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Research Paper

Formulation and Characterization of Mouth Dissolving Tablets of Ezetimibe by Frosta Technique Using Ezetimibe: Hydroxypropyl-β-cyclodextrin Solid Dispersion

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Highly plastic granules that can be compressed into tablets at low pressure were developed to make mouth dissolving tablets (MDTs) by compression method. In formulation of MDTs by Frosta technique, perlitol SD 200, maltrin QD M 580 and sucrose solution (40% W/V) were used as plastic material, water penetration enhancer and a wet binder respectively. Maltrin QD M 580 and pearlitol SD 200 were mixed in different proportions (10:90, 20:80, 30:70, 40:60 and 50:50). Wet binder (sucrose solution, 40% w/v) was used because it preserved the porous structure of maltrin QD M 580 and give better mechanical strength. Mouth dissolving tablets (batches MT1-MT5) were prepared by wet granulation method using optimized Ezetimibe: Hyroxypropyl-β-cyclodextrin solid dispersion (1:3 ratio, Batch SD3). The prepared Ezetimibe: Hyroxypropyl-β-cyclodextrin solid dispersion were characterized by Fourier transform infrared spectroscopy, differential scanning calorimetry, and powder X-ray diffraction and reveals reduction in drug crystallinity which might be responsible for improved dissolution properties. Evaluation of the tablets showed that all the tablets were found to be within official limits and the optimized batch MT3 (Containing 30% maltrin QD M 580 and 70% pearlitol SD 200) exhibited a disintegration time of 13.67 sec, percentage friability of 0.435%, wettability of 12 sec and 99.88 % drug release at the end of 45 minutes. The stability study conducted as per the ICH guidelines for six months and the formulations were found to be stable. The results concluded that mouth dissolving tablets of Ezetimibe successfully prepared by Frosta technique and improve the bioavailability of drug.

Key words: Ezetimibe, Hyroxypropyl-β-cyclodextrin, Maltrin QD M 580, Mouth dissolving tablet, Frosta Technique.

INTRODUCTION

Ezetimibe (EZE) is chemically 1-(4-fluorophenyl)-3(R)-[3-(4-fluorophenyl)-3(S)- hydroxypropyl]-4(S)-(4-hydroxyphenyl)-2-azetidinone. EZE reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine[1]. Due to its very high hydrophobic character, EZE exhibits highly erratic and very low dissolution profile in gastrointestinal fluids. Together with permeability, the solubility and/or dissolution rate of a drug are key determinants of its oral bioavailability. It is generally considered that compounds with very low aqueous solubility will show dissolution rate-limited absorption and hence poor absorption, distribution and target organ delivery[2]. Improvement of aqueous solubility in such a case is a valuable goal to improve therapeutic efficacy.

To enhance the solubility of those drugs scientists over the world are inventing various approaches. Formulation approaches such as micronization, modification of crystal habits, complexation, using surfactants and co-solvents, solid dispersions, etc have been extensively studied. A well established method to improve the solubility and bioavailability of poorly soluble drugs is solid dispersion technology [3, 4]. Cyclodextrins are powerful carriers for improving the

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therapeutic efficacy of drugs with poor aqueous solubility through inclusion complexes. Hydroxypropyl-β-cyclodextrin (HP-β-CD), a chemical derivative of β-CD, is the most accepted representative of hydroxyalkylated derivatives as a hydrophilic drug carrier because of its amorphousness, high water solubility and solubilizing power than β-CD, low cost and low toxicity[5].

Innovative drug delivery systems known as melt in mouth or mouth dissolving tablets (MDT) are novel types of tablets that disintegrate/disperse/dissolve in saliva. Their characteristic advantage, such as administration without water anywhere anytime, leads to their suitability for geriatric and pediatric patients. They are also most suitable for drugs that undergo extensive fist pass metabolism. The benefits, in terms of patient compliance, rapid onset of action as the drug goes directly into systemic circulation and good stability, make these tablets popular as a dosage form of choice on the current market. However, a major challenge is to develop mouth-dissolving tablets of poorly soluble drugs[6].

