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Formulation and Evaluation of Fast Dissolving Tablet of a Model Anti-Diabetic Drug By Inclusion Complexation Using Beta Cyclodextrin

Mahalingan K.[1], Ganesh R.S.*[1], Ronak Patel[2], Umashankar M.S[1]

1. Department of Pharmaceutical Technology, Krupanidhi College of Pharmacy, #12/1, Chikkabellandur, Carmelram Post, Bangalore-570035 Karnataka, India

2. Department of Pharmaceutics, Krupanidhi College of Pharmacy,#12/1, Chikkabellandur, Carmelram Post, Bangalore-570035,Karnataka, India

ABSTRACT

In the present investigation an attempt was made to formulate fast dissolving tablets using BCS class II drug Repaglinide, ie low solubility and high permeability to form an inclusion complex to improve the dissolution rate, thus enhancing the bioavailability. Beta-CD inclusion complex was made in varying ratios 1:1, 1:3 and 1:5 of drug and polymer by solvent evaporation method. The complexes were evaluated for phase solubility, drug content and drug release. Phase solubility study revealed AL type indicating linear increase in solubility with increase in the carrier concentrations. The inclusion complex 1:1 ratio prepared by spray dried was studied for drug content uniformity which was ranging from 85-98%, FTIR showed no any compatibility of the drug and beta-CD; DSC and XRD showed distinct loss of drug crystallinity accounting for enhancement in the dissolution rate. SEM revealed spherical shape of the inclusion complex. The drug release study was carried out in 0.1N HCL using USP type paddle dissolution apparatus revealed to be 93% within 5 mins. The FDT was formulated by direct compression method six batches of tablets were prepared with varying ratios of superdisintegrants (F1-F6). The tablets were evaluated for hardness, friability, weight variation, disintegration which was found within the official range, drug content ranging from 89-94%. The formulation F3 containing Crosspovidone was optimized which showed maximum drug release of 98% within 10 mins. Kinetics of drug release from all the tablets followed zero order release with non-Fickian type diffusion.

Key words: Repaglinide, Beta- Cyclodextrin, Spray drying and fast dissolving tablets

*Corresponding Author Email: ganesh.kle@gmail.com

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INTRODUCTION

Drug absorption from the gastrointestinal (GI) tract can be limited by a variety of factor with the most significant contributors being poor aqueous solubility and or poor membrane permeability of drug molecule The Biopharmaceutics Classification System (BCS) is a drug development tool that allows estimation of the contribution of three fundamental factors including dissolution, solubility and intestinal permeability, which govern the rate and extent of drug absorption from solid oral dosage forms[1-3].

Repaglinide is a non –Sulphonyl urea oral hypoglycemic agent used in the management of type -2 diabetes mellitus , Chemically it is {(S) – 2-ethoxy -4-[2-[3-methyl -1-[2 -(1 -piperidinyl) phenyl] butyl] amino]-2-oxoethyl] benzoicacid}. Repaglinide is a BCS class -2 drug with bioavailability following oral administration is low (60%). BCS class -2 compound are low soluble but highly permeable, and exhibits bioavailability that is limited by dissolution rate. It has short biological half life of less than one hour and rapidly eliminated from body. The dissolution rate of BCS class-2 drug substances may be accelerated by improvement of wetting characteristics of the drug[4].

Diabetes mellitus is a chronic disorder of carbohydrate, fat and protein metabolism. A defective or deficient insulin secretary response, which translates in to impaired carbohydrate (glucose) use, is a characteristic feature of diabetes mellitus, as the resultant hyperglycemia. Diabetes is a chronic condition that affects about 3% of the world population approximately 100 million people. If not adequately managed; diabetes can result in a wide range of complications that have clinical, social and economic implications[5,6].

β-cyclodextrin is a white crystalline powder, molecular weight of 1135, it is stable in the solid state if protected from high humidity. It is commonly used as solubilizing agent as well as stabilizing agent[7]. The complex formation is almost always associated with a relatively large negative ΔH (standard free energy change) and ΔS (standard entropy change) that can be either positive or negative. Also, complex formation is largely independent of the chemical properties of the guest (i.e., drug) molecules. The association of binding constants with substrate polarizability suggests that Van der Waals forces are important in complex formation. Hydrophobic interactions are associated with a slightly positive ΔH and a large positive ΔS; therefore, classical hydrophobic interactions are entropy driven, suggesting that they are not involved with cyclodextrin complexation since, as indicated, these are enthalpically driven processes. The main driving force for complex formation could, therefore, be the release of

enthalpy-rich water from the cyclodextrin cavity. The water molecules located inside the cavity cannot satisfy their hydrogen-bonding potentials; therefore, they are of higher enthalpy. The energy of the system is lowered when these enthalpy-rich water molecules are replaced by suitable guest molecules which are less polar than water[8-10].

