the solution of β-cyclodextrin was poured into the mixture of atenolol-poloxamer 188 until a suspension was formed. This mixture was stirred at 500 rpm and heated on 50ºC for 6 hours to evaporate the solvent. The results of this process were the slurry paste, then the slurry paste dried in a tray dryer at 50ºC until the moisture content of the powder was 2-4%. The dried inclusion complexes powder was pulverized and passed through a no. 60 sieve and stored in airtight container until further use.

CHARACTERIZATION OF TERNARY INCLUSION COMPLEXES OF ATENOLOL-B-CYCLODEXTRIN-POLOXAMER 188

Infrared spectrum analysis

Infrared spectrum analysis of atenolol, β-cyclodextrin, poloxamer 188, and the inclusion complexes were performed to predict the possible interaction between the host molecules (atenolol), guest molecules (β-cyclodextrin), and surfactant (poloxamer 188). This study also beneficial to predict the functional groups of these molecules, which induced the interaction. Infrared spectrum of these samples was recorded using Fourier Transform Infrared spectrophotometer (Jasco FT-IR/4200) over a wave number 4000-400 cm^{-1}(Jagdale, Dehghan, & Paul, 2019).

Differential scanning calorimetry study

The samples of atenolol, β-cyclodextrin, poloxamer 188, and the inclusion complexes were subjected to DSC studies. Approximately 4 mg of samples was placed in platinum crucible, then analyzed using Mettler Toledo differential scanning calorimeter. The samples were heated and scanned at 10ºC/minutes in the range of 40ºC to 200ºC. The samples was flowed by nitrogen 40 ml/minutes(Ghosh, Biswas, & Ghosh, 2011).

X-ray powder diffraction study

X-ray diffraction spectrum of atenolol, β-cyclodextrin, poloxamer 188, and the inclusion complexes were recorded using Philips x-ray diffractometer in the range 2Θ 5-50º. X-ray diffraction study of inclusion complexes was performed to analyze the difference of the crystalline structure among atenolol as pure drug, β-cyclodextrin, poloxamer 188 and inclusion complexes of atenolol-β-cyclodextrin-poloxamer 188(Akbari, Valaki, Maradiya, Akbari, & Vidyasagar, 2011).

Scanning electron microscopy

The scanning electron microscopy photograph of atenolol, β-cyclodextrin, poloxamer 188, and the inclusion complexes were obtained by Hitachi scanning electron microscope. The samples were impregnated with gold to produce a protective layer during the scanning process at 15 kV(Doile et al., 2008).

Drug content analysis

The inclusion complexes powder was weighed 266.8 mg (equivalent to 50 mg of atenolol) transferred into 100.0 ml volumetric flask. 10 ml of methanol was added to the volumetric flask containing inclusion complexes, and sonicated for 5 minutes to get clear solution. Acetic acid buffered pH 4,6 was quantitatively added to the volumetric flask. Appropriate dilution was performed to this solution and the drug content of inclusion complex was calculated by analyzing the absorbance of this solution using UV-Vis spectrophotometer at λ 274 nm (Chandrasekhar et al., 2013) .

In vitro dissolution study

Dissolution study of atenolol and inclusion complexes were performed using the USP dissolution test apparatus type II (paddle method). Atenolol was weighed 50 mg and the inclusion complexes were weighed equivalent to 50 mg of atenolol. Dissolution medium in this study was 900 ml acetate buffer pH 4,6 and the rotation speed of apparatus was 50 rpm. The dissolution medium was maintained 37±0.5°C during this study. An aliquot of 10 ml samples were withdrawn in predetermined intervals (1,3,5,13,45, and 60 minutes) and replaced with the fresh dissolution medium. Diluted samples from each time interval were then assayed to determinate the concentration of atenolol by measuring the absorbance at 274 nm using UV-visible double beam spectrophotometer (Shimadzu UV-1800). The dissolution studies were performed until 60 minutes to obtain a dissolution profile and calculate the dissolution parameters, including % drug release (%Q), area under dissolution curve (AUC), and % dissolution efficiency (%DE).

DATA ANALYSIS

The dissolution parameters of the inclusion complexes (% drug release, area under curve (AUC), and dissolution efficiency (%DE) were analyzed using one way analysis of variance (ANOVA). The results are considered as statistically significant when $P < 0.05$.

RESULTS

Characterization of solid dispersions

The solid state characterization of atenolol, β-cyclodextrin, poloxamer 188, and inclusion complexes were performed using Fourier

Transform Infrared Spectroscopy (FT-IR), Differential Scanning Calorimetry (DSC), Powder X-ray Diffractometer (PXRD), and Scanning Electron Microscopy (SEM).