The Frosta technology is based on the compression of highly plastic granules at low pressures to prepare MDTs [7]. The highly plastic granules are composed of three components: a plastic material, a water penetration enhancer and a wet binder. Each of the three components plays an essential role in obtaining tablets with higher strength and faster disintegration time than the other MDTs. The key benefits of the Frosta technology are: fast disintegration in the mouth: within 5–40 sec depending on the tablet size, low manufacturing cost, simple processing, strong mechanical property: friability <1% and multi-tablet packaging: dozens of tablets in one bottle.

The purpose of this study was to improve the solubility and dissolution rate of Ezetimibe by forming a binary complex with Hydroxypropyl-β-cyclodextrin (HP-β-CD) by kneading method and to formulate its mouth dissolving tablets by Frosta technique.

MATERIALS AND METHODS:

The drug Ezetimibe, Hydroxy propyl-β-Cyclodextrin (HP-β-CD), Maltrin QD M 580 and Pearlitol SD 200 was procured from Ranbaxy Lab Ltd. Gurgaon (HR). All other chemicals were procured locally and were of analytical grade.

Preparation of solid dispersion by kneading method

Inclusion complex of Ezetimibe and hydroxylpropyl β-cyclodextrin (HP-β-CD) in different molar ratios (1:1, 1:2, 1:3 and 1:4) was prepared by kneading method. An accurately weighed amount of hydroxylpropyl β-cyclodextrin (HP-β-CD) was taken in glass mortar and kneaded with small amount of water to make slurry. Ezetimibe was added slowly into the slurry with continuous kneading. Once all the drug was incorporated into the slurry, the thick slurry was then kneaded for 45 min. The slurry was taken into the petri dish and dried at 50 ^{0}C.

Table 1: Abbreviations used to designate different solid dispersion batches

S. No	Batches	Diacerein: Hydroxy propyl- β-cyclodextrin ratio
1	SD1	1:1
2	SD2	1:2
3	SD3	1:3
4	SD4	1:4

The dry powder was pulverized and passed through sieve # 100 and stored in dessicator. Different batches of Ezetimibe: HP-β-CD solid dispersion is shown in table 1

Characterization of solid dispersions

I. Estimation of drug content[8]

Solid dispersions of Ezetimibe were tested for drug content uniformity. Solid dispersion equivalent to 10 mg of drug was weighed and transferred to 50 ml volumetric flask and volume was made up to mark with acetate buffer pH 4.5 (containing 0.45 % w/v SLS). The solution was sonicated for about 10 minutes and filtered using Whatman filter paper no. 41. The filtrate was suitably diluted with acetate buffer pH 4.5 and analysed against blank solution by spectrophotometrically at 232 nm. This was done in triplicates and the average drug contents were estimated.

II. In-vitro drug release profile

In vitro dissolution test for Ezetimibe solid dispersions was performed in triplicate using USP dissolution apparatus type II (paddle method). The medium was 900 ml of acetate buffer pH 4.5 (containing 0.45 % w/v SLS), maintained at 37° C ± 0.5° C. The paddles were rotated at 75 rpm. The solid dispersions equivalent to 10 mg of Ezetimibe were taken in muslin cloth and tied to the paddle. Sample (10ml) was withdrawn at different time intervals (5, 10,15,30,45 and 60 minutes) and replaced with the same amount of acetate buffer pH 4.5 to maintain the perfect sink conditions. Sample (10ml) was filtered and the drug absorbance was measured at wavelength of 232nm against blank using a double beam spectrophotometer.

Ezetimibe: HP-β-CD inclusion complex having a ratio of 1:3 (batch SD3) prepared by kneading method showed highest in-vitro drug release (99.87%) and high drug content (98.77%) was selected as optimized batch and further characterized by FTIR, DSC and X-ray diffraction studies.

III. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of Ezetimibe, Hydroxy propyl β-cyclodextrin (HP-β-CD) and solid dispersion of ezetimibe with HP-β-CD (optimized batch SD3) was recorded using ATR spectrophotometer (Bruker-Alpha E). Samples were scanned from 4000 to 600 cm^{-1}.