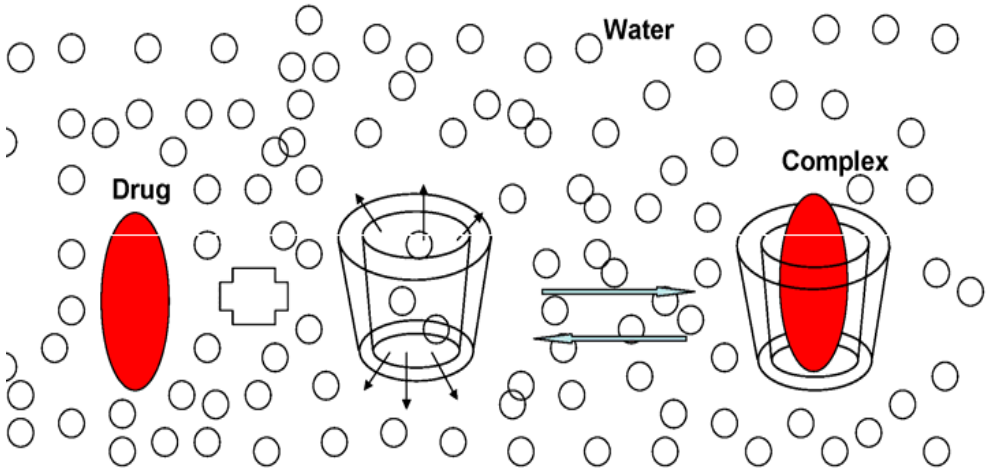

Figure 1.Schematic presentation of the process of complex formation

Nearly 35% of the general population, especially the elderly patients and children suffer from dysphasia or difficulty in swallowing, which results in high incidence of noncompliance and ineffective therapy. Swallowing problems also are very common in young individuals because of their poorly developed muscular and nervous systems[11]. Other groups who may experience problems in swallowing conventional oral dosage forms are the patients with tremors of extremities, mentally ill, developmentally disabled, non co-operative patients and patients with reduced liquid intake or patients suffering from nausea. The swallowing problems are also common in some cases such as patients with motion sickness, sudden episodes of allergic attack or coughing and due to lack of water[12, 13].

To overcome these problems, formulators have considerably dedicated their effort to develop novel drug delivery systems (NDDS) which enhance safety and efficacy of drug molecule and to achieve better patient compliance. One such approach is 'Oral dispersible Tablets', which disintegrate or dissolve in saliva and are swallowed without water as tablet disintegrate in mouth, this could enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx, esophagus. This leads to an increase in the bioavailability by avoiding first pass metabolism[14].

The centre for drug evaluation and research states an orally dissolving tablet to be "A dosage form containing medicinal substances, which disintegrates rapidly usually within a matter of

seconds, when placed upon tongue." This system is recognized with other synonyms like fast dissolving tablets; melt in mouth tablets, porous tablets, rapidly disintegrating tablets, quick dissolving, and rapiments tablets. Despite various nomenclatures the function and concept of all these Drug Delivery System (DDS) is similar[15].

The main objective of the present work is to formulate fast-dissolving tablets of poorly soluble repaglinide by inclusion complex. To improve the solubility characteristics of Repaglinide, due to its low aqueous solubility and poor dissolution can cause formulation problem and limit its therapeutic application by delaying the rate of absorption. Complexation technique can be used to improve the in vitro dissolution properties of poorly water soluble drug[16].

MATERIALS AND METHODS

Materials:

Repaglinide was gift sample from Biocon Bangalore.β-Cyclodextrin from signet pharma mumbai. Crosspovidone from Colorcon Asia Pvt Ltd, Crosscarmellose-sodium Loba chemical Mumbai ,Sodium Starch Glycollate. Were gift sample from Meggle Germany. All other reagents used were of analytical grade.

Method:

Phase solubility Studies: Accurately weighed samples of REP (12 mg) in quantities exceeding its aqueous solubility was shaken at room temperature with aqueous solutions of β cd (0.1N HCL) of pH1.2 in increasing concentrations (2–12 mM), for a period of 144h (6 days), until equilibrium was established. The samples were filtered through a 0.45 µm membrane filter and suitably diluted with 0.1N HCL before analysis. The results were evaluated in terms of complex stability constant. The stability constant of Repaglinide-β cd complex was calculated using Higuchi-Connor's equation.

$$\mathbf{K_{(1:1)} = Slope / S_O (1\text{-}slope)}$$

S_0= intrinsic solubility of Repaglinide in0.1N HCL. "Slope" was calculated from phase solubility diagram.

Drug-Excipient Interaction Studies

Fourier Transform Infrared Spectroscopy (FTIR):

A Fourier transform infrared spectrum (FTIR) was used to identify the formation of complex. Samples were analyzed by potassium bromide pellet method in an IR spectrophotometer (Shimadzu, FTIR 1300) in the region between 4000-400 cm^{-1}.

Differential Scanning Calorimetry:

The thermal behavior of Repaglinide and cyclodextrin inclusion complexes was studied using Differential Scanning Calorimetry in order to confirm the formation of solid complex. When guest molecules are incorporated in the cyclodextrin cavity or in the crystal lattice, their melting, boiling and sublimation points are usually shifted to a different temperature or disappear within the temperature range.

X-Ray diffraction study:

X-Ray diffraction were performed and interaction of the drug with cyclodextrins using a PW 1720 X-ray generator and a PW 1710 diffractometer control (Philips Electronic Instrument). The scanning range (2θ) was from 5° to 90°, and the scan step and scan speed were 0.04° and 0.02°/s, respectively.

Formulation of inclusion complexes

These inclusion complexes were prepared by using different method: Physical mixture method: In this method Repaglinide and β CD in molar ratio (1:1) are taken were weighed and mixed in a mortar for 5 min to obtain a homogenous powder blend, passed through sieve no. 80 and stored in desiccator .