Infrared spectrum analysis

The FT-IR spectrum of atenolol, β-cyclodextrins, poloxamer 188, and the ternary inclusion complexes are shown in Figure 1. The FT-IR spectrum of pure drug was characterized by several functional groups including –CO-NH specified at 3177.15 cm^{-1} (N-H stretching) and 1613.16 cm^{-1}(C=O stretching), asymmetric C-H stretching at 2921.63 cm^{-1}, and –N-CO deformation at 1515.78 cm^{-1}.β-cyclodextrins spectrum exhibited specific absorption bands at 3398.92 (O-H stretching band), 1645.95 cm^{-1} (O-C, C=O), 1416.46 cm^{-1} (O-H *bending*, α-CH2 *bending*, CH2 *deformation*), 1336.43 cm^{-1} (O-H *bending*), 1157.08 cm^{-1} (C-C-C *bending*), 1028.84 cm^{-1}(C-O), 938.199 cm^{-1}, 859.132 cm^{-1}, 755.959 cm^{-1} (=C-H & =CH2 *stretching*, C-H bending &*ring puckering*) dan 707.747 cm^{-1} (cis-RCH=CHR). Poloxamer 188 spectrum was characterized by broad bands at 3458.71 cm^{-1} which is indicated as –O-H stretching, -CH_3 stretching at 2889.09 cm^{-1}, and C-O stretching bands at 1107.9 cm^{-1}, 1242.9 cm^{-1}, 1281.47cm^{-1}. In the case of ternary inclusion complexes, the specific carbonil bands (C=O) of atenolol was dissapeared. There were several new specific bands in the inclusion complexes, characterized at 2065.39 cm^{-1} and 2064.42 cm^{-1}. This phenomenon indicated a possible interaction between atenolol and β-cyclodextrins. Interaction between atenolol and β-cyclodextrin was predicted as the formation of hydrogen bonding between –C=O-NH groups in atenolol molecules and hydroxyl (-OH) groups of β-cyclodextrins(Gite, 2014). The effect of poloxamer 188 concentrations in the inclusion complexes revealed no significant difference between three different ratios, which has been prepared.

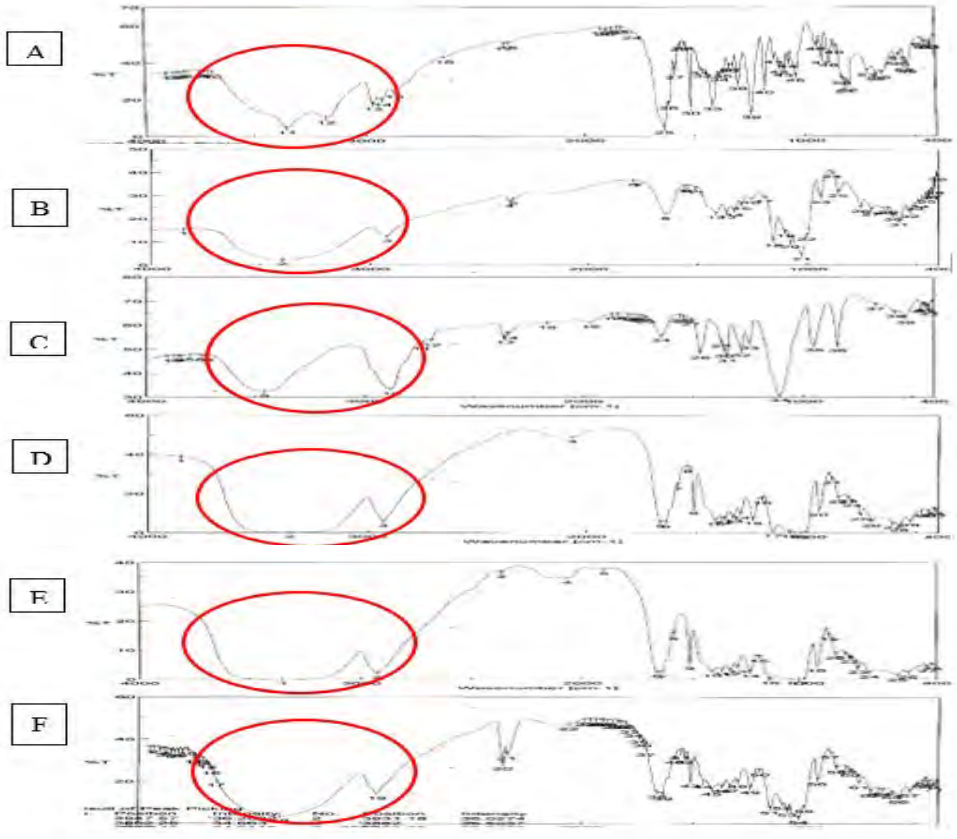

Fig.1: Infrared spectrum of (A) atenolol, (B) β-cyclodextrin. (C) poloxamer 188, ternary inclusion complexes (D) (1 :1 :0.0075), (E) (1 :1 :0,0015), (F) (1 :1 :0.0025)

