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FORMULATION AND EVALUATION OF CARVEDILOL FAST DISSOLVING TABLETS

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ABSTRACT

Carvedilol a poorly water soluble drug undergoes extensive first pass metabolism, which reduces its bioavailability to 25-30%. Fast dissolving tablets of Carvedilol were prepared with the purpose of delivering the drug directly into the systemic circulation and bypassing the hepatic first pass metabolism with a concomitant increase in bioavailability. The solubility of Carvedilol was improved by forming inclusion complex with cyclodextrin which was then further used for the formulation of Fast dissolving tablet. All the three superdisintegrant showed good compressibility, good compatibility, flowability and stability. Formulation C3 of Ac-Di-sol superdisintegrant required minimum disintegration time, wetting time Compared to Formulations of Crosspovidone, or Sodium-starch glycoate with same concentration. Formulation of Ac-Di-sol superdisintegrant (C3) had maximum Formulation of Ac-Di-sol superdisintegrant (C3) have maximum water absorption ratio, drug release than all other formulation and 98.4% release in 10 min.

KEYWORDS: Carvedilol, Superdisintegrats, Fast dissolving Tablets

INTRODUCTION

Carvedilol is an alpha and a beta adrenoreceptor-blocking agent used in the treatment of various cardiovascular disorders such as angina pectoris, cardiac arrhythmia and hypertension. Carvedilol is indicated for the treatment of mild to severe chronic heart failure, Left ventricular dysfunction following myocardial infraction in clinically stable patients and hypertension. Carvedilol is a poorly water-soluble oral antihypertensive agent, with problems of variable bioavailability and bio-equivalence related to its poor water-solubility. In present work attempt will be made to design and evaluation of Fast dissolving tablets of Carvedilol for the effective management of angina pectoris, hypertension etc. In view of substantial first pass effect and its shorter plasma half life therefore is an ideal drug candidate for Fast dissolving drug delivery system.To formulate the fast dissolving dosage form of Carvedilol to Improve patient compliance, Ease of administration, Increase bioavailability of drug and avoid first pass effect.

MATERIALS AND METHODS

Carvedilol procured from Zydus Cadila, Ahmedabad, Betacyclodextrin gifted from Micro Advance Research centre, Bangalore, Cross carmellose Sodium, Cross povidone ,Sodium starch glycolate, Microcrystalline cellulose Procured from Signet chemicals pvt.ltd ,Mumbai.

Preparation of the Fast dissolving tablet of Carvedilol: The tablet consisted of drug: β-CD complex, super disintegrant like Ac-di-sol/ Polyplasdone-XL /Primojel, Avicel pH102, talk, Magnesium stearate, Lactose, Dextrose, Sorbitol, Xylitol, Aerosil, Strawberry. These ingredients were weighed and mixed stoichometrically to obtain the final formulation. The weight of the tablet in all formulations was kept constant to 130mg. All the batches were prepared by direct compression method using the 27-station rotary punch tablet compression machine using 7 mm biconvex plain on both side die-punches set. The variables maintained in the formulation were the different types of super-disintegrant and their concentration (in mg) in the formulation.

Firstly inclusion complex of Carvedilol and β- cyclodextrin in the ratio of 1:4 was prepared. The inclusion complex was prepared by kneading method. 1gm of Carvedilol was placed in the mortar and 4gm of β-cyclodextrin mixed to it, and then organic solvent methanol was added. Slowly grind the mixture of Carvedilol, β-cyclodextrin and organic solvent methanol still paste is not prepared. Once paste was prepared paste was dried at 50^0C. Completely dried complex used for the preparation of fast dissolving tablet. Tablets were prepared from blends by direct compression method. All the ingredients including drug were passed through mesh no. 60 excepting lubricants. Lubricants were passed through mesh no.80. Lubricants were added at the time of compression. Blend is mixed uniformly by manually for 30 minutes. Tablets of convex faced weighing 130mg each with 3.3mm thickness and 7mm in diameter.

Table.1.Formulation of Fast dissolving tablet of Carvedilol

INGREDIENTS	C1	C2	C3	C4	C5	C6	C7	C8	C9
Drug: β-CD complex (mg)	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5
Ac-Di-Sol (mg)	4	6	8	-	-	-	-	-	-
Cross povidone(mg)	-	-	-	4	6	8	-	-	-
Sodium starch glycolate (mg)	-	-	-	-	-	-	4	6	8
Lactose (mg)	18	18	18	18	18	18	18	18	18
Sorbitol (mg)	16	16	16	16	16	16	16	16	16
Xylitol (mg)	10	10	10	10	10	10	10	10	10
Avicel pH102 (mg)	27	25	21	27	25	21	27	25	21
Talk (mg)	2	2	2	2	2	2	2	2	2
Mg stearate (mg)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Flavour (Strawberry)	3	3	3	3	3	3	3	3	3
Aerosil	5	5	5	5	5	5	5	5	5
Total	150	150	150	150	150	150	150	150	150

***In vitro* dissolution studies:** Dissolution rate was studied by using USP type-II apparatus (USP XXIII Dissolution Test Apparatus at 50 rpm) using 900ml of phosphate buffer pH (6.8) as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°C. The absorbance of filtered solution was measured by UV spectrophotometric method at 223nm and concentration of the drug was determined from standard calibration curve. As the method of preparation of tablets changed to sublimation, the dissolution of the drug from the tablets prepared by camphor sublimation method was quicker than those prepared by other method. This may be due to their lowest hardness and the porous structure is responsible for faster water uptake, hence it facilitates wicking action of crosscarmellose sodium in bringing about faster disintegration.

