Research Article

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Solubility enhancement and formulation of rapid disintegrating tablet of Febuxostat Cyclodextrin complex.

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ABSTRACT

Febuxostat is a non-purine, xanthine oxidase inhibitor. It is a BCS class II drug. It exhibits poor bioavailability of about 49% which is attributed to its poor solubility. The present work was aimed at overcoming these two limitations. Drug-ß-cyclodextrin and Hydroxy propyl ß-cyclodextrin complex were prepared and characterized by FTIR, DSC and PXRD studies. Saturation solubility study was carried out to evaluate the increase in the solubility of febuxostat. In vitro studies showed that the solubility and dissolution rate of febuxostat were significantly improved by complexation with ß-cyclodextrin and Hydroxy propyl ß-cyclodextrin with respect to drug alone. The inclusion complexes with ß-CD prepared by spray drying method showed highest solubility (305.09%) and fast dissolution profile while inclusion complexes with HP-ß-CD prepared by co-evaporation method showed highest solubility (330.24%) and it was incorporated into rapid disintegrating tablet. The tablets were prepared by using three different superdisintegrants, crosspovidone, sodium starch glycolate and croscarmellose sodium by direct compression. Tablets were evaluated for the hardness, friability, assay, thickness, disintegration time and average weight. Tablets shows enhance dissolution rate as compared to pure febuxostat.

Key words: Febuxostat, ßCD, HPßCD, superdisintegrants, Cogrinding complex, coevaporation complex.

1.INTRODUCTION:

Poorly water soluble drugs present significant challenges during dosage form designing due to their inadequate solubilization in digestive fluids.[1,2]

Cyclodextrin complexation process has been emerged as effective tool to increase solubility of poorly soluble drugs.[3,4]

Febuxostat[2-[3-cyano-4-(2-methylpropoxy)-phenyl)-4-methylthiazole -5-carboxylic acid, is a BCS class II drug, solubility and rate of dissolution are the rate limiting step in its absorption. Febuxostat (FBX) is a non-purine, xanthine oxidase inhibitor.[5]

Thus aim of the present work is to improve solubility of drug through complexation cyclodextrin and to formulate the rapid disintegrating tablet of the prepared complexes by direct comparison method using various superdisintegrants.

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2. MATERIALS AND METHODS:

2.1. Material

Febuxostat (FBX) was obtained as gift sample form Emcure Pharmaceuticals, Pune. The complexing agent betacyclodextrin (ß-CD) & hydroxyl propyl betacyclodextrin (HP-ß-CD) were purchased from Gangwal chemicals, mumbai. All other chemicals and solvent used were of pharmaceutical and analytical grade.

2.2. Phase solubility studies[6]

Phase solubility studies were carried out at room temperature, in triplicate according to method reported by Higuchi and Connors. Excess amount of FBX was added to double distilled water containing various concentration of ß-CD & HP-ß-CD (0-0.005M) in a series of stoppered conical flasks and shaken for 48 hr on a rotary flask shaker. The suspensions were filtered through whatman filter paper and assayed for FBX using UV spectrophotometer (Varian Cary 100, Australia) at 314 nm against blank prepared using same concentration of ß-CD and HP-ß-CD in double distilled water.

2.3. Preparation of the physical mixture

Physical mixtures(PM), FBX:ß-CD (1:1) and FBX:HP-ß-CD (1:1), were prepared by simple blending in a glass mortar.

2.4. Preparation of solid inclusion complexes[7,8,9]

Inclusion complexes of FBX:ß-CD (1:1) and FBX:HP-ß-CD (1:1) were

prepared by, A] Kneading method (Kn), B] Co-grounding (CG), C] Coevaporation method (CE), D] Melting method (MELT), E] Freeze–Drying Method (FD), F] Spray drying method (SD).

2.5 Evaluation of Solid Complexes

2.5.1. Determination of drug content[10]

Drug: cyclodextrin complex equivalent to 10 mg of drug was stirred with 100ml of methanol. From this the concentration of 10 µg/ml was prepared and the drug content was determined spectrophotometrically at 314 nm using methanol as blank.

2.5.2. Saturation Solubility Studies[11]

Excess amount of drug, PM and inclusion complexes were added to the 250 ml conical flasks containing 25 ml of double distilled water. The sealed flasks were shaken for 24hr at room temperature followed by equilibrium for three days. Then, the aliquots were withdrawn through whatman filter paper. The concentration of FBX was determined by UV spectrophotometer at 314 nm.

2.6. Characterization of the physical mixture and inclusion complexes

2.6.1. UV spectroscopic study

Complex formation between FBX and cyclodextrins were studied by UV spectroscopic method. 10mg FBX were weighed accurately and dissolved in 100ml methanol. Diluted suitably and spectra of drug recorded at 314 nm. Same method was used only FBX –cyclodextrins complex.

2.6.2. Fourier Transform Infrared spectrophotometry [FT-IR]

FT-IR has been employed as a useful tool to identify the drug excipient interaction. Samples were analyzed by potassium bromide pellet method in an IR spectrophotometer (Varian, Australia) in the region between 4000 to 400 cm-1.