Differential scanning calorimetry study

Differential scanning calorimetry study is beneficial to analyze the thermal characteristics of atenolol, carrier, surfactant, and the inclusion complexes of these components. DSC termograms explained the melting point of atenolol, β-cyclodextrin, and poloxamer 188 respectively, were 153.90°C; 124.27°C; and 52.05°C. The DSC termograms of ternary inclusion complexes and pure component showed

in Figure 2. Pure atenolol showed a single sharp endothermic peak at 153.90°C, regarding its melting point. Preparation of atenolol into ternary inclusion complexes using β-cyclodextrin, and poloxamer 188 induced the alteration of atenolol endothermic peak. There were three endothermic peaks in the inclusion complexes, corresponding to atenolol, cyclodextrin, and poloxamer 188. The specific endothermic peak of atenolol was shifted to the lower value in the termogram of inclusion complexes. Moreover, the entalphy of ternary inclusion complexes also revealed a reduction compare to the entalphy of pure atenolol. The shifting of endothermic peak of atenolol and the reduction of entalphy in ternary inclusion complexes, indicating the interaction between drug, carrier, and surfactant(Badr-Eldin et al., 2008). The lower endothermic peak of atenolol in ternary inclusion complexes compared to the pure drug, indicating an alternation of crystal behavior lead to amorphous system or solubilisation of drug into the melted carrier (Patil, Belgamwar, Patil, & Surana, 2013).

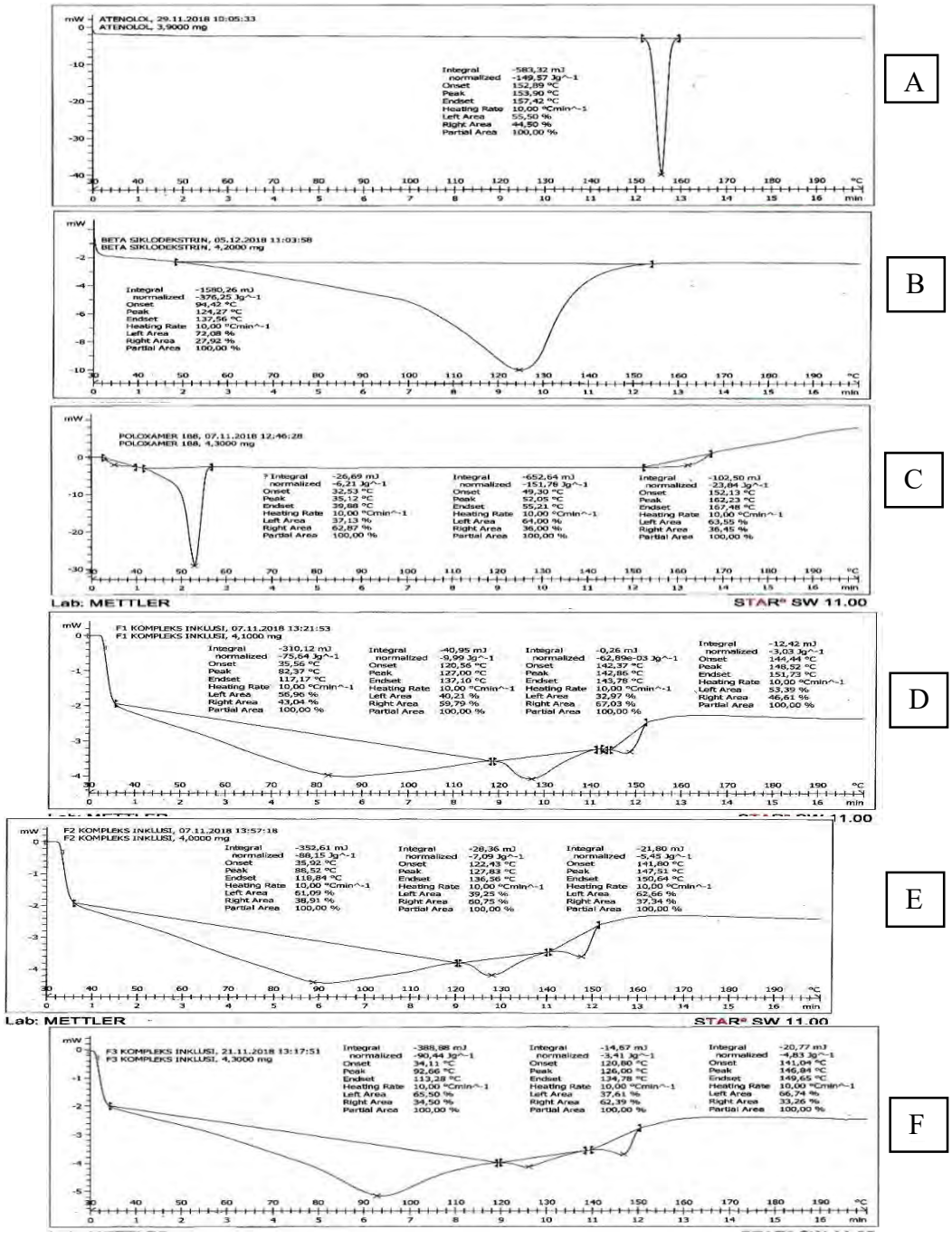

Fig.2: DSC termogram of (A) atenolol, (B) β-cyclodextrin. (C) poloxamer 188, ternary inclusion complexes (D) (1 :1 :0.0075), (E) (1 :1 :0,0015), (F) (1 :1 :0.0025)