IV. Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) analysis of the samples (Ezetimibe, HP-β-CD and solid dispersion of ezetimibe with HP-β-CD: optimized batch SD3) was carried out on a DSC-60 (Shimadzu Corporation, Japan). Samples were heated under nitrogen atmosphere on an aluminum pan at a heating rate of 10ºC per min over the temperature range of 50 - 300ºC.

V. Powder X-ray diffraction studies (PXRD)

This technique is extremely reliable to evaluate the changes in the crystalline phase and amorphization of solid drug as a result of excipient or carrier interactions. Crystallinity is indicated by the presence of sharp peaks that are absence in case of amorphous drugs.[9, 10]

The powder X-ray diffraction (XRD) of Ezetimibe, HP-β-CD and solid dispersion of ezetimibe with HP-β-CD (optimized batch SD3) was recorded using an X-ray diffractometer (Goniometer PW3050). The scanning rate was 10^0/min and diffraction angle (2θ) was 5-50^0. Amongst, all the solid dispersion batches (SD1-SD4), the optimized solid dispersion batch SD3 prepared by kneading method at molar ratio of 1:3 (Ezetimibe: HP-β-CD) was selected for formulating into mouth dissolving tablets.

Preparation of mouth dissolving tablets of Ezetimibe by Frosta technique

In formulation of MDTs by frosta technique, perlitol SD 200, maltrin QD M 580 and sucrose solution (40%) were used as plastic material, water penetration enhancer and a wet binder respectively. Maltrin QD M 580 and pearlitol SD 200 were mixed in different proportions (10:90, 20:80, 30:70, 40:60 and 50:50) as listed in table 2. Wet binder (sucrose solution, 40%) was used because it preserved the porous structure of maltrin QD M 580 and give better mechanical strength.

Mouth dissolving tablets were prepared by wet granulation method using optimized Ezetimibe: HP-β-CD solid dispersions (batch SD3), maltrin QD M580, pearlitol SD 200, talc and magnesium stearate. The composition of tablets is shown in the table 2. All the ingredients (except talc and magnesium stearate) were passed through #60 separately, weighed, mixed in geometrical order in a poly bag for 10 minutes and then the blend was transferred into mortar. Sucrose solution (40% w/v) was gradually added to the mixture and the wet mass was prepared with hand. The wet mass was passed through a # 14 screen and was spread on a tray to dry at 50°C for one hour. The dry granules was forcedly passed through a # 18 screen and mixed with lubricant and glidant (# 60) for further 5 minutes in a poly bag. Then, finally the granules were compressed using 8 mm flat round punches on a 10-station rotary tablet machine (Ratnakar, Ahmedabad, India). A batch of 50 tablets was prepared for all the designed formulations.

Evaluation of mouth dissolving tablets

Weight variation test was carried out as per IP 2010. The hardness of the tablets was measured using a Monsanto hardness tester and friability was measured using a Roche Friabilator[11]. Wetting time and water absorption ratio of mouth dissolving tablets was carried out by using the method given by Bi et al. (1996)[12]. In this method a piece of tissue paper folded twice placed in a petri dish containing 6 ml of water. A tablet is placed on the paper, and the time for complete wetting was measured. The wetted tablet was then weighed and the water absorption ratio was calculated using the equation ($R = 100 (W_b - W_a) / W_a$), Where W_a and W_b are the weights of tablets before and after water absorption respectively. Disintegration test was carried by using the method given by Madgulkar AR et al. (2009)[13]. Drug content was determined by the method given by khemchand et al. (2013)[8].

In vitro drug release studies

In vitro dissolution test for mouth dissolving tablets was performed in triplicate using USP dissolution apparatus type II (paddle method). The medium was

Table 2: Composition of MDTs of Ezetimibe: HP-β-CD solid dispersion prepared by Frosta technique using 40% w/v sucrose solution as binder

S.No	Ingredients (mg/tab.)	MT1	MT2	MT3	MT4	MT5
1	Eze: HP-β-CD Solid dispersion*	40.5	40.5	40.5	40.5	40.5
2	Maltrin QD M580	9.15	18.30	27.45	36.60	45.75
3	Pearlitol SD 200	82.35	73.20	64.05	54.90	45.75
4	Sucrose solution (40% W/V)	15	15	15	15	15
5	Magnesium Stearate	1.5	1.5	1.5	1.5	1.5
6	Talc	1.5	1.5	1.5	1.5	1.5
	Total	**150**	**150**	**150**	**150**	**150**