2.6.3. Powder X-ray Diffractometry [PXRD]

X-Ray Diffraction pattern, the sample was placed into aluminum holder and the instrument was operated between initial and final 2? angle of 5-50^0 respectively.

2.6.4. Differential Scanning Calorimetry [DSC]

Differential scanning Colorimetery was performed on a METTLER DSC 30. The samples analyzed by heating at scanning rate of 20^{0}C/ minute over a temperature range 25 to 300^0 C.

2.7. In-vitro dissolution studies[12]

Drug release studies were performed in triplicate at 37 ± 0.5^{0}C employing USP apparatus II at 100 rpm. Dissolution study was carried out in two dissolution media (Phosphate buffer of pH 6.8 and double distilled water). Dissolution studies were performed on pure drug (40 mg) and the complexes containing an equivalent amount of the drug. Aliquots of the periodically withdrawn samples (5 mL) were analyzed spectrophotometrically at 314 nm, and were replaced with an equal volume of plain dissolution medium.

2.8. Formulation of tablets[13]

Co-grinding complex of ß-CD and co-evaporation complex of HP-ß-CD were selected for the formulation of tablets. Tablets were prepared by direct compression method and the various formulae used in the study are shown in Table 1. The drug, diluents, superdisintegrant were passed through sieve ? 40. All the above ingredients were properly mixed. Magnesium stearate was passed through sieve ? 80. The powder blend was compressed into tablets on 8-station Rotary Tablet Machine Minipress-II (Rimek Ltd.).

2.9. Evaluation of Super Disintegrating Tablets:

2.9.1. Evaluation of powder blend

The powder blend was evaluated for flow properties. Different tests that were carried out are bulk density (s_b), tapped density (s_t), compressibility index, and Hausner ratio.

Table 1. Formulae used in the preparation of tablets.

Ingredients (mg/tab)	F1 (6%)	F2 (8%)	F3 (10%)	F4 (6%)	F5 (8%)	F6 (10%)	F7 (4%)	F8 (6%)	F9 (8%)
Drug:ß-CD / Drug:HP-ß-CD complex	80	80	80	80	80	80	80	80	80
MCC PH102	50	50	50	50	50	50	50	50	50
Mannitol	48	44	40	48	44	40	52	48	44
CRP	12	16	20	-	-	-	-	-	-
SSG	-	-	-	12	16	20	-	-	-
CCS	-	-	-	-	-	-	8	12	16
Sod. Saccharin	5	5	5	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5	5	5	5
Total weight	200	200	200	200	200	200	200	200	200

CRP: *Crosspovidone,* ***CCS:*** *Croscarmellose sodium,* ***SSG:*** *Sodium starch glycolate.*

2.9.2. Evaluation of Tablet

Hardness of the tablets was evaluated using a Monsanto hardness tester. The friability of tablets for each batch was determined using automated USP friabilator Roche friabilator. The tablets were subjected to tests like uniformity of drug content, and weight variation tests single dose preparation as per US Pharmacopeia (USP).

2.9.3. Disintegration Time, Wetting Time and Water Absorption Ratio Studies

For determination of disintegration time (D.T.), one tablet was placed in beaker containing 10ml phosphate buffer of pH 6.8 and the time required for complete dissolution (with mild shaking) was measured. On the other hand, the wetting time was measured as follows: A sample of the final tablet was placed in petri dish (10 cm in diameter) containing 10 ml water at room temperature. The wetting time is that necessary for the complete wetting of the tablet. The wetted tablet was then weighed. Water absorption ratio, R, was determined according to the following equation:

R = 100 x Wa - Wb / Wb ……(1)

Where, Wb = weight of tablet before water absorption
Wa = weight of tablet after water absorption, respectively.

2.9.4. *In vitro* Dissolution

In vitro dissolution studies of rapid disintegrating tablets were performed by using USP type II apparatus at 100 rpm, using dissolution media (0.1 N HCl) maintained at 37±0.5 ^{0}C. Aliquot of dissolution medium was withdrawn at a specific time intervals and it was filtered. Absorption of solution was checked by UV spectroscopy, and drug content was determined.

2.9.5. Assay Method

Twenty tablets were weighed accurately and powdered. Tablet powder equivalent to 10 mg of drug was stirred with 100ml of methanol for 60 minutes, then the solution was filtered and treated as stock solution (100 µg/ml drug). From this further dilutions were done for each formulation. Absorbances were measured and the concentration of drug in the tablet was determined spectrophotometrically at 314 nm using methanol as blank.

2.9.6. Stability Testing

Temperature dependent stability studies were carried out on the optimized batches such as CRP 6%, SSG 8% and CCS 4% . They were packed in Alu–Alu pouches and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies in stability chambers (Thermolab).

(i) 30 + 2^o C and RH 65 % + 5% (ii) 40 + 2^o C and RH 75 % + 5%
The tablets were withdrawn after a period of 7, 14 days, 1, 2 and 3 month and analyzed for visual defects, hardness, disintegration time and percentage assay.

2.9.7. Infra Red Spectroscopy Study of Tablet:

IR studies were carried out using KBr Discs to check drug-excipient compatibility. The reference standard was compared with that of the formulation.