X-ray powder diffraction study

X-ray powder diffraction study was performed to analyze crystal structure and configuration of the crystal lattice. The X-ray powder difractogram among pure atenolol, β-cyclodextrin, and poloxamer 188 were evaluated to identify the alteration of drug crystallinity prior to inclusion complexes and after inclusion complexes. Crystalinity was determined by comparing representative peak heights in the difractogram (Akbari et al., 2011). X-ray difraction study find out that there were some reduction of atenolol peak intensity in ternary inclusion complexes compare to the pure atenolol. This condition indicated that there was an alteration of drug crystalinity lead to amorphous system. It revealed that atenolol molecule entrapped in the β-cyclodextrin cavity (Badr-Eldin et al., 2008). The formation of an amorphous system proves that the drug formed ternary inclusion complexes. On the other hand, the increased of poloxamer proportion in inclusion complexes was not exhibited a different X-ray pattern of the inclusion complexes. X-ray difractogram of atenolol, β-cyclodextrin, and inclusion complexes showed in Figure 3.

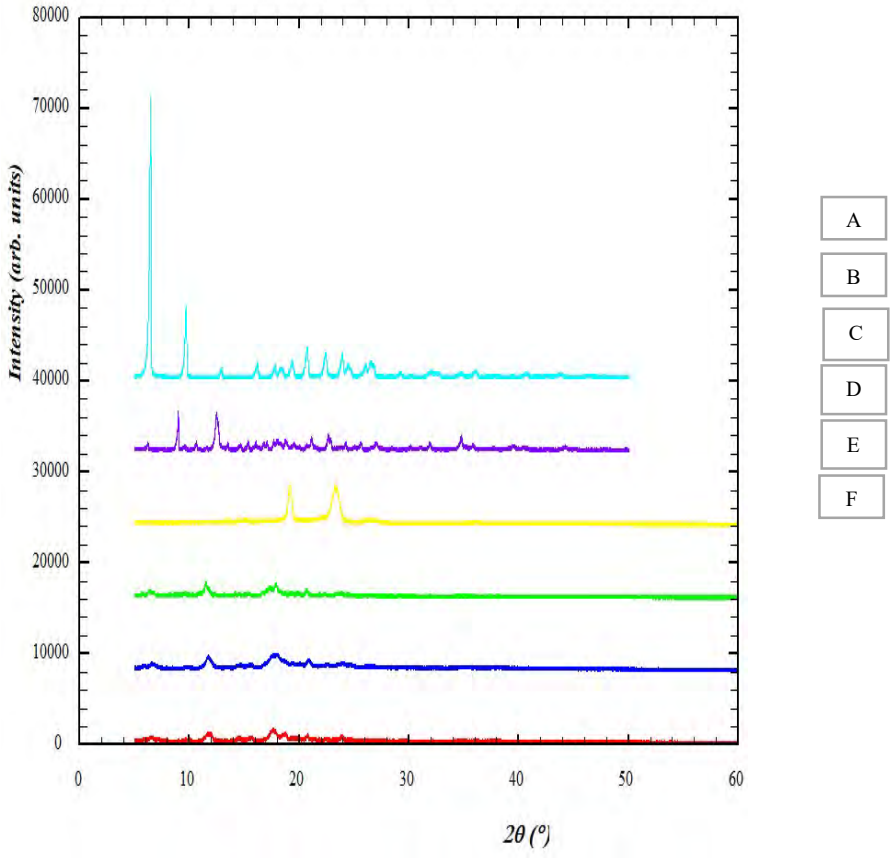

Fig.3 : DSC termogram of (A) atenolol, (B) β-cyclodextrin. (C) poloxamer 188, ternary inclusion complexes (D) (1 :1 :0.0075), (E) (1 :1 :0,0015), (F) (1 :1 :0.0025)

Scanning Electron Microscopy

Scanning electron photomicrograph of atenolol, β-cyclodextrin, poloxamer 188, and ternary inclusion complexes were observed to determine the alteration of surface morphology among pure drug, carrier, surfactan, and inclusion complexes. Photomicrograph of atenolol showed extangular shape, β-cyclodextrin showed cubical shape, and poloxamer 188 showed rounded grape shaped. The ternary inclusion complexes of atenolol showed that atenolol was entrapped in the cubical structure of β-cyclodextrin and poloxamer 188 attached on the surface of β-cyclodextrin. The scanning electron micrograph also revealed the decrease of crystallinity due to formation of ternary inclusion complex and molecular dispersion of the drug inside the carrier, respectively(Antony Muthu Prabhu et al., 2012). The scanning electron photomicrograph of atenolol, β-cyclodextrin, poloxamer 188, and ternary inclusion complexes showed in Figure 4.