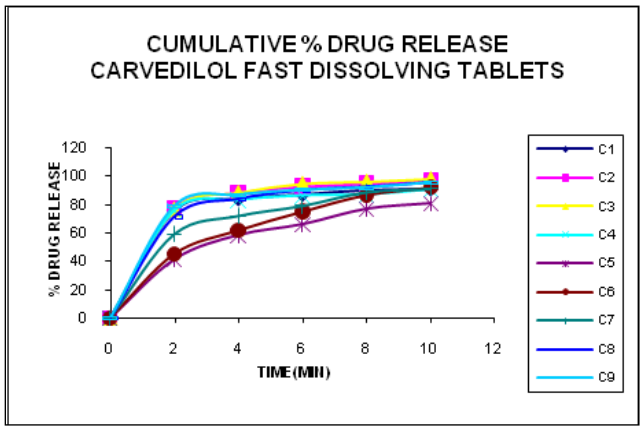

Figure.1. Cumulative % drug release carvedilol fast dissolving tablets(c1-c9)

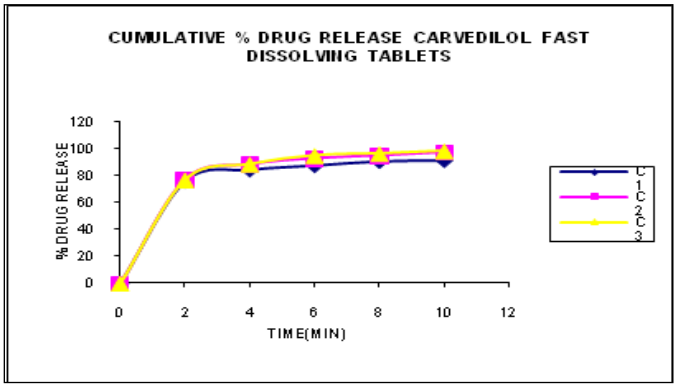

Figure.2.Cumulative % drug release carvedilol fast dissolving tablets(c1-C3)

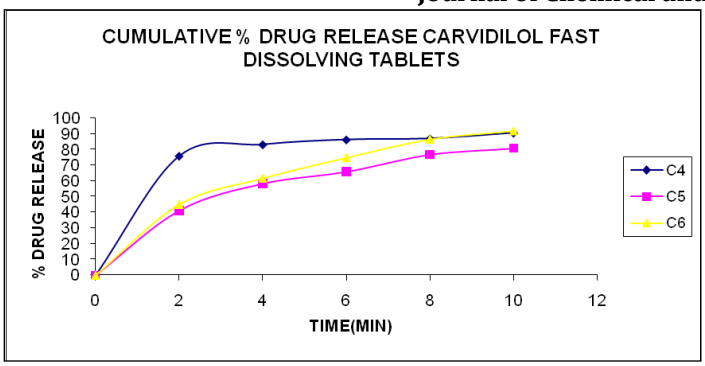

Figure.3.Cumulative % drug release carvedilol fast dissolving tablets (c4-c6)

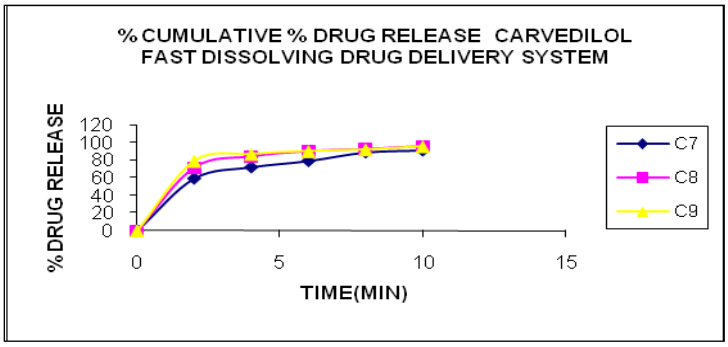

Figure.4.Cumulative % drug release carvedilol fast dissolving tablets(c7-c9)

CONCLUSION

Formulation of Ac-Di-sol superdisintegrant (C3) had maximum Formulation of Ac-Di-sol superdisintegrant (C3) have maximum water absorption ratio, drug release than all other formulation in 10 min. Stability study conducted for a period of 45 days as per I.C.H. Guidelines for an optimized formulation of C3. All these three formulations did not show any significant difference in formulations physical or chemical parameter.From this study it can be concluded that Carvedilol can be successfully complexed with Beta-cyclodextrin to prepare fast dissolving tablets.

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