Solvent evaporation method: It was prepared by co-evaporation of drug– β CD of 1:1. 1:3 and 1:5 in methanol–water (1:1 v/v) solutions on a water bath at 50°C. Each solid product was sieved through 80# and same fraction was used for the following tests.

Spray drying: Spray drying technique was used for the preparation of inclusion complexes of Repaglinide: β CD with inlet temperature110 ^{0}C and an outlet 80^{0}C, aspiration speed 80-90 rpm, feed rate 12ml/min. In this method water and ethanol mixture about 1:1 ratio was used for solvation of cyclodextrins and this solution was spray dried using Labultima spray dryer model LU222. After spray-drying, resulting powder was collected by cyclone separation and transferred to glass vials and kept stored in desiccators.

In Vitro dissolution characteristics of Repaglinide-β-Cyclodextrin complexes: Repaglinide is predominantly in a unionized form in acidic medium. Hence 0.1 N HCL of pH1.2 was selected as the dissolution medium. Repaglinide inclusion complexes of the ratios 1:1, 1:3 and 1:5 prepared by solvent evaporation method equivalent to 20mg in each ratio was used for the dissolution studies. Dissolution experiments were carried out in an USP XXIII paddle apparatus in 0.1 N HCL of pH1.2 at 37◦C using 50 rpm. A 5ml amount of dissolution medium was withdrawn at intervals of 5, 10, 15, 20, 30, 45 min. An equal amount of fresh dissolution medium was replaced immediately after withdrawal of the test sample. Test samples were filtered through

a 0.45 µ whattman filter and suitably diluted. The absorbance of diluted samples was estimated for amount of Repaglinide dissolved by measuring in UV/VIS spectrophotometer at 240nm.

Preparation of 1:1 drug-β-CD ratio of inclusion complex by spray drying method: Based on the in vitro dissolution study of the 3 ratios prepared by solvent evaporation method, the least ratio 1:1 which showed least dissolution hence this ration was further subjected for spray drying

Scanning electron microscopy (SEM):

The morphologic properties of the spray-dried powders of 1:1 ratio of Repaglinide and β-Cyclodextrin were characterized by scanning electronic microscopy (JEOL, Model JSM 840).

Strategies for Development of Fast Dissolving Tablets

Drug inclusion complex 1:1 ratio prepared by spray dried method was selected for further development into FDT. Drug-beta CD inclusion complex and MCC were weighed and passed through # 60 mesh Sifted components were mixed homogeneously for 15 min (Blend-I). Mannitol, Superdisintegrant were weighed and passed through # 44 mesh, sifted components were mixed homogeneously for 10 min. (Blend-II). Blend-II was mixed with Blend-I, mixing was continued for 1 hour. Magnesium stearate and talc were weighed and passed through 120#mesh and mixed with blend-1-blend-2 mixture by tumbling for 10 mins. The prepared blend was compressed. It shows in **Table 1.**

Table 1: Formulation of inclusion complexes

S. No	Ingredients	F1 (mg/tab)	F2 (mg/tab)	F3 (mg/tab)	F4 (mg/tab)	F5 (mg/tab)	F6 (mg/tab)
1	Drug-βcd inclusion complex1:1(SD) equivalent to 2mg	9	9	9	9	9	9
2	Crosscarmellose sodium	4	8				
3	Crosspovidone			4	8		
4	Sodium starch glycollate					4	8
5	Mannitol	40	36	40	36	40	36
6	Avicel pH101	90	90	90	90	90	90
7	Magnesium stearate	5	5	5	5	5	5
8	Talc	3	3	3	3	3	3
	TOTAL	151	151	151	151	151	151

In vitro dissolution study

Medium : 900 ml; 0.1 N Hydrochloric acids

Apparatus : USP-II (paddle)

RPM : 50

Temperature : 37°C ± 0.5°C

Time : 30 minutes

Analysis of Release Mechanism

The *in vitro* dissolution data mentioned in Table No.6 was fitted to zero order, first order, Higuchi release model and Korsemeyer Peppas model to analyze the mechanism of drug release from the matrix tablets (**Table 2).**

Table 2: Equations used to compare dissolution profiles.

Method	Parameter/equation
Zero order	% dissolution =kt
First order	% dissolution =100(1- e^{-kt})
Higuchi	%dissolution= $kt^{0.5}$
Korsemeyer-Peppas model	$Mt/M\infty = Kt^n$

[a] m_α is the initial drug amount (100%, when represented as percentage); m_t the amount of drug remaining at a specific time (calculated as percentage of m_α); *k the rate constant; t is the time*

RESULTS AND DISSCUSIONS

Solubility determination:

The solubility of pure Repaglinide at pH 1.2, 6.8 and 7.4 was found to be 3.15, 0.294 and 0.149mg/ml respectively. The study showed that solubility of Repaglinide decreases as pH increases .The maximum solubility was observed at pH1.2. The results are shown in **Table 3.**

Table 3: Solubility studies of Repaglinide in different pH

pH	Solubility of Repaglinide in mg/ml
0.1N HCL(1.2)	3.15
6.8	0.294
7.4	0.149

Phase solubility study:

The entire phase solubility diagram showed the concentration of Repaglinide in pH 1.2 buffer increases as a function of increase in concentration of beta-Cyclodextrin. All the curves obtained in the present studies are classified as AL type according to Higuchi and Connors because of linear increase in the solubility with the value of R^2 closed to unity. β-Cyclodextrin has hydrophobic internal cavity and hydrophilic outside surface due to arrangement of hydroxyl group, this arrangement permits the cyclodextrin to accommodate a drug molecule forming an inclusion complex primarily improving the solubility of the drug molecule. The stability constant, Ks was found to be 1857 M-1 in case of beta cyclodextrin, which are within the range (200- 5000m-1) .This indicate that complex are quite stable . The data are presented in the table based on the phase solubility diagram. B-CD complex of the drug is more effective in solubilizing Repaglinide in aqueous media. (Table 4 and Figure 2)

Table 4: Phase solubility studies of Repaglinide: β- Cyclodextrin complexes.

Concentration of β-Cyclodextrin in mmol/L	concentration of Repaglinide in mmol/L
2	2.6
4	4.9
6	6
8	8.2
10	10.1
12	11.0

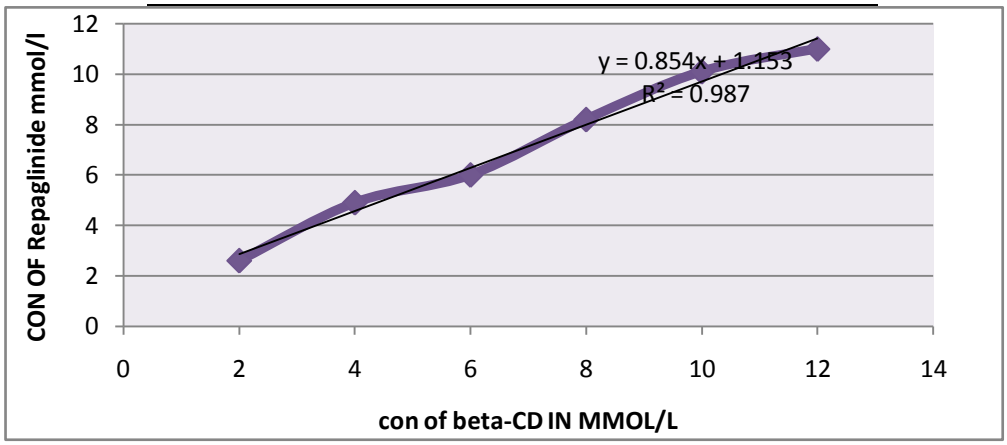

Figure 2: Phase solubility curve

FTIR Specctroscopy:

The FTIR spectral characterization of drug and beta cyclodextrin in the ratio 1:1 prepared by spray dried method showed the functional group of the drug remaining intact. Spectroscopic characterization of Repaglinide with the excipient in the ratio 1:1 showed no any incompatibilities **(Figure 3-5).**