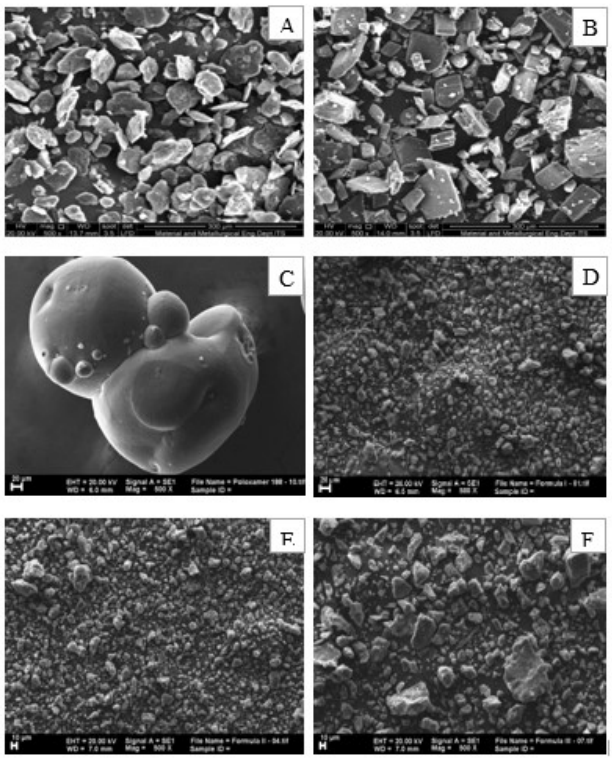

Fig.4: SEM photomicrograph of (A) atenolol, (B) β-cyclodextrin, (C) poloxamer 188, ternary inclusion complexes (D) (1 :1 :0.0075), (E) (1 :1 :0.0015), (F) (1 :1 :0.0025)

Scanning electron photomicrograph of ternary inclusion complexes with 1 :1 :0.0075 ratio (formula 1) and 1 :1 :0.0015 ratio (formula 2) showed that atenolol was dispersed in β-cyclodextrin as smaller particles compared to the pure drug. The reduction of particle size, increased surface area, and contribute to enhance drug dissolution(Kumar, Murthy, Sameeraja, & Narayan, 2016). However, atenolol in formula 3 (1 :1 :0.0025) was dispersed in a larger size, like a broken fragment. The larger size of drug particles in formula 3, caused slightly different of dissolution characteristics compare to two other formulas.

Drug content analysis

Drug content analysis was performed in this study to ensure drug content uniformity in inclusion complexes powder. Drug content analysis is an approach to control the quality and effectifity of inclusion complexes served as starting material in the field of dosage form formulation. The results of % drug content in formula 1 (1 :1 :0.00075) were99.33±0.60%, formula 2 (1 :1 :0.0015) were 99.25±0.13%, formula 3 (1 :1 :0.0025) were92.82±0.13%. All of the inclusion complexes formulation showed the presence of high drug content, above 90%. It indicated that atenolol was homogeneously dispersed in the inclusion complex powder. The requirement of atenolol content in the powder for formulation was 98%-102%, according to Pharmacopeia. Based on this requirement, the formula I and formula II can be developed further as starting material in the dosage form formulation. Formula III can not be utilized as starting material because the drug content was lower than 98%.

In vitro dissolution study

In vitro dissolution study was performed to predict the drug release profile and dissolution parameter of these inclusion complexes. Dissolution is a rate limiting step in the absorption process, in the case of poorly water soluble drugs(Jagdale et al., 2019). Therefore, dissolution parameters have strong correlation with the ability of drug to readily absorb and available in the blood. The inclusion complexes performed an enhancement of % drug release compare to pure drug. Formula 1, formula 2, and formula 3 showed respectively 90.94±5.46%, 89.89±4.12%, and 82.35±5.34% atenolol release after 15 minutes. The pure drug of atenolol only showed 77.39±20.58% after 15 minutes. The dissolution profile of these formulas showed in Figure 1. The dissolution parameters of formula 1, formula 2, formula 3, and atenolol have been tabulated in Table 1.