3. DATAANALYSIS:

3.1. Phase-solubility studies

The values of apparent stability constant, Ks, between each drug–carrier combination were computed from the phase-solubility profiles, as described below:

$$Ks = \frac{Slope}{Intercept(1-Slope)} \quad \ldots\ldots\ldots\ldots(2)$$

The values of Gibbs free energy of transfer, ΔGo_{tr}, of Febuxostat from aqueous solution of the carriers were calculated according to the following relationship[14]:

$$\Delta Go_{tr} = -2.303RT.\log\frac{S_o}{S_s} \quad \ldots\ldots\ldots\ldots(3)$$

Where, S_o and S_s are the molar solubilities of febuxostat in 1% w/v aqueous solution of the carrier, respectively.

4. RESULTSAND DISCUSSION:

4.1. Phase Solubility Analysis

Phase solubility diagrams for FBX with ß-CD and HP-ß-CD in distilled water are shown in fig.1 and fig.2. The solubility of FBX increased in linear fashion as a function of the concentration of ß-CD and HP-ß-CD, showing A_L –type phase solubility diagram with slopes of less than unity. According to Higuchi and Connors, these A_L type solubility curves indicate the first order dependency of the interaction on the concentration of CD and the formation of soluble FBX-ß-CD and FBX-HP-ß-CD complexes with stoichiometric ratio of 1:1. The values of the stability constants for ß-CD was 446.33 , while $K_{1:1}$ value of HP-ß-CD was 1449.1

The negative nature of the Gibbs free energy changes (? Gtr°) for FBX-ß-CD (-5.9356, -6.3290, -6.4500, -6.3618, -6.7908 & -6.9655) and for FBX-HP-ß-CD (-5.9356, -6.1792, -6.3490 ,-6.3763, -6.7315 and -6.8711)for 0,0.001, 0.002, 0.003, 0.004 & 0.005 moles/ml of water respectively) are indicative of the spontaneity of the process. The endothermic heats of solution further explain the increase in solubility with temperature.

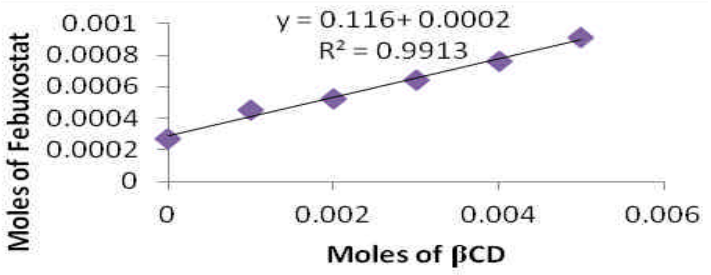

Fig.1. Phase solubility analysis plot for inclusion complexes (Drug:ß-CD)

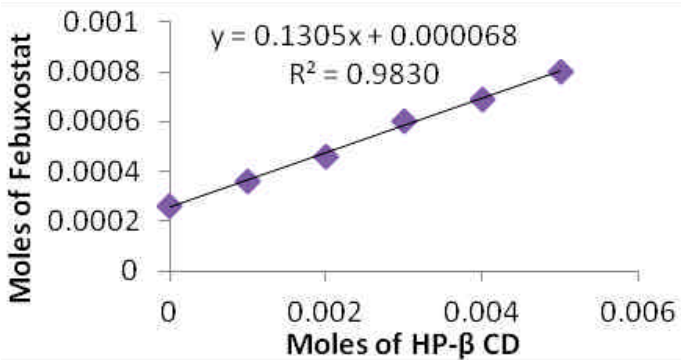

Fig.2. Phase solubility analysis plot for inclusion complexes (Drug:HP-ß-CD)

4.2. Evaluation Complexes:

4.2.1. Drug Content in drug:ß-CD(1:1) and drug:HP-ß-CD(1:1) complex

Percentage drugs content of the complexes are shown in Table 3 was found within the range of 82 to 96%. The maximum percent drug content was found to be 97.02 % and 92.4% in the drug:ßCD(1:1) and drug:HPßCD(1:1) in spray-dried complex.

4.2.2. Saturation solubility study:

The saturation solubility data for drug and complexes are presented in Table 3. The solubility showed a steep increase from 11.97 µg/ml to 36.52 µg/ml for ß-CD complexes while 39.12 µg/ml for HP-ß-CD complexes .The spray- dried complex of ß-CD and freeze-dried complex of HP-ß-CD shows maximum saturation solubility (36.52 µg/ml, 39.51µg/ml).

Table 2. Percentage drug content and saturation solubility of drug:ßCD(1:1) and drug:HPßCD(1:1) complex

Complexes	% increase in Solubility	
	ß-CD	HP-ß-CD
Drug	……..	……..
Physical mixture	126.98%	136.17%
Kneading	213.86%	268.58%
Co-grounding	233.24%	268.33%
Co-evaporation	208.68%	330.24%
Melt	178.52%	210.94%
Freez Drying	280.11%	330.11%
Spray Drying	305.09%	326.81%

4.2.3. FTIR

Fig.4 illustrates the FT-IR spectra of the samples under study. The chemical interaction between the drug and the cyclodextrin often leads to identifiable changes in the infrared profile of dispersion. Drug spectrum shows prominent peaks at 2928 cm^{-1} for CH, 2231cm^{-1} for C≡N, 1714 cm^{-1} for C=O, 1629 cm^{-1} for C=N and 1516 cm^{-1} for C=C. Physical mixture of drug with ß-CD (1:1) and drug: HP-ß-CD complexes shows the prominent peaks of drug, but there was reduction in peak intensity of drug peak which was obscured by cyclodextrin peak indicating formation of complexes.