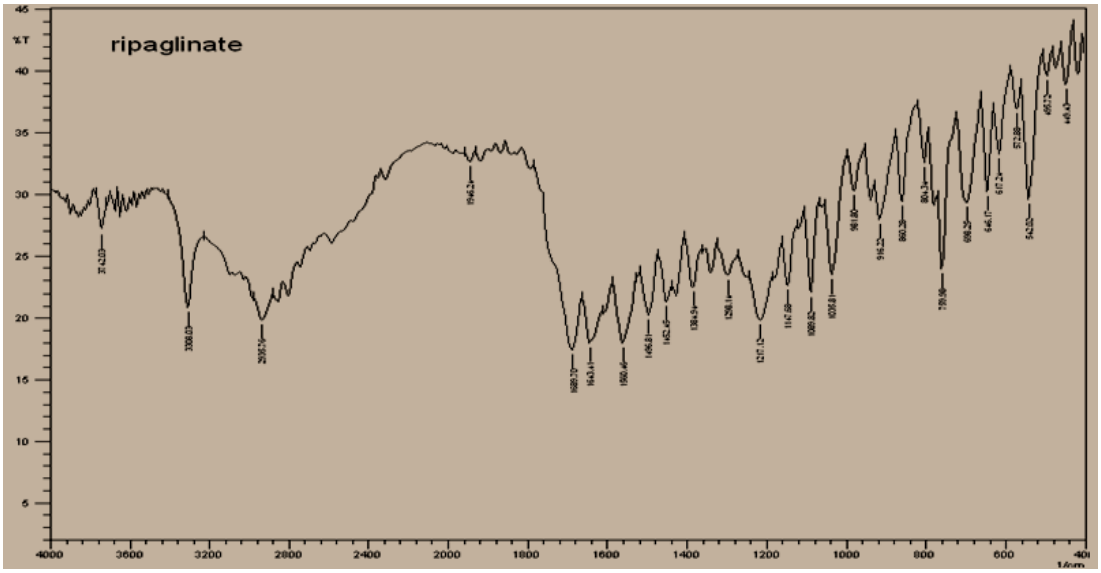

Figure 3: FTIR Spectrum of Repaglinide pure drug

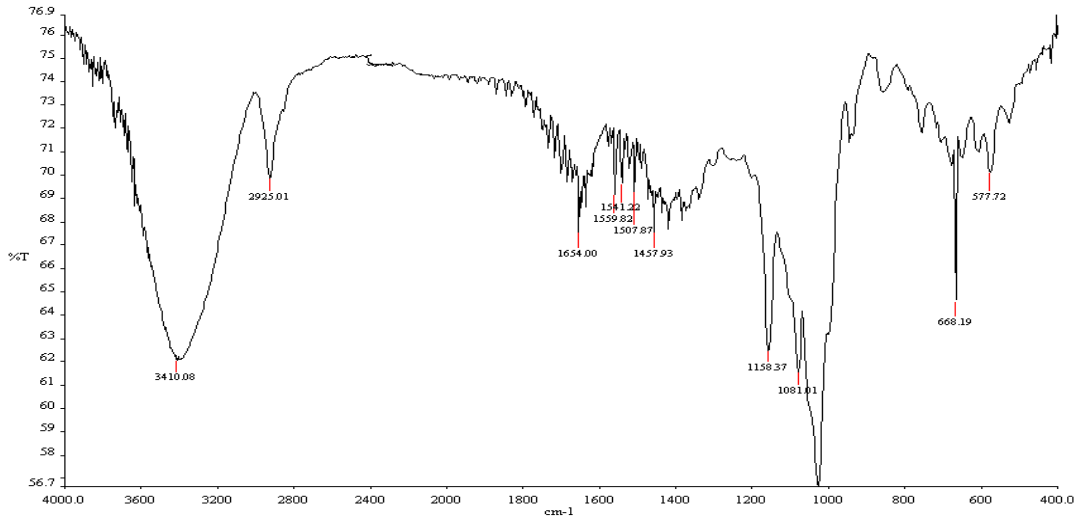

Figure 4: FTIR Spectrum of β-CD

Figure 5: FT-IR spectrum of 1:1 ratio of Repaglinide: β-CD Spray dried

Xray Diffraction Study:

The X-RD pattern of inclusion complex 1:1 prepared by spray drying method .The result are shown in **figure 6**. The X-RD pattern of spray drying complex is totally diffused indicating the formation of complex which is amorphous in nature.

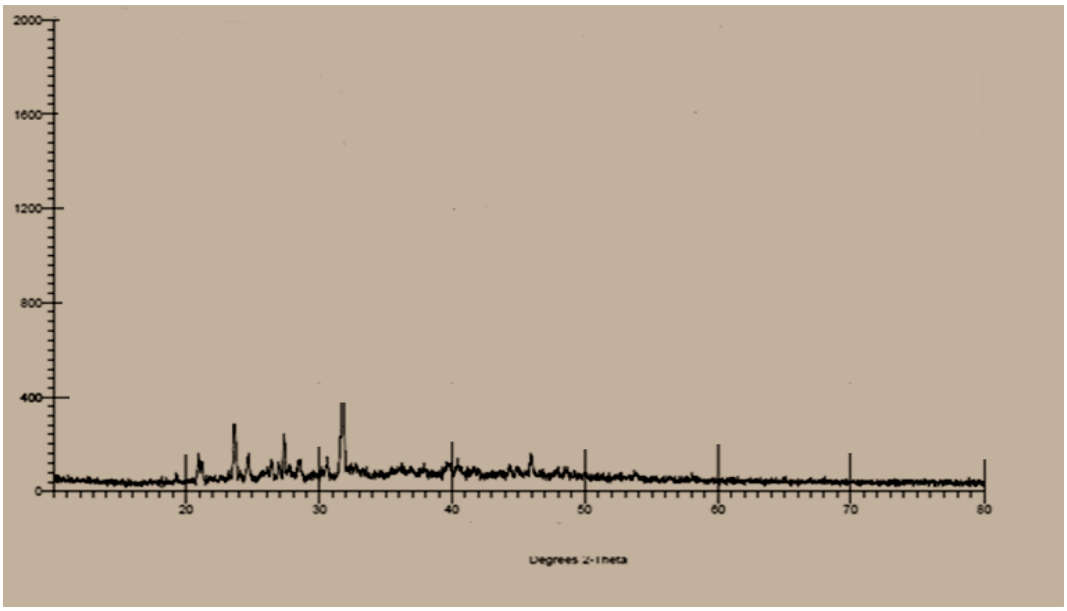

Figure 6: X-ray diffractometer of Spray dried 1:1 ratio of Repaglinide :β-CD

Diffraction scanning Calorimetry:

The thermogram of the complex is presented in figure showed a less intense endothermic peak of Repaglinide at 134.5^{o}C prepared by spray drying method **(Figure 7).**