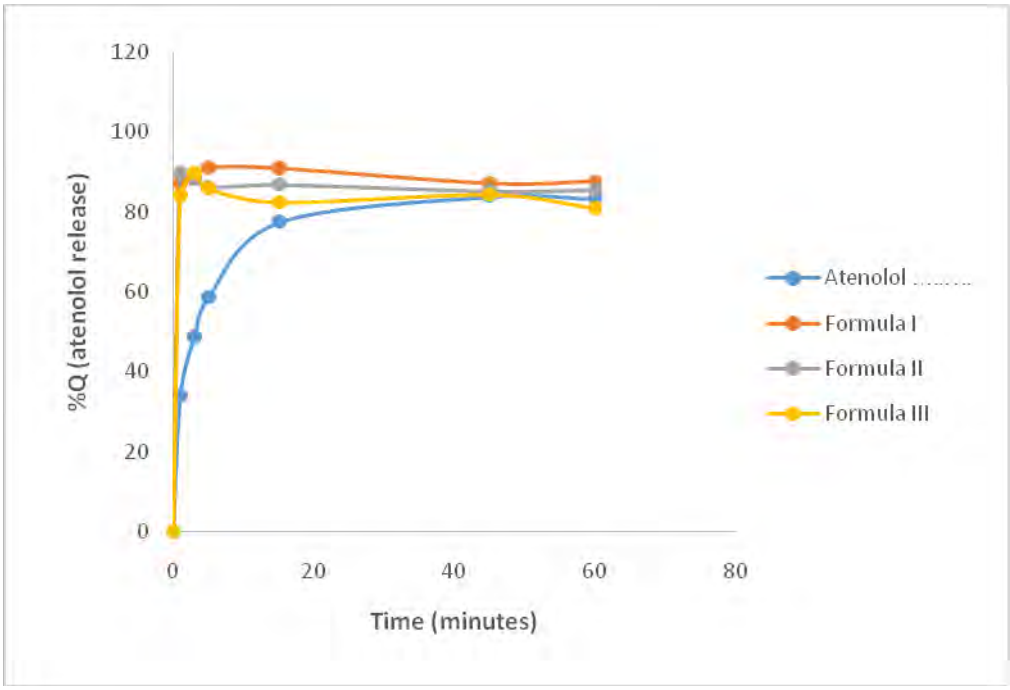

Fig.5: Dissolution profile of atenolol and ternary inclusion complexes

Table 2 : Dissolution parameters of atenolol and ternary inclusion complexes (formula 1, formula 2, and formula 3)

Sample	Area under curve (AUC)	% Dissolution efficiency (%DE $_{60\ minutes}$)
Atenolol powder	4378.42±2.55	75.97%±4.20
Inclusion complex formula 1 (1 :1 :0.00075)	5528.15±160.60	92.82%±7.50
Inclusion complex formula 2 (1 :1 :0.0015)	5618.68±477.36	94.58%±2.84
Inclusion complex formula 3 (1:1:0.0025)	5530.67±286.92	88.78%±7.21

The inclusion complexes of atenolol-β-cyclodextrin-poloxamer 188 showed higher dissolution efficiency compare to atenolol powder. The results of statistical analysis using one-way ANOVA revealed that the dissolution parameters (AUC and % dissolution efficiency) of ternary inclusion complexes were significantly differentcompared to the puredrug atenolol ($P<0.05$). The dissolution efficiency of ternary inclusion complexes folded 1.2 times than the atenolol powder. In the presence of β-cyclodextrin, the hydrophobic part of drug molecule can be interacted with hydrophobic region of β-cyclodextrin cavity. This interaction promotes the hydrophilic region of β-cyclodextrin assembled to interact with aqueous environment. The hydrophilic region increase the wettability of atenolol, then atenolol dissolved in the aqueous medium. Poloxamer 188 played a role to lower the surface tension of the drug and aqueous medium, so that the solubilization process of the drug has been occurred. Poloxamer 188 also served to enhance the hydrogen bonds between drug and carrier and decrease cristallinity of the product(Jagdale et al., 2019). This phenomenon also can be analyzed from the results of characterization using XRD, SEM, FT-IR, and DSC. Due to the decrease of crystallinity and high degree of interaction between atenolol and β-cyclodextrin through hydrogen bonding, these inclusion complexes displayed a higher degree of dissolution parameters.

The dissolution efficiency of ternary inclusion complexes was increased slightly according to the increase of poloxamer concentration in formula 1 to formula 2. Poloxamer 188 employed to enhance the solubilizing efficiency of β-cyclodextrin by interacting with the functional

groups presented in the exterior part of β-cyclodextrin(Kulkarni, Dias, & Ghorpade, 2019). Due to this phenomenon, the synergistic effect of β-cyclodextrin poloxamer 188 exhibited enhancement on dissolution efficiency. Incorporation of the two water soluble carriers contributes to increase amorphousness of the drug, as confirmed by DSC and XRD data (Nirmala, Ashok Chakradhar, & Sudhakar, 2016). The concentration of poloxamer 188 in the preparation of ternary inclusion complexes also affects the dissolution parameters. Poloxamer 188 concentrations play significant role to reduce the contact angle of poorly water soluble drugs and increased wettability (Szafraniec et al., 2019). The escalation of poloxamer 188 concentrations in a mixture, caused the dissolution rate of the drugs increased. The improvement in dissolution parameters is possibly caused by several factors, such as the strong hydrophilic character of β-cyclodextrin, the optimal dispersion of atenolol to β-cyclodextrin, the alteration of crystalline based structure of the amorphous form, and the molecular hydrogen bond between atenolol and β-cyclodextrin lead to partial miscibility of the drugs (Jagdale et al., 2019).

