Research Article

Design and Evaluation of Fast Dissolving Tablets of Clobazam using Complexation Technique

Dhanalakshmi B*[1], M.Vidyavathi[2], K. A.Sridhar[3]
[1, 3] East West College of Pharmacy, Bharath Nagar, Bangalore, Karnataka, India.
[2] Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visva Vidyalayam, Tirupati, A.P., India.
***Corresponding author's E-mail:** pharmadhana55@gmail.com

Received: 22-05-2018; **Revised:** 18-06-2018; **Accepted:** 08-07-2018.

ABSTRACT

Clobazam is a new 1, 5-benzodiazepine used for the treatment of epilepsy. The objective of present study was to formulate and evaluate taste masked fast dissolving tablets of Clobazam to increase the palatability and bioavailability of the drug. In the present work, an attempt was made to mask the taste by forming inclusion complexes using complexation technique. Taste improvement of drug with HP-β-Cyclodextrin was done by simple complexation approach using physical and kneading methods at various ratios of drug:HP-β-Cyclodextrin 1:0.5, 1:1, 1:1.5, 1:2, 1:2.5, 1:3(PF1-PF6, KF1-KF6). Taste perception study was carried and the best taste masked ratio of 1:2 of kneading mixture (KF4) was selected based on bitterness score and characterised by FTIR to identify the compatibility between drug and carrier. Tablets were prepared with KF4 by direct compression technique using superdisintegrants like lycoat and ludiflash (FLY1-FLY3, FLU1-FLU3). Prepared Tablets were evaluated for different properties like drug content, hardness, friability, disintegration time and In-vitro dissolution study. Different formulations showed disintegration time in the range of 20 to 75S. Among all formulations, FLY3 showed 99% drug release within 10min. Thus FLY3 was considered as the best among the prepared formulations, to which stability studies were conducted. The stability data confirmed the selected FLY3 tablets are stable as one not shown any changes in the results of different parameters before and after storage at 400C ±20 C/75% ± 5% RH for 3 months in stability chamber.

Keywords: Clobazam, HP-β-Cyclodextrin, Superdisintegrants, Lycoat and Ludiflash.

INTRODUCTION

Fast dissolving tablets are gaining prominence as new dosage forms as, these dosage forms dissolve or disintegrate in oral cavity within a minute without the need of water or chewing. [1] In spite of tremendous development in drug delivery technology, oral route remains perfect route for administration of therapeutic agents because of low cost of therapy, ease of administration, accurate dose, self medication and pain avoidance, leading to high level of patient compliance. Tablets and capsules are the most popular dosage forms [2] but main drawback of such dosage forms is dysphasia or difficulty in swallowing. This problem led to development of novel solid dosage forms such as fast dissolving tablets.[3]

Taste of pharmaceutical product is important parameter in governing the patient compliance with oral dosage form. Thus taste masking of oral pharmaceutical formulations has become important tool to improve patient compliance and especially the quality of treatment.[4, 5] HP-β-Cyclodextrin is the most widely used complexing agent for inclusion type complexes to mask the taste of drugs. Cyclodextrins (CD) are cyclic oligosaccharides with a hydrophilic outer surface and a lipophilic central cavity and have the ability to form inclusion complexes with a wide range of substrates.[6] This complex forming ability of cyclodextrins has been widely exploited in the pharmaceutical field for various applications, including taste –masking of bitter drugs.[7]

The complexing agent is capable of masking the bitter taste of the drug by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste buds thereby reducing the perception of bitter taste.[8]

Clobazam is used for the treatment of epilepsy. Since Clobazam has bitter taste, to improve the patient compliance, an attempt was made to mask the bitter taste of the drug by complexation with HP-β-cyclodextrin and formulate fast dissolving tablets of Clobazam by using superdisintegrants like lycoat and ludiflash. The aim of present study was formulation and evaluation of taste masked fast dissolving tablets of Clobazam to increase the palatability and bioavailability of the drug.