* Ezetimibe: HP-β-CD (1:3) solid dispersion equivalent to 10 mg of ezetimibe

900 ml of acetate buffer pH 4.5 (containing 0.45% SLS), maintained at 37° C ± 0.5° C. The paddles were rotated at 75 rpm. Sample (10 ml) was withdrawn at different time intervals (5, 10, 15, 30, 45 and 60 minutes) and replaced with the same amount of acetate buffer pH 4.5 to maintain the perfect sink conditions. Sample (10 ml) was filtered and the absorbance was measured at wavelength of 232 nm against blank using a double beam spectrophotometer.

Accelerated stability studies

The stability studies were performed on the most promising mouth dissolving tablet formulation MT3 according to ICH (International Conference on Harmonization) guidelines for six months[14]. The study was performed by keeping the prepared tablets in air tight high density polyethylene bottles and placed in a desiccator containing saturated solution of sodium chloride, which gave a relative humidity of 75±5%. The desiccator was placed in a hot air oven maintained at 40±2°C and samples were withdrawn at 30, 90 and 180 days. All the parameters (friability, disintegration time, wetting time, water absorption ratio, drug content and in-vitro drug release) of formulation were measured at predetermined time interval.

RESULTS AND DISCUSSION

Characterization of solid dispersions

I. Estimation of drug content

The results of estimation of drug content (%) from sold dispersions of Diacerein with HP- β-CD are shown in table 3.The drug content was found in the range of 97.30 to 98.82% (SDI- SD4) indicating the acceptability of kneading method for preparation of solid dispersions. Low values of standard deviation in drug content of solid dispersion indicated uniform drug distribution in all the prepared batches.

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Table 3: Drug content (%) from solid dispersion batches SD1 to SD4

	SD1	SD2	SD3	SD4
Drug content (%)*	97.30±1.10	98.82±0.93	98.77±0.87	97.65±1.35

*(Mean± S.D.): n=3

II. In vitro drug release profile

Dissolution studies of pure Ezetimibe and all prepared solid dispersions were carried out in acetate buffer pH 4.5 (containing 0.45% w/v SLS). It is evident that the onset of dissolution of pure Ezetimibe was very low. The drug released from pure Ezetimibe was only 49.30% in 60 minutes during the in vitro dissolution study, suggesting a strong need to enhance the dissolution of Ezetimibe.

The in vitro dissolution profiles of the pure Ezetimibe and solid dispersions containing various ratios of Ezetimibe to HP-β-CD (SD1-SD4) are shown in fig. 1.

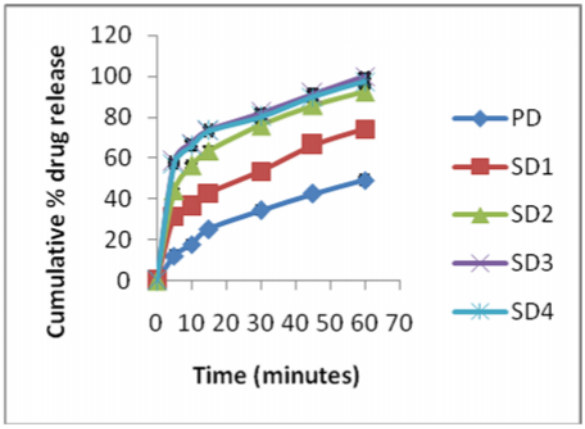

Fig. 1: In vitro drug release from Ezetimibe: HP β-CD solid dispersion in acetate buffer pH 4.5

The solid dispersions prepared by kneading method in the ratios of 1:1, 1:2, 1:3 and 1:4 (Ezetimibe: HP-β-CD) were showed 74.26 %, 92.42%, 99.87% and 97.35% drug release respectively at the end of 60 minutes. However, the inclusion complex at a molar ratio of 1:3 (SD3) achieved maximum dissolution rate of the drug. Possible mechanisms of improved dissolution rates of complexes include reduction of crystallite size, a solubilization effect of carrier, conversion of drug to amorphous state and finally the combination of the above methods. On further increasing the amount of HP-β-CD in solid dispersion i.e. formulations at 1:4 ratio (SD4) showed slightly decrease in dissolution rate, this might be due to the higher amount of carrier itself takes time to dissolution and viscosity of HP-β-CD increased as the concentration increased.

III. Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectra of Ezetimibe, HP-β-CD, and solid dispersions of Ezetimibe with HP-β-CD are shown in figure 2 A, B, C respectively.The IR spectra of Ezetimibe-HP-β-CD complexes showed considerable differences when compared with those of their corresponding constituents. The principal absorption peaks of Ezetimibe at 3267.30, 2937.75, 1885.19, 1271.18 and 1162.78 cm^{-1} shifted to a slightly lower frequency at 3230.02, 2925.62, 1844.33, 1270.52 and 1152.54 cm^{-1} respectively. The peaks at 1218.97 and 1357.19 shifted to a slightly higher frequency at 1219.33 and 1358.40 cm^{-1} respectively and broadening of these peaks were also observed. The observed shifts and broadening of the peaks clearly indicated the presence of host–guest interactions and formation of drug dispersion as a consequence of the interaction with HP-β-CD.

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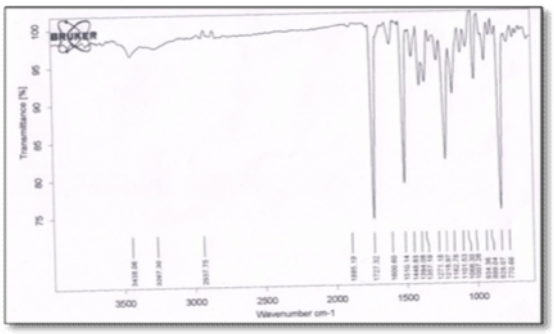
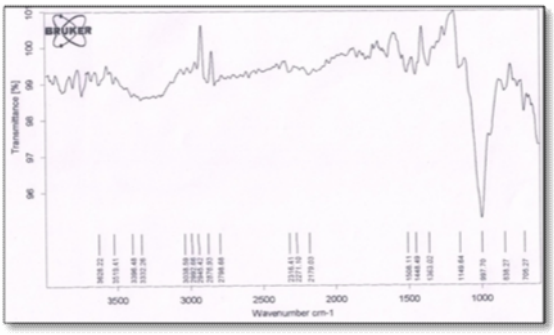
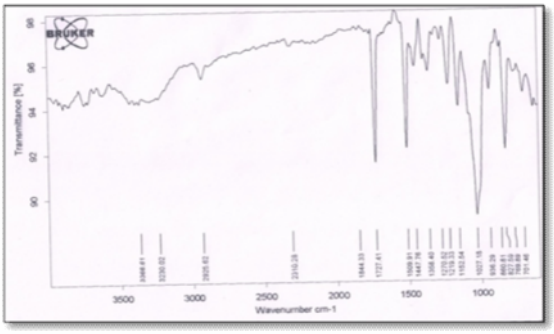


A. Ezetimibe



B. Hydroxy propyl β-cyclodextrin (HP-β-CD)



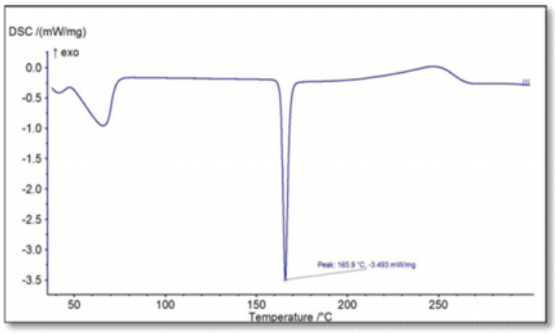
C. Solid dispersion of Ezetimibe with HP-β-CD (Optimized batch, SD3)

Fig. 2: FTIR spectra of Ezetimibe (A), Hydroxy propyl β-cyclodextrin (B) and solid dispersion of Ezetimibe with HP-β-CD (C)

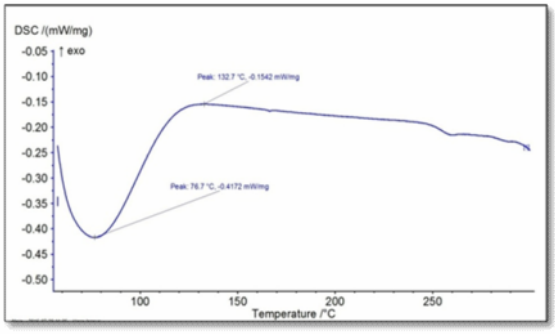
The binary system of Ezetimibe-HP-β-CD did not show any new peaks, indicating the absence of chemical bond formation in binary system.