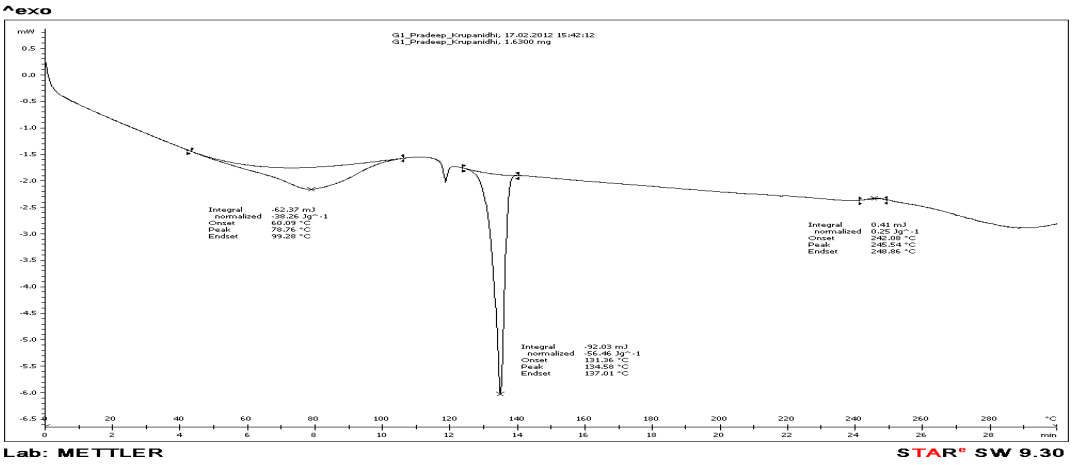

Figure 7: DSC of 1:1 ratio of Spray dried Repaglinide :β-CD

Scanning Electron Microscopy Studies:

SEM data of Repaglinide-β- CD prepared by spray drying showed images of particle with spherical shape (**Figure 8).**

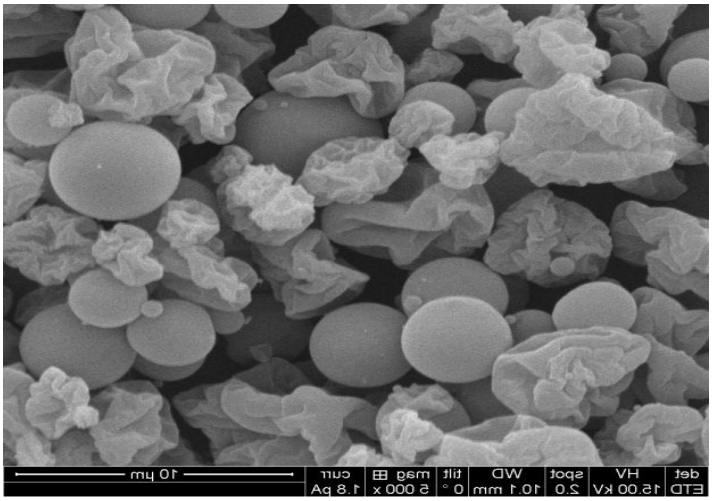

Figure 8: SEM of 1:1 ratio of Repaglinide :β-cd

In vitro dissolution study:

Dissolution profile of physical mixture and inclusion complex by solvent evaporation method were determined. The cumulative percentage of drug release was shown in the **Table 5**. In case of physical mixture (1:1) the percentage of drug released was found to be 76% in 45 minutes. The inclusion complex prepared by solvent evaporation method using beta- Cyclodextrin as carrier in the ratio of 1:1 showed 81% drug release respectively at 45 minutes, where as the formulation ratio of 1:3 showed 89% of drug release within 30 minutes and 1:5 ratio showed 90% of drug release at 45 minutes .The increased dissolution rate may be due to the higher solubility of beta–Cyclodextrin in dissolution medium and better wettability of Repaglinide in the formulations.

Further the inclusion complex in the 1:1 ratio was prepared by spray dried method which showed improved solubility than pure drug, physical mixture, and inclusion complex prepared by solvent evaporation methods by the three ratios. The inclusion complex of the Drug-β-Cyclodextrin (1:1) ratio by spray dried method showed maximum percentage of drug release which was finally considered for the formulation of Fast dissolving tablet shown in table 5 and **Figure 9-11** for immediate drug release of the Repaglinide.

Table 5: In Vitro Dissolution profile

Time(min)	% Drug Release in 900ml 0.1N Hydrochloric Acid 50 RPM,					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	47	49	52	29	19	23
10	90	89	98	63	41	45
15	113	111	115	103	68	81

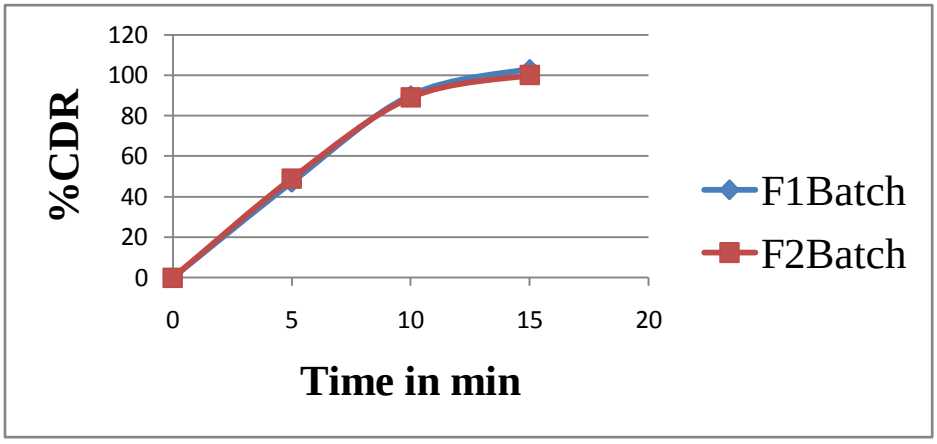

Figure 9: Dissolution studies of the FDT of Spray dried 1:1 ratio of drug β-CD of F1-F2 batch