MATERIALS

Clobazam was purchased from Lake Chemicals, Bangalore. Lycoat, Ludiflash purchased from Colorcon Pvt, Ltd. All other chemicals and solvents used were of pharmaceutical and analytical grade obtained from commercial sources.

METHODS

Preparation of inclusion complexes

Clobazam inclusion complexes were prepared by physical mixing and kneading methods using different ratios of drug: HP-β-Cyclodextrin as shown in table1. Methanol was used as common solvent for preparation of inclusion complexes.

Physical mixture

Accurately weighed amount of drug and HP-β-Cyclodextrin were taken into glass mortar and then mixed for 10 minutes to get a good mixture of drug and polymer. Then the product was stored in the desiccator for further study[9].

Kneading method

Accurately weighed amount of drug and HP-β-Cyclodextrin were taken into glass mortar and then water, methanol mixture (20:80) was added in small quantities and the mixture was needed for 45 minutes then dried in oven at 40^0 C. The product obtained was pulverized, passed through mesh (#) 80 and stored in desiccator for further study[9].

Table 1: Ratio of different complexes

Complex code		Ratio of Drug: HP- β-Cyclodextrin
Physicalmixture method	Kneading method	
PF1	KF1	1:0.5
PF2	KF2	1:1
PF3	KF3	1:1.5
PF4	KF4	1:2
PF5	KF5	1:2.5
PF6	KF6	1:3

Evaluation of HP-β-cyclodextrin inclusion complexes

Drug content

An accurately weighed amount of complex mixture (equivalent to 10 mg of Clobazam) was dissolved in methanol in 10 ml of volumetric flask and made up to the final volume. The absorbance of diluted solution was measured at 232 nm by UV- Spectro photometer against appropriate blank and % drug content was calculated using standard graph.

In-vitro dissolution study of complex

Dissolution study of samples (equivalent to 10 mg Clobazam) was performed using USP type II dissolution test apparatus by paddle method. The dissolution test was performed three times using 900 ml of phosphate buffer of pH 6.8 at 37^0c ± 5^0c at 50 rpm. A sample 5 ml of dissolution media was withdrawn from dissolution apparatus at regular interval of 5 min up to 1 hour. The same quantity of sample was replaced with fresh dissolution medium. The samples were filtered through 0.45 µm membrane filter, and absorbance of these samples was determined at λmax 232 nm using UV-Visible spectrophotometer.

Evaluation of taste of complex

Taste masking ability of prepared formulations was evaluated by taste panel of six human volunteers. In this test volunteers were given a little amount of pure drug (2mg) and equivalent sample from HP-β-Cyclodextrin complex formulations to taste and evaluate the bitterness and give their response after 10 seconds, but instructed not to swallow it. Then the sample was spitted out followed by rinsing the mouth with distilled water and a gap of 30 min was allowed between successive tests. The response was evaluated on a scale from 0-4. 0-good, 1-tasteless, 2-slightly bitter, 3-bitter, 4-very bitter. Each volunteer was asked to assess the taste of both drug and the complex and to give scores. The average of scores of volunteers was calculated and the best taste masked complex was selected based on the least score obtained.

Formulation of fast dissolving tablets by direct compression method

Fast dissolving tablets of Clobazam were prepared using best HP-β-Cyclodextrin inclusion complex of Clobazam selected based on taste by direct compression method. The calculated amounts of th best taste masked drug complex (KF4- 1:2) equivalent to 10 mg Clobazam, superdisintegrants and other excipients were taken according to the composition given in Table 2. All the ingredients were passed through sieve # 60 mesh separately. Then the ingredients were mixed in plastic container and compressed into tablets of 200 mg using 12mm, flat punches on 16 station rotary tablet punching machine. (Rimek mini press)

Evaluation of blends

The powder blend was evaluated for its flow properties such as angle of repose, bulk density, tapped density, compressibility index, and hausners ratio.