IV. Differential Scanning Calorimetry (DSC)

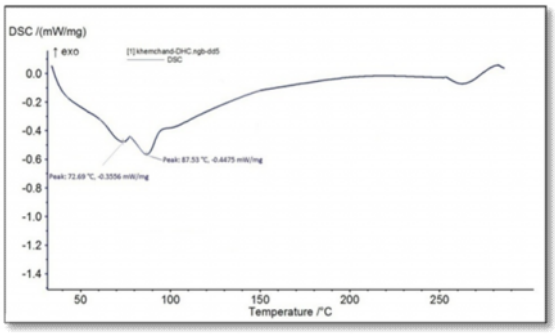
In order to confirm the formation of inclusion complex, thermal behavior of Ezetimibe and its complex with HP-β-CD was studied using DSC. The thermogram of Ezetimibe, HP-β-CD and complex with HP-β-CD are shown in the figure 3 A, B & C respectively. Ezetimibe



A. Ezetimibe



B. Hydroxy propyl β-cyclodextrin



C. Solid dispersion of Ezetimibe with HP-β-CD (Optimized batch, SD3)

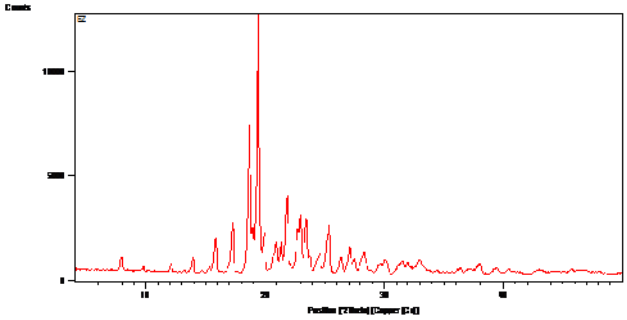
Fig. 3: DSC spectra of Ezetimibe (A), Hydroxy propyl β-cyclodextrin (B) and solid dispersion of Ezetimibe with HP-β-CD (C)

showed an endothermic peak at 165.90 ºC corresponding to its melting point. The DSC thermogram of HP-β-CD exhibited broad endothermic peak at 76.70 ºC attributed to the evaporation of

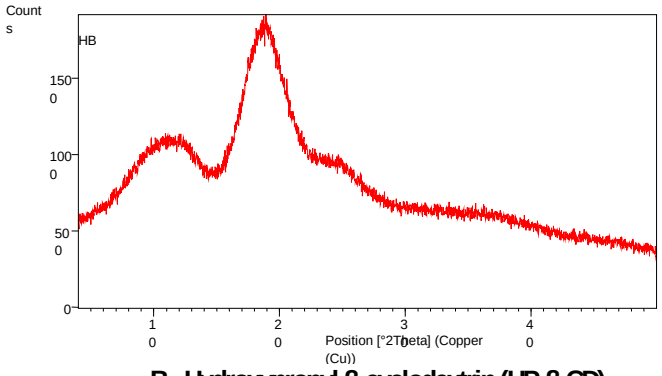
absorbed water. The melting peak of Ezetimibe was totally disappeared in thermogram of solid dispersion, indicating the absence of crystalline drug in solid dispersion and suggesting that Ezetimibe was molecularly dispersed and converted completely to an amorphous form.