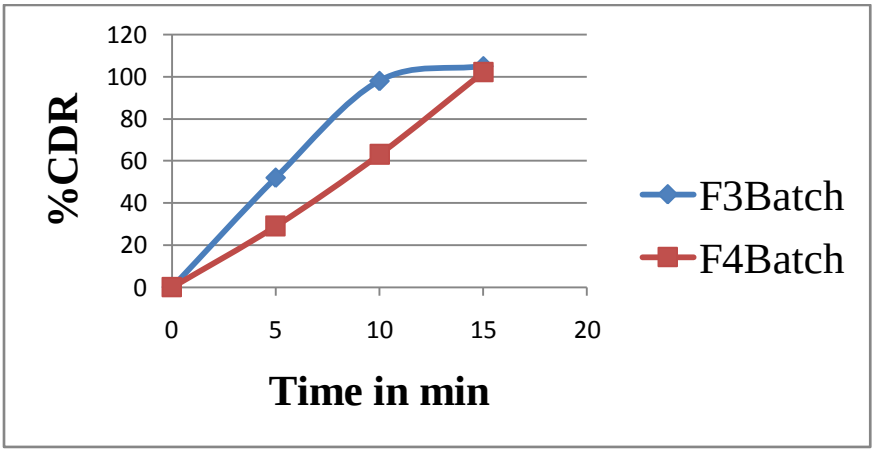

Figure 10: Dissolution studies of the FDT of Spray dried 1:1 ratio of drug β-CD of F4-F5 batch

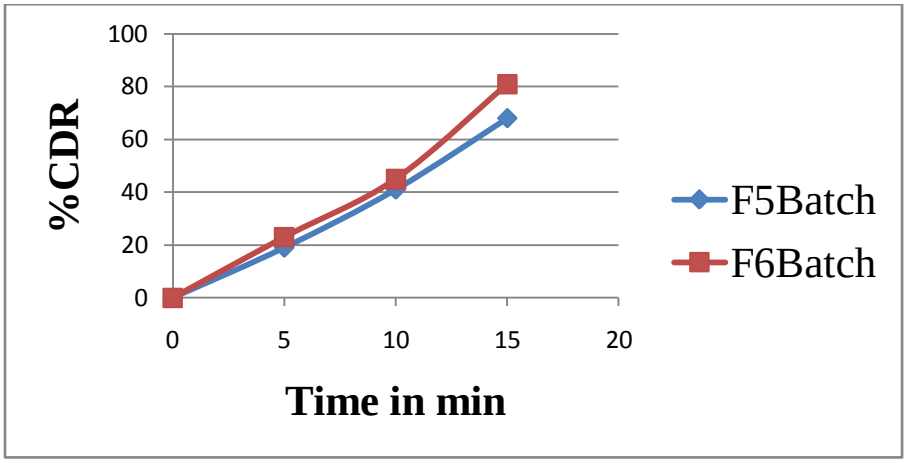

Figure 11: Dissolution studies of the FDT of Spray dried 1:1 ratio of drug β-CD of F5-F6 batch

Formulation and evaluation of Fast dissolving tablets of drug-beta Cyclodextrin complex (1:1) prepared by spray dried method.

Direct compression method was used to prepare the fast dissolving tablets of Drug-β-CD (1:1) inclusion complex, Crosscarmellose sodium, Crosspovidone, Sodium starch glycollate in three different ratios were used as disintegrants, mannitol as sweetening agent, magnesium stearate and talc were used as lubricants.

Pre-compression parameters:

The pre-compression parameters of the formulation F1 to F6 prepared by the direct compression method showed bulk density 0.5-0.55 g/cm^3 and angle of repose 28.0-35.3^{o}C **(Table 6).**

Table 6: Pre-compression parameters of Direct Compression method

Formulation code	Bulk density (g/cc) ± SD,	Tapped density (g/cc) ± SD,	Angle of repose ± SD	Carr's index (%) ± SD,	Hausner's Ratio ± SD
F1	0.51 ± 0.007	0.65 ± 0.01	35.36 ± 0.20	21.53 ± 0.39	1.27 ± 0.04
F2	0.52 ± 0.007	0.63 ± 0.01	33.46 ± 2.08	17.46 ± 1.20	1.21 ± 0.03
F3	0.55 ± 0.007	0.65 ± 0.01	30.20 ± 0.88	15.38 ± 2.51	1.18 ± 0.03
F4	0.53 ± 0.007	0.64 ± 0.02	30.1 ± 1.70	17.18 ± 1.20	1.20 ± 0.03
F5	0.50 ± 0.007	0.67 ± 0.01	28.43 ± 1.48	25.37 ± 1.58	1.34 ± 0.03
F6	0.54 ± 0.007	0.66 ± 0.02	28.04 ± 1.34	18.18 ± 2.20	1.22 ± 0.03

Post compression parameters:

The prepared tablets of F1 to F6 were subjected to hardness test as per IP. The hardness of all formulations was found to be in the range 3-4.5 ±1 kg/cm^2. The percentage friability of all the formulations was found to be not more than 0.68% which was found within 1% limit. The result of friability test indicated that the tablets were mechanically stable. The weight variation of the tablets was carried out as per IP by taking the average weight of 10 tablets. The weight of all

tablets was in between of 141-151.0mg. As the weight of the tablets was 151.0mg, the acceptable weight variation range is 147-152mg. Hence all the tablet formulations were within the Pharmacopeia limits. The % drug content of all the tablets was found to be between 89.0-93.1% of Repaglinide which is within the acceptable limits. Wetting time of all the formulations ranges from 21-55 sec but for F3 it was found to be least of only 21±1.1secs. Water absorption ratio of all the formulations ranges from 67-85 but for F3 it was of the highest of 85 ±1.13 (**Table 7).**