However, in this study showed a little bit contrary, regarding to formula 3. The increased of poloxamer 188 concentrations caused the dissolution parameter became smaller compare to the other formulas. The formation of gel like structure of poloxamer 188 in the microenvironment level of the ternary inclusion complex was expected to provoke this condition(Emal et al., 2012). A gel microenvironment hindrance the drug movement, so that formula 3 showed less drug release compared to the lower concentration of poloxamer 188 (formula 1 and formula 2). The decreased of atenolol release in formula 3 was also confirmed by SEM photomicrograph, which indicated that the drug was dispersed in bigger constituent compare to the other formulas.This result revealed poloxamer concentration in the formula must be optimized well. In this study, the optimum ratio of atenolol- β-cyclodextrin-poloxamer 188 was found at 1 :1 :0.0015 molar ratio. This study also revealed that poloxamer 188 was possible to use in the lower concentration for enhancing dissolution characteristics of the drug.

CONCLUSION

Atenolol is an antihypertensive drug with low water solubility characteristics, hence the dissolution process is the rate limiting step of the absorption process. Based on this study, the formation of ternary inclusion complexes between atenolol-β-cyclodextrin-poloxamer 188 were able to enhance the dissolution of atenolol. The percentage of drug release and dissolution efficiency ($DE_{60\ minutes}$) of atenolol from ternary inclusion complexes were higher than atenolol pure drug. The ternary inclusion complexes gave higher enhancement in dissolution efficiency (1.2 folds) of atenolol. This phenomenon was also confirmed from DSC, FT-IR, X-ray, and SEM results. The results explained the ternary inclusion complex systems prepared employing β-cyclodextrin and poloxamer 188 observed with lower crystallinephase compare to the pure drug. The alteration of crystallinity of this system might be caused by interaction between atenolol, β-cyclodextrin and poloxamer 188 through the hydrogen bonding. The concentration of poloxamer 188 also influenced the dissolution and physical characteristics of inclusion complexes. The increased of poloxamer 188 concentrations in ternary inclusion complexes did not always provide linear impact to the dissolution efficiency of the drugs. The formation of gel like structure of poloxamer 188 on the microenvironment level of ternary inclusion complex with 1 :1 :0.0025 ratio was expected to hinder the drug release from this system. This phenomenon was also confirmed by SEM photomicrograph, which described the dispersion of atenolol was in bigger granules compare to the other formulas. Thus, the optimum ratio of atenolol, β-cyclodextrin and poloxamer 188 in this study was 1 :1 :0.0015.

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REFERENCES

1. A. A. E., . A. A., & . E. A. E. (2012). Complexation of Naproxen With Beta-Cyclodextrin With and Without Poloxamer 407 To Enhance Drug Dissolution. *Journal of Applied Pharmacy*, *4*(04), 178–191. https://doi.org/10.21065/19204159.4.178
2. Akbari, B. V., Valaki, B. P., Maradiya, V. H., Akbari, A. K., & Vidyasagar, G. (2011). Effect of Types of Cyclodextrin on Rosuvastatin Calcium Inclusion Complex. *Indian Journal of Pharmaceutics*, *2*(1), 1–8.
3. Antony Muthu Prabhu, A., Subramanian, V. K., & Rajendiran, N. (2012). Excimer formation in inclusion complexes of β-cyclodextrin with

salbutamol, sotalol and atenolol: Spectral and molecular modeling studies. *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, *96*, 95–107. https://doi.org/10.1016/j.saa.2012.04.044