V. Powder X-ray diffraction studies (PXRD)

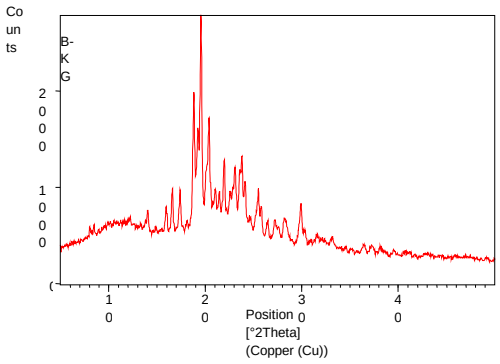
The XRD patterns of Ezetimibe, HP-β-CD and Ezetimibe–HP-β-CD inclusion complexes are shown in figure 4 A, B & C respectively. The powder X-ray diffraction pattern of pure Ezetimibe exhibited a series of intense peaks at 2θ value of 7.9, 13.89, 15.81, 17.22, 18.66, 19.39, 20.64, 21.80, 22.91, 23.42, 24.52 and 26.32, which were indicative of their crystallinity. Due to amorphousness of HP-β-CD, no major peaks



A. Ezetimibe



B. Hydroxypropyl β-cyclodextrin (HP-β-CD)



C. Solid dispersion of Ezetimibe with HP-β-CD (Optimized batch, SD3)

Fig. 4: X-ray diffraction patterns of Ezetimibe (A), Hydroxy propyl β-cyclodextrin (B) and solid dispersion of Ezetimibe with HP-β-CD (C)

were observed in spectra of HP-β-CD. Diffraction patterns of inclusion complexes of Ezetimibe-HP-β-CD in the ratio of 1:3 prepared by kneading showed the characteristic peaks of Ezetimibe but the intensity and number of drug peaks are reduced, indicating a decrease in drug crystallinity. These results suggested the amorphization of the drug and formation of amorphous inclusion complexes.

Evaluation of mouth dissolving tablets

The data obtained for post-compression parameters such as weight variation test, hardness, friability, disintegration time, wetting time, water absorption ratio and drug content of batches MT1- MT5 are shown in the table 4. Tablets obtained were of uniform weight with acceptable weight variation limits as per IP specification i.e., below 7.5 %. Hardness of tablets was found to be 4.0 to 7.0 kg/cm^2. Friability was found to be less than 1%. Disintegration time was found to be in the range of 13.67 to 22.33 seconds. In batches MT1-MT5, fast disintegration

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Table 4: Evaluation parameters Ezetimibe: HP-β-CD mouth dissolving tablets prepared by Frosta technique (MT1-MT5)

Batches	WVT (mg)***	H (kg/cm²)**	F (%)	DT (sec) *	WT (sec)*	WAR (%)*	DC (%)*
MT1	151±2.17	7.0±1.04	0.384	22.33±2.08	17.0±1.0	41.56±2.10	100.18±0.42
MT2	148±1.98	6.16±0.75	0.421	18.0±1.0	15.67±1.73	44.87±1.25	98.37±1.18
MT3	150±1.15	5.33±0.98	0.435	13.67±1.73	12.0±2.0	50.21±1.36	99.83±0.78
MT4	149±2.57	4.16±0.75	0.510	16.0±2.0	14.33±2.08	53.66±0.90	97.90±1.22
MT5	150±1.28	4.0±0.54	0.516	19.33±0.57	16.0±1.0	58.80±1.47	100.30±0.66

(Mean ±S.D), ***n=20, **n=6, *n=3,
WVT= Weight variation test, H= Hardness, F= Friability DT= Disintegration time, WT= Wetting time, WAR= Water absorption ratio, DC= Drug content

might be due to the preservation of porous structures of Maltrin QD M580 by using binder solutions with high sucrose concentration (40%). As the proportion of Pearlitol SD 200 decreased, the tablet hardness as well as the tablet disintegration time decreased. The low hardness of tablets made of 60:40 and 50:50 (Maltrin QD M 580 and pearlitol SD 200) granules may be due to the loss of the granule plasticity resulting from dissolution of a large portion of Maltrin QD 580 during granulation. Water absorption ratio and wetting time was found to be in the range of 41.56 to 58.80 % and 12 to 17 seconds respectively. Drug content was found to be in the range of 97.90 to 100.30 %, which was within acceptable limits. Granulation. Water absorption ratio and wetting time was found to be in the range of 41.56 to 58.80 % and 12 to 17 seconds respectively. Drug content was found to be in the range of 97.90 to 100.30 %, which was within acceptable limits.