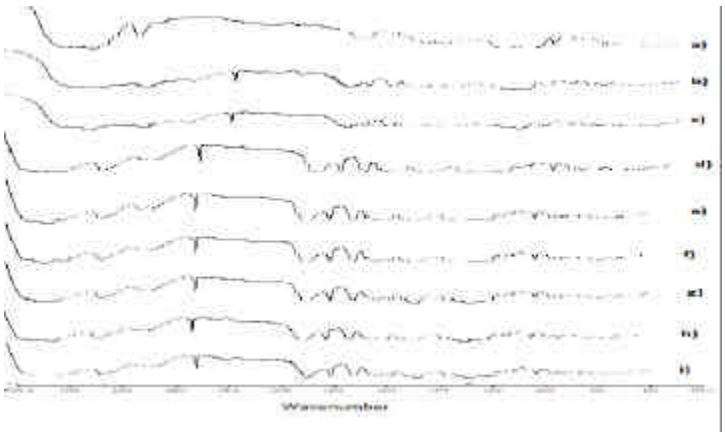

Fig.3. IR spectral analysis of a)Febuxostat b) BCD c)physical mixture d) kneading method e)coevaporation method f)co-grounding, g) spray Drying, h) melting method i)freeze Drying .

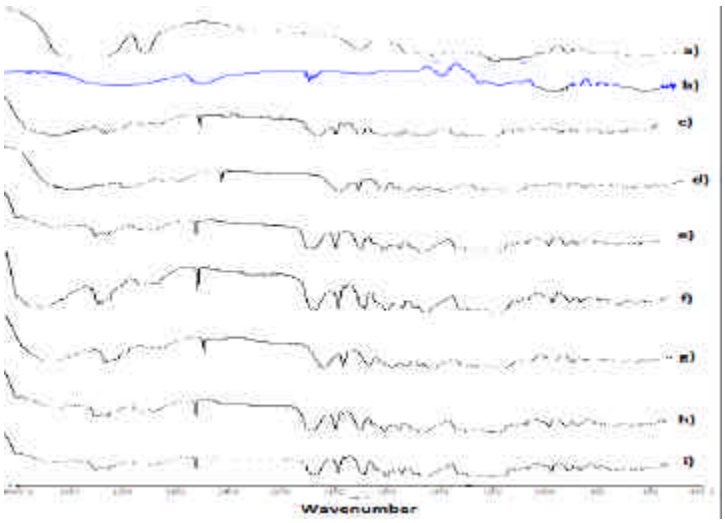

Fig.4. IR spectral analysis of a)Febuxostat b) HPBCD c)physical mixture d) kneading method e)coevaporation method f)co-grounding, g) spray Drying, h) melting method i)freeze Drying .

4.2.4. X-ray Diffractometry [XRD]

Powder X-ray diffraction spectroscopy has been used to assess the degree of crystallinity of the given sample. When complexation of drug and ß-CD / HP-ß-CD are formed, the overall number of crystalline structure is reduced and the number of amorphous structures is increased. The final product sample shows less number as well as less intensity of peaks. This shows that overall crystallinity of complexes is decreased and due to more amorphous nature, the solubility is increased. XRD patterns are shown in Fig.5 & 6. FBX showed its highly crystalline nature, as indicated by the numerous distinctive peaks at 2θ values was 25.9, 26.8, and 29.9. The peaks at 2θ values 5-15 was due to the sample holder The XRD of pure febuxostat showed numerous distinctive peaks that indicated a high crystallinity. The diffractograms of complexes were found to be more diffuse compared to drug, there is no characteristic peak i.e formation of amporphous solid state (inclusion complex formation).

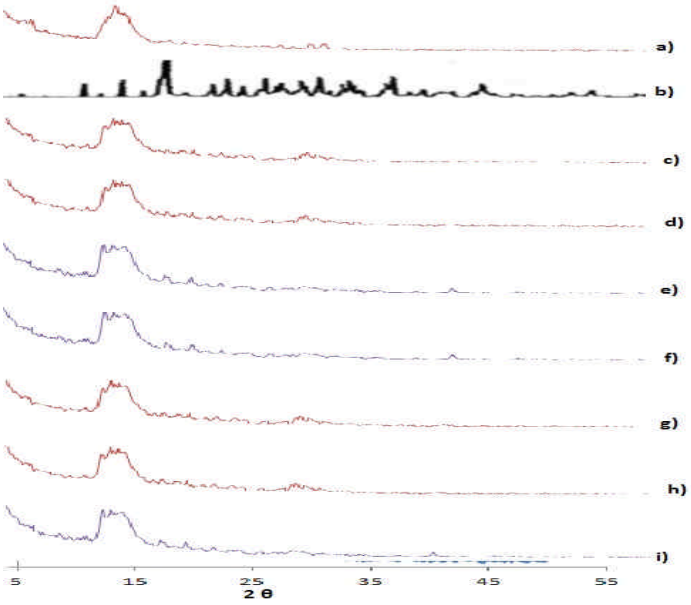

Fig.5. X-Ray Diffraction of a)Febuxostat b) BCD c)physical mixture d) kneading method e)coevaporation method f)co-grounding, g) spray Drying, h) melting method i)freeze Drying .