Table 7: Post-compressional parameters for Direct Compression method

Formulation code	Hardness * (Kg/cm^2)±SD	Friability (%)	Thickness* (mm)± SD	Weight variation* (mg)± SD	In-vitro Disintegrating time (sec) *	Wetting time* (sec) ± SD	Water absorption ratio*± S.D	Drug Content* (%)± SD
F1	3.9 ± 0.306	0.52	3.3 ± 0.05	147 ± 1.78	65	42 ± 1.11	81 ± 1.54	93.51 ± 0.72
F2	4.0 ± 0.200	0.66	3.1 ± 0.12	152 ± 1.32	70	36 ± 1.0	83 ± 1.86	90.48 ± 0.91
F3	4.2 ± 0.115	0.49	3.2 ± 0.06	150 ± 0.56	55	21 ± 1.15	85 ± 1.35	93.41 ± 1.07
F4	4.1 ± 0.231	0.48	3.2 ± 0.08	147 ± 1.97	60	33 ± 0.57	73 ± 1.20	92.06 ± 0.39
F5	3.92 ± 0.306	0.57	3.3 ± 0.05	146 ± 0.65	65	32 ± 1.15	70 ± 1.57	89.38 ± 1.23
F6	3.89 ± 0.315	0.67	3.2 ± 0.08	151 ± 1.93	79	55± 0.57	67 ± 1.21	91.12 ± 0.73

***Average of three determinations**

Disintegration time:

Disintegration time of all formulations was carried out it was found within the range of 55-79 secs but for F3 it was found to be the least of 55 seconds **(Figure 12).**

In- vitro dissolution study of directly compressible fast dissolving tablets: Dissolution study of each of the complex was carried out to observe the release pattern of the drug from the complex. The dissolution studies were carried out in 0.1 N HCL, to simulate the gastric pH condition. The result was presented in the Table 5. From the overall data of the in vitro dissolution studies among all formulations, F1 to F6, formulation F3 batch showed the maximum percentage of drug release i.e. 98% within10 minutes. From the above studies it was observed that as the concentration of superdisintegrants increased the drug release also increased in case of Crosspovidone and decreased in case of crosscarmellose sodium and Sodium Starch Glycollate.

Drug release kinetic studies from different formulation:

In vitro drug release data for all formulation F1to F6 were subjected to release kinetic studies according to zero order, first order equation and korsemeyer–Peppas model to ascertain the mechanism of drug release. The R^2 and n values were given in Table 8. Among the zero order and first order equation the value of regression correlation coefficient R2 were found to be higher in zero order equation. Hence the drug release from all the formulations followed zero

Initial

20 Second

40 second

45 second

55 second

Figure 12: In-vitro Disintegrating time of tablets of F3 batch prepared by direct compression method

Table 8: Kinetic profile of dissolution data of formulation F1-F6 Batch

R2 Values					
Formulation	**Zero order**	**First order**	**Korsemeyer-Peppas**	**Higuichi**	**n value**
F1	0.9993	0.9371	1.0000	0.9569	0.937
F2	0.9966	0.9518	1.0000	0.9692	0.861
F3	0.9988	0.8849	1.0000	0.9608	0.9143
F4	0.9979	0.9688	1.0000	0.9233	1.1193
F5	0.9937	0.986	1.0000	0.925	1.109
F6	0.9948	0.9850	1.0000	0.9516	0.9683

order release kinetics. In case of korsemeyer-peppas model, the result indicated that release exponent 'n' values are more than 0.5 which indicates non-fickian type of diffusion mechanism of drug release. So, overall data showed that all the formulations followed zero order of drug release with non-fickian diffusion mechanism.

CONCLUSION

The formulations were prepared with beta Cyclodextrin using 3 different methods. All the formulated complexes had shown drug content above 95%, substantial increase in the aqueous solubility of the water-insoluble drug. Phase solubility studies of Repaglinide with β CD illustrate the solubility enhancement. The stability constant K (1:1) of Repaglinide- β CD complex was found to be 1857.8mol-1. The in vitro dissolution studies of Repaglinide- β CD complexes prepared by Physical mixture, Solvent evaporation, and Spray drying methods showed drug release of 101 % respectively. At the end of 10 min the complexes prepared with cyclodextrin by Spray drying showed better release of 102 % compared to pure Repaglinide release of 50%. Hence the Repaglinide-β CD formulation prepared by Spray drying was the effective formulation compared to other polymers prepared by various methods. Hence Repaglinide B- cyclodextrin 1:1 binary system along with the use of super disintegrants could be considered for formulation of fast dissolving tablets Repaglinide. The formulation F3 showed the maximum percentage of drug release 98% at the end of 10 minutes. The characterization of fast dissolving tablet of Repaglinide formulation F3 containing crosspovidone as super disintegrant is considered as the most acceptable formulation. The release kinetics of all formulations was fitted to different kinetic model; from the above studies it was observed that all the formulations followed zero order kinetics with non-fickian type of diffusion.

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