In vitro drug release studies

Figure 5 showed the dissolution profiles of mouth dissolving tablets prepared from Ezetimibe: HP-β-CD solid dispersion using 40% w/v (MT1-MT5) sucrose solution as binder. The cumulative percentage drug release of formulation batches MT1-MT5 was found to be in the range of 84.06 to 100.17 % at the end of 60 minutes. The lowest release (MT1- 84.06 %) was seen with tablets containing 10% maltrin QD M 580 and 90% pearlitol SD 200 while tablets containing 30% maltrin QD M 580 and 70% pearlitol SD 200 showed highest drug release (batch MT3-100.17%) at the end of 60 minutes. The dissolution profile data indicated that the cumulative % drug released was increased as the concentration of matrin QD M 580 increased from 10-30% in batches MT1-MT5. This increased in drug released might be due to highly porous structure of maltrin QD M 580 which makes the tablets highly porous and increased the dissolution rate. As the concentration of maltrin QD M 580 increased above 30 % in batches MT4-MT5, the in-vitro drug release was decreased that might be occurs due to loss of granules plasticity and granules became hard. The formulation MT3 containing 30% maltrin QD M 80 and 70% pearlitol SD 200 showed

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Table 5: Accelerated stability studies of the optimized formulation MT3 at 40 ± 2 °C/ 75 ± 5 % RH for six months

Parameters	Days			
	0	30	90	180
Friability (%)	0.435	0.437	0.445	0.472
Disintegration time (sec)*	13.67±1.73	14.0±1.0	15.33±1.52	16.0±1.0
Wetting time *	12.0±2.0	12.0±1.0	12.67±0.57	13.33±1.15
Water absorption ratio*	50.21±1.36	50.10±0.87	49.15±1.43	48.28±2.38
Drug content (%)*	99.83±0.78	99.60±0.94	99.22±1.36	98.86±1.55
In vitro drug release in 60 Minutes*	100.17±0.72	99.63±1.05	99.08±1.46	98.35±1.33

*(Mean± S.D.): n=3

good hardness, least weight variation, low wetting and disintegration time and showed 99.88% drug release in 45 minutes was selected as optimized batch and used for accelerated stability studies.

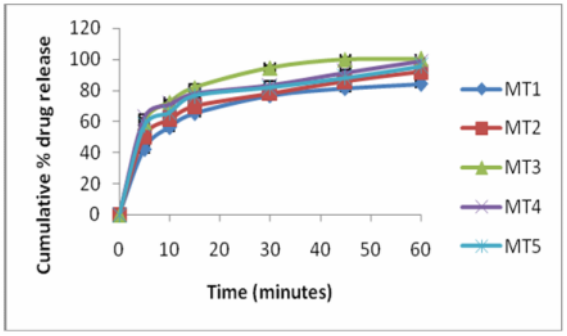

Fig. 5: In vitro drug release (%) from Ezetimibe: HP-β-CD MDTs prepared by Frosta technique (MT1-MT5)

Accelerated stability studies

No significant variation (1 to 3%) in drug release and other evaluation parameters were observed at accelerated conditions of 45 ± 2º C with 75 ± 5% RH. Therefore, it was concluded that the batch MT3 was stable over the chosen temperature and humidity for 6 months. The results are shown in table 5

CONCLUSION

The present study concluded that Hydroxy propyl β-cyclodextrin is a suitable carrier for the preparation of Ezetimibe solid dispersions. FTIR and DSC study demonstrated absence of any notable interaction between Ezetimibe and HP-β-CD. PXRD data showed conversion of Ezetimibe from crystalline to an amorphous form which is responsible for the enhanced solubility. The optimal batch (MT3) exhibited a disintegration time of 13.67 sec, percentage friability of 0.435%, wettability of 12 sec and 100.17 % drug release in 60 minutes. The key properties of the Frosta tablet are its highly porous structure offering fast disintegration in the mouth and yet enough mechanical strength due to the highly plastic granules. The Frosta tablets are expected to improve patient compliance, provide a rapid onset time of action and increase bioavailability. So, Frosta is a novel technique for formulation of mouth dissolving tablets.

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