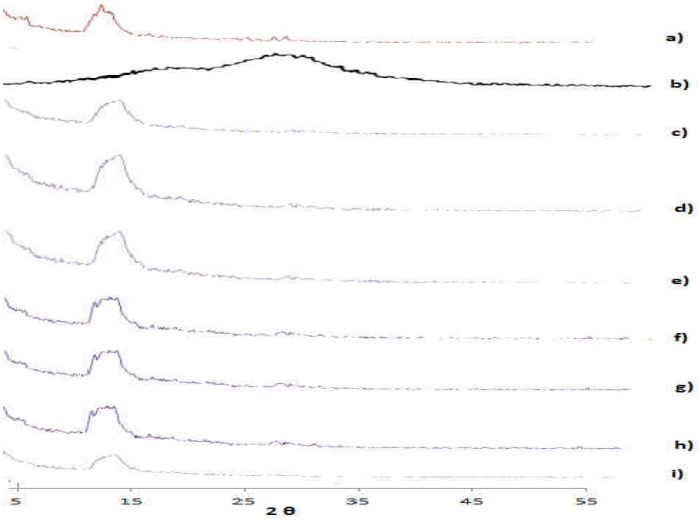

Fig.6. X-Ray Diffraction of a)Febuxostat b) HPBCD c)physical mixture d) kneading method e)coevaporation method f)co-grounding, g) spray Drying, h) melting method i)freeze Drying .

4.2.5. DSC

DSC enables the quantitative detection of all processes in which energy is required or produced (i.e., endothermic or exothermic phase transformations). Thermograms for drug and complexes are shown in Fig.7 & 8. DSC studies showed that endothermic peaks for pure febuxostat, ß-CD and HP-ß-CD were obtained at 205°C , 85.11°C and 280°C respectively. Thermogram of drug: ß-CD (1:1) and drug: HP-ß-CD (1:1) complex showed reduction in the intensity of peak of FBX and shift of endothermic peak of ß-CD and HP-ß-CD. These indicate successful complexation with ß-CD and HP-ß-CD. Thus, DSC studies confirm the inclusion complexation of drug with ß-CD and HP-ß-CD.

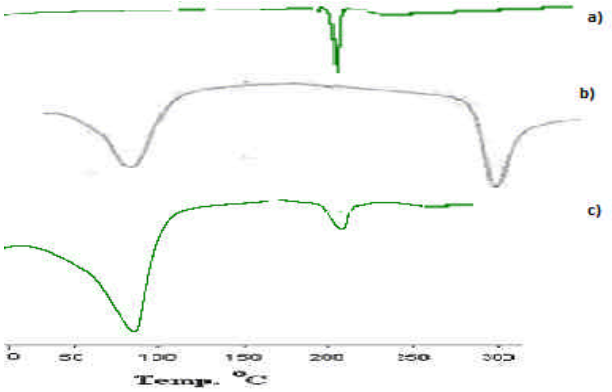

Fig.7: DSC study of a) Pure Febuxostat, b) pure BCD, c) cogrounding complex.

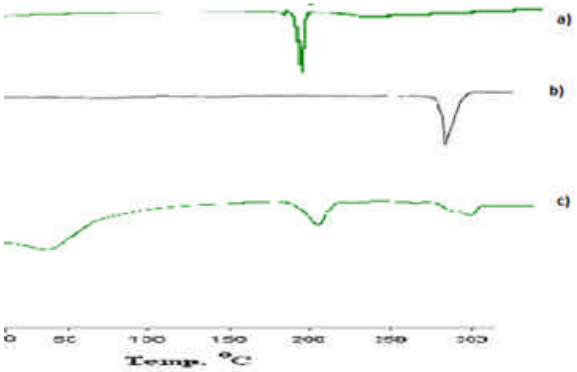

Fig. 8: DSC study of a) Pure febuxostat, b) pure HPBCD, c) coevaporation complex.

4.3. In vitro release profile of complexes

Dissolution profiles of pure FBX and complexes are presented in Fig.9, Fig.10, Fig.11 and Fig.12. It is evident that the complexation technique has improved the dissolution rate of febuxostat to a great extent. From in vitro release study, Fig.9, Fig.10, Fig.11 and Fig.12, it was found that the complex prepared as 1:1 by co-grinding method of drug:ß-CD and co-evaporation method of drug:HP-ß-CD has shown improve in dissolution behavior as compare to drug and other complexes. This might be due to the inclusion complex formation, which indicates the improved solubility phenomenon.