4. Badr-Eldin, S. M., Elkheshen, S. A., & Ghorab, M. M. (2008). Inclusion complexes of tadalafil with natural and chemically modified β-cyclodextrins. I: Preparation and in-vitro evaluation. *European Journal of Pharmaceutics and Biopharmaceutics*, *70*(3), 819–827. https://doi.org/10.1016/j.ejpb.2008.06.024
5. Bhowmik, A., Nijhu, R. S., Ahmed, T., & Sultana, S. (2013). Design and development of atenolol matrix tablet employing natural and synthetic polymers. *Journal of Applied Pharmaceutical Science*, *3*(9), 103–108. https://doi.org/10.7324/JAPS.2013.3919
6. Borodi, G., Bratu, I., Dragan, F., Peschar, R., Helmholdt, R. B., & Hernanz, A. (2008). Spectroscopic investigations and crystal structure from synchrotron powder data of the inclusion complex of β-cyclodextrin with atenolol. *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, *70*(5), 1041–1048. https://doi.org/10.1016/j.saa.2007.10.021
7. Buha, S. M., Baxi, G. A., & Shrivastav, P. S. (2012). Liquid Chromatography Study on Atenolol--Cyclodextrin Inclusion Complex. *ISRN Analytical Chemistry*. https://doi.org/10.5402/2012/423572
8. Carneiro, S. B., Duarte, F. Í. C., Heimfarth, L., Quintans, J. D. S. S., Quintans-Júnior, L. J., Júnior, V. F. D. V., & De Lima, Á. A. N. (2019). Cyclodextrin-drug inclusion complexes: In vivo and in vitro approaches. *International Journal of Molecular Sciences*, *20*(3), 1–23. https://doi.org/10.3390/ijms20030642
9. Chandrasekhar, P., Shahid Muhammad, S., & Niranjan Babu., M. (2013). Formulation and Evaluation of Oral Dispersible Tablets of Anti Hypertensive Drug Atenolol. *International Journal of Pharmacy*, *3*(2), 79–84.
10. Doile, M. M., Fortunato, K. A., Schmücker, I. C., Schucko, S. K., Silva, M. A. S., & Rodrigues, P. O. (2008). Physicochemical Properties and Dissolution Studies of Dexamethasone Acetate-β-Cyclodextrin Inclusion Complexes Produced by Different Methods. *AAPS PharmSciTech*, *9*(1), 314–321. https://doi.org/10.1208/s12249-008-9042-z
11. Ghosh, A., Biswas, S., & Ghosh, T. (2011). Preparation and Evaluation of Silymarin β-cyclodextrin Molecular Inclusion Complexes. *Journal of Young Pharmacists*, *3*(3), 205–210. https://doi.org/10.4103/0975-1483.83759
12. Gite, S. . (2014). Development and Evaluation of Mucoadhesive Tablets of Atenolol and It's B-Cyclodextrin Complex. *Asian Journal of Biomedical and Pharmaceutical Sciences*, *4*(37), 25–32. https://doi.org/10.15272/ajbps.v4i37.595
13. Jagdale, S. K., Dehghan, M. H., & Paul, N. S. (2019). Enhancement of dissolution of fenofibrate using complexation with hydroxy propyl β-cyclodextrin. *Turkish Journal of Pharmaceutical Sciences*, *16*(1), 48–53. https://doi.org/10.4274/tjps.60490
14. Kulkarni, A., Dias, R., & Ghorpade, V. (2019). Freeze dried multicomponent inclusion complexes of quercetin: Physicochemical evaluation and pharmacodynamic study. *Marmara Pharmaceutical Journal*, *23*(3), 403–414. https://doi.org/10.12991/jrp.2019.148
15. Kumar, M. A., Murthy, P. N., Sameeraja, N. H., & Narayan, P. N. (2016). Dissolution rate enhancement of entacapone and formulation of its oro- dispersible tablets: Applying statistical design. *Indian Journal of Pharmaceutical Education and Research*, *50*(4), 549–562. https://doi.org/10.5530/ijper.50.4.7
16. Li, D. X., Han, M. J., Balakrishnan, P., Yan, Y. D., Oh, D. H., Joe, J. H., … Choi, H. G. (2010). Enhanced oral bioavailability of flurbiprofen by combined use of micelle solution and inclusion compound. *Archives of Pharmacal Research*, *33*(1), 95–101. https://doi.org/10.1007/s12272-010-2231-9
17. Nirmala, D., Ashok Chakradhar, P., & Sudhakar, M. (2016). Preparation and characterization of Pitavastatin solid dispersions. *Research Journal of Pharmacy and Technology*, *9*(5), 555–558. https://doi.org/10.5958/0974-360X.2016.00105.0
18. Patil, P. H., Belgamwar, V. S., Patil, P. R., & Surana, S. J. (2013). Solubility Enhancement of Raloxifene Using Inclusion Complexes and Cogrinding Method. *Journal of Pharmaceutics*, *2013*, 1–9. https://doi.org/10.1155/2013/527380
19. Qiu, Y., Chen, Y., Zhang, G., Liu, L., & Porter, W. (2009). *Developing solid oral dosage forms. Pharmaceutical theory and practice. Libro. Developing Solid Oral Dosage Forms*. https://doi.org/http://dx.doi.org/10.1016/B978-0-444-53242-8.00009-6
20. Szafraniec, J., Antosik, A., Knapik-Kowalczuk, J., Chmiel, K., Kurek, M., Gawlak, K., … Jachowicz, R. (2019). The self-assembly phenomenon of poloxamers and its effect on the dissolution of a poorly soluble drug from solid dispersions obtained by solvent methods. *Pharmaceutics*, *11*(3). https://doi.org/10.3390/pharmaceutics11030130

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