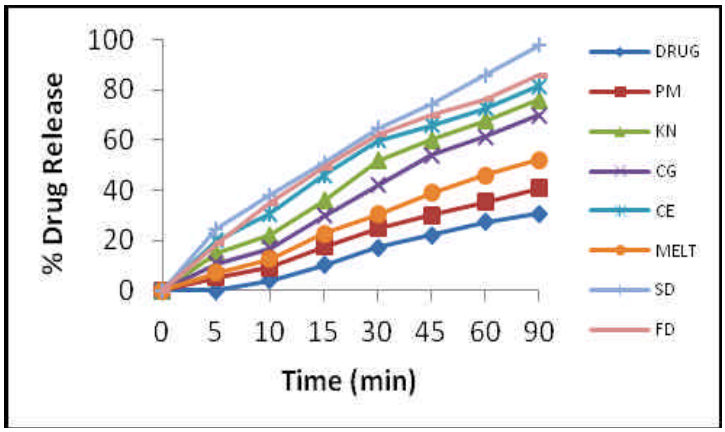

Fig.9. % drug release of drug and its complexes in Distilled Water (Drug:ß-CD complex)

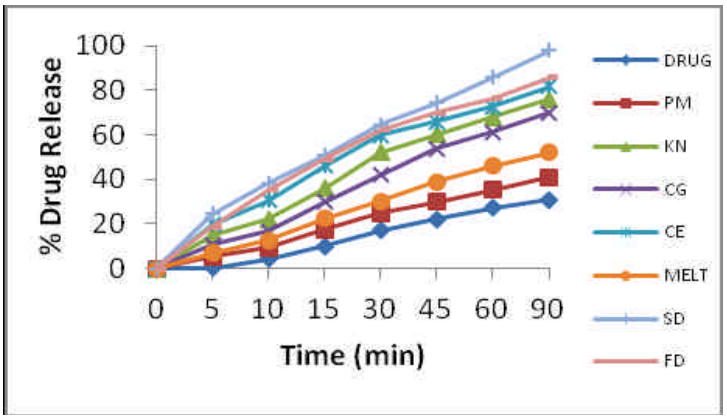

Fig.10. % drug release of drug and its complexes in Phosphate buffer pH 6.8 (Drug:ß-CD complex)

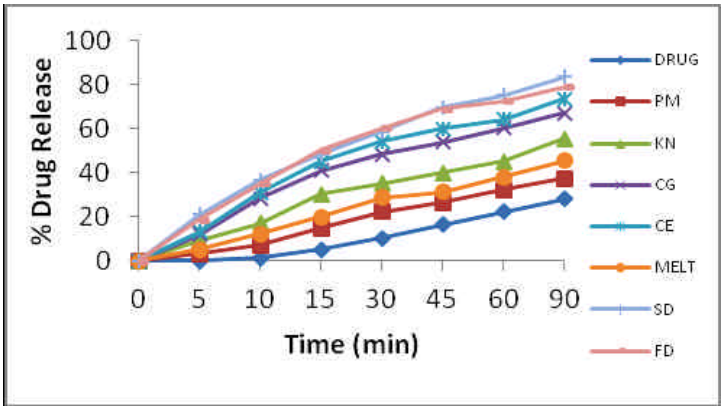

Fig. 12. % drug release of drug and its complexes in Phosphate buffer pH 6.8(Drug:HP-ß-CD complex)

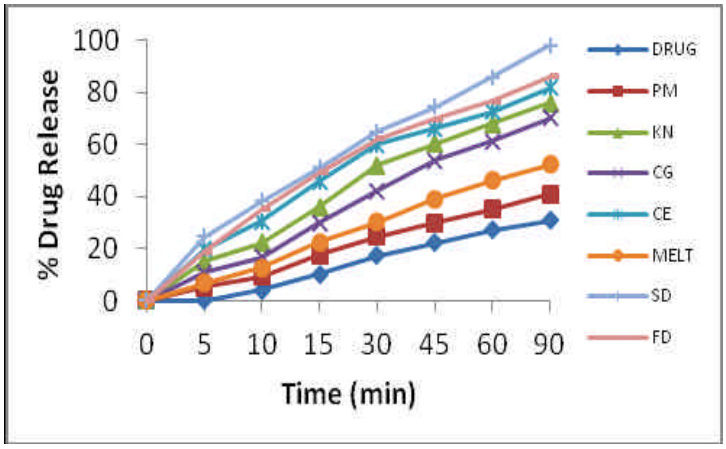

Fig.11. % drug release of drug and its complexes in Distilled Water (Drug:HP-ß-CD complex)

4.4. Evaluation of Rapid Disintegrating Tablets

Three different superdisintegrants, Crosspovidone(CRP), Sodium starch glycolate and crosscarmellose sodium (CCS) with different concentrations (each 4%,6%, 8%, 10%) were tried to achieve fast dispersion of tablets.

Micromeritic properties of tablet powder were calculated. Bulk density, tap density were found to be in the range of 0.64-0.7647 & 0.7784-0.8965. Hausners Ratio was found to be less than 1.25, it showed good flow. Carr's index was in the range of 18-21; hence it was fair to passable.

Table 3. Evaluation of Rapid Disintegrating Tablet

Formulation		Hardness **(Kg/cm²)	Friability (%)	Thickness** (mm)	D.T (min) **	Average Weight (mg) *	Water Absorption ratio	% Assay
Control		3.23±0.11	0.63 ±0.01	3.33±0.51	4.5±0.127	202±0.6324	168.4±0.12	97.35±0. 26
CRP 6%	ß-CD	3.3±0.032	0.78±0.21	3.3±0.05	1.60±0.57	202.3±0.27	125.1±0.17	95.5±0.43
	HPß-CD	2.63±0.152	0.62 ±0.52	3.02±0.02	1.5±0.57	201±0.25	124.1±0.25	98.5±0.43
CRP 8%	ß-CD	3.20±0.10	0.79±0.11	3.2±0.53	0.51±0.07	203±0.25	134.9±0.57	95.28±0.15
	HPß-CD	2.56±0.032	0.65 ±0.23	3.01±0.02	0.40±0.07	205±1.00	135.4±0.97	98.28±0.25
CRP 10%	ß-CD	3.63±0.15	0.62±0.51	3.2±0.22	1.12±0.57	202±0.79	159.4±0.11	96.35±0. 26
	HPß-CD	2.50±0.10	0.69±0.32	3.4±0.02	1.2±0.57	202±0.702	168.4±0.12	97.35±0. 26
SSG 6%	ß-CD	3.62±0.158	0.75±0.42	3.1±0.02	3.34±0.036	202±0.76	94.4±0.84	96.01±0.35
	HPß-CD	3±0.100	0.73 ±0.81	3.2±0.03	2.20±0.024	201±0.763	90.4±0.84	97.01±0.15
SSG8%	ß-CD	3.53±0.152	0.82±0.13	3.02±0.01	2.4±0.026	204±1.14	98.9±0.42	97.02±0.23
	HPß-CD	3.23±0.152	0.71 ±0.15	3.2±0.03	1.55±0.134	205±1.04	98.2±0.12	97.12±0.43
SSG10%	ß-CD	3.2±0.100	0.85±0.51	3.02±0.02	2±0.05	202±1.11	112.4±0.25	97.15±0.21
	HPß-CD	3.1±0.100	0.72±0.21	3.4±0.03	1.10±0.124	203±1.32	122.4±0.28	98.15±0.21
CCS4%	ß-CD	3.23±0.15	0.78±0.41	3.1±0.02	2.15±0.012	205.3±0.82	136.4±0.80	96.28±0.25
	HPß-CD	3.2±1.06	0.63±0.52	3.4±0.04	3.05±0.24	204.3±0.52	135.4±0.97	98.28±0.25
CCS6%	ß-CD	3.36±0.05	0.64±0.62	3.02±0.01	1.30±0.577	202.8±1.058	135.0±1.64	97.03±0.35
	HPß-CD	3.4±0.89	0.72±0.36	3.1±0.02	2.50±0.15	201.8±1.058	138.0±1.64	97.2±0.55
CCS 8%	ß-CD	3.46±0.01	0.68±0.72	3.02±0.02	1.45±0.027	204.86±0.41	154.0±0.64	96.50±0.15
	HPß-CD	3.1±0.19	0.89±0.92	3.2±0.03	2.45±0.22	205.86±0.592	152.0±0.64	98.59±0.29

** average ± sd, n = 20, ** average ± sd, n = 6.*

All the formulations exhibited white color, odorless, flat circular in shape with smooth surface. Hardness of tablets prepared by direct compression was 3.19-3.63 kg/cm2. The friability of all formulations was found to be less than 1.0 % and hence the tablets with lower friability may not break during handling on machines and or shipping.

Disintegration time is very important for rapid disintegrating tablet which is desired to be less than 3 min. Disintegration time of prepared rapid disintegrating tablet was in the range of 0.40 to 3.34 min. Formulation CRP (10%) & CCS (8%) shows minimum D.T, but it was observe that all the three conc. shows D.T within 1 min. So, CRP(6%) & CCS (4%) were selected for the stability study. Also, the formulation SSG (10%) shows minimum D.T. SSG (8%) shows D.T. which is lower than SSG (6%), but nearly similar to SSG (10%). Thus, SSG 8% was selected for the stability study.

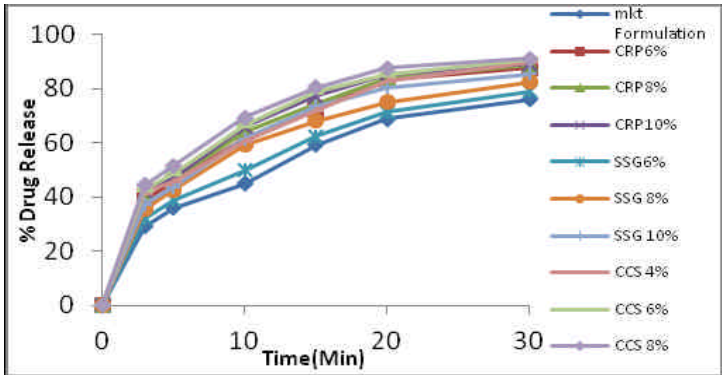

Fig. 13: % drug release from tablet in 0.1N HCl (Drug:ß-CD)

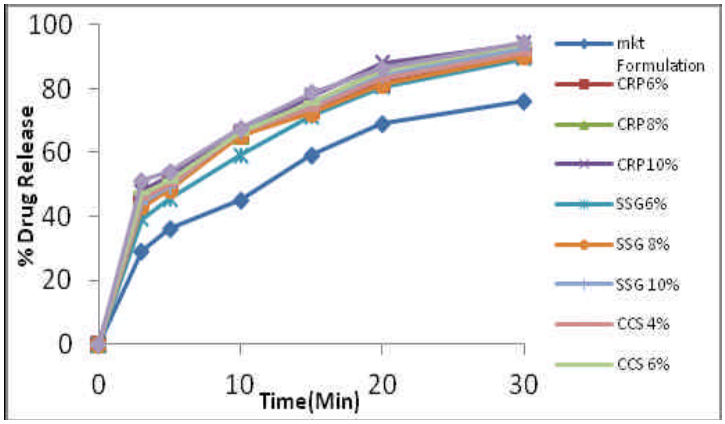

Fig.14. % drug release from tablet in 0.1 N HCl (Drug:HP-ß-CD)

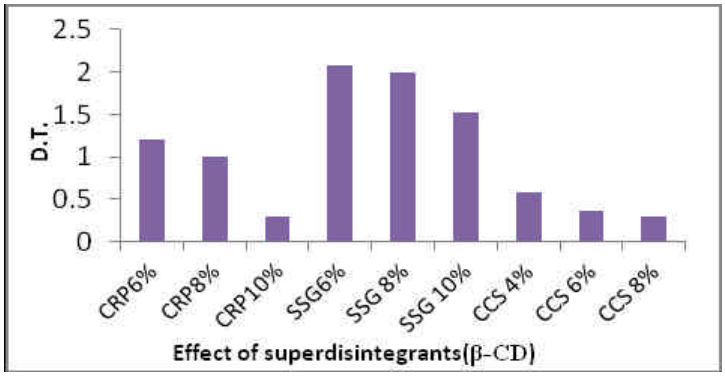

Fig.15. Effect of concentration of superdisintegrants.

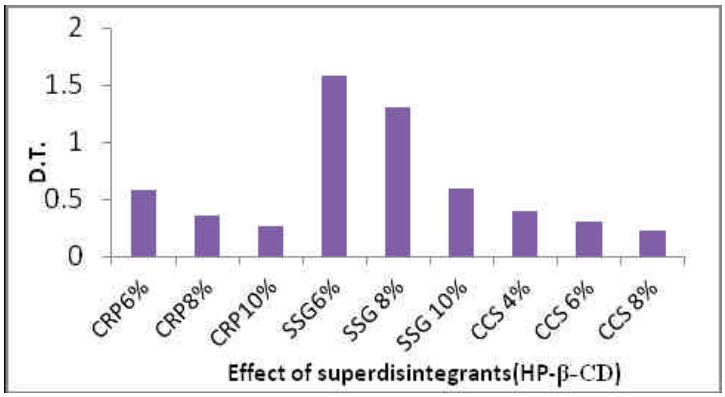

Fig.16. Effect of concentration of superdisintegrants.

Crosspovidone shows a decrease in D.T. as concentration increases. This was because CRP shows capillary mechanism of disintegration. When in contact with water it replaces the air absorbed by particles. This weakens the intermolecular bond and breaks the tablet into smaller particles. At 8% CRP showed decrease in D.T as compare to 6% but there is no significant increase in D.T of 10 %, hence 8% CRP was selected. SSG shows a decrease in D.T. as concentration increases. 10% SSG showed reduction in D.T compare to 6% and 8%, hence 10% SSG was selected. As compared to other superdisintegrants, CCS shows much better disintegration time drop and is much effective than others, 4% CCS was selected.

4.5. Stability testing

From the stability data Table 8 and Table 9 for batch CRP (6%) ,SSG(8%) and CCS(4%) it can be concluded that there were no significant changes in hardness, disintegration time & assay, so optimized batches i.e. CRP (6%) ,SSG(8%) and CCS(4%) are said to be stable. Hence, this product can be kept for a period of one year or more.

5. CONCLUSION:

ß-CD and HP-ß-CD formed 1:1 complexes with febuxostat as indicated by A_L type plot in phase solubility study. Inclusion complexes of febuxostat made by different methods exhibited following order for enhancement of their solubility, freeze drying > spray drying > kneading > coevaporation > melting > co-grounding >physical mixture. DSC and XRD confirmed the inclusion complex formation. The inclusion complexes with ß-CD prepared by spray drying method showed highest solubility (36.52 µg/ ml) and fast dissolution profile while inclusion complexes with HP-ß-CD prepared by co-evaporation method showed highest solubility (39.53 µg/ ml). Disintegration time decreased with the increase in concentration of superdisintegrants. Formulations CRP(6%) SSG(8%) and CCS(4%)showed faster disintegration.

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