Angle of Repose

Angle of repose was determined using fixed funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (θ) was calculated using an equation $\theta = \tan^{-1}(h/r)$.

Bulk Density

It was determined by pouring the blend in to a graduated cylinder. The bulk volume (V_b) and weight of the powder (M) was determined. The bulk density was calculated using an equation, apparent bulk density $=M/V_b$.

Tapped Density

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. Then the tapped density was calculated using an equation, Tapped density $=M/V_t$.

Compressibility index (I)

Compressibility index I was calculated using an equation,

$$I = V_{b-} V_{t/} V_{bx} 100.$$

Hausner's ratio: Hausner's ratio was calculated using an equation, Hausner's ratio (H) =Tapped density / Bulk density.

Evaluation of fast dissolving tablets

The tablets were evaluated for following parameters

Thickness

Thickness was measured by vernier callipers. Five tablets of each formulation were randomly taken and their thickness was measured by placing between two arms of vernier calliper and the average thickness was determined in mm.

Hardness

The crushing strength of tablets was measured by using Monsanto hardness tester. It was expressed in Kg/cm². Five tablets of each formulation were randomly picked and hardness of the each tablet was determined. Then the average hardness was calculated.[10]

Weight variation test

Twenty tablets were selected at random and average weight was determined using an electronic balance. Tablets were weighed individually and compared with an average weight. Then variation in weight of each tablet from an average weight was calculated.[11]

Drug content

Ten tablets were powdered and blend equivalent to 10 mg of Clobazam was weighed and dissolved in phosphate buffer pH of 6.8. The solution was filtered through 0.45 µm membrane filter and drug content was analyzed at λmax of 232nm usingUVspectrophotometer.[12]

Friability test

The friability of tablets was measured in Roche friabilator. Preweighed twenty tablets were placed in friabilator and operated at 25 rpm for 4 min and weighed again after dedusting. Percentage loss in friability was calculated using an equation given below. The loss should not be more than 1%.

% loss in friability= (Initial weight- Final weight)/Initial weight× 100

In-vitro disintegration test

The test was carried out with 6 tablets using tablet disintegration test apparatus. Phosphate buffer of pH 6.8 at 37^0 c ± 2^0 c was used as a disintegration media and time in seconds taken for complete disintegration of tablet with no residue remaining on mesh of apparatus was noted as its disintegration time.[12]

In-vitro dissolution study

Percent drug dissolved from fast dissolving tablets was determined by USP dissolution test apparatus using paddle method. The dissolution test was performed three times using 900 ml of phosphate buffer of pH 6.8 at 37^0C ± 5^0c at 50 rpm. A sample 5 ml of dissolution media was withdrawn from dissolution apparatus at regular interval of 2 min upto 10 min. The same quantity of sample was replaced with fresh dissolution medium. The samples were filtered through 0.45 µm membrane filter,[13] and absorbance of these samples was determined at λmax 232 nm using UV-Visible spectrophotometer. Then the % drug dissolved was calculated using calibration curve.

Wetting time

Wetting time of tablets was measured using petridish method. Six circular tissue papers of 10 cm diameter were placed in a petridish. 10ml of water containing dye was added to petridish. A tablet was carefully placed on the surface of tissue paper. Time required for water to reach the upper surface of the tablet was noted as wetting time.[14]

Drug-excipient compatibility study

FTIR spectra of pure drug Clobazam and best formulations FLY3 were obtained using IR spectrophotometer and compared. The samples were prepared with KBr. The sample scanning range was 4000 to 500 cm^{-1}

Stability study

Accelerated stability studies were carried out at 40^0c ±2^0 c/75% RH for 3 months. Stability studies were carried out as per ICH stability testing guidelines (ICH guidelines). The optimized formulation FLY3 tablets was stored in aluminium capped clear glass vials and were subjected to a storage condition of 40^0C ±2^0 C/75% ± 5% RH for 3 months in stability chamber. The samples were withdrawn at time intervals of 0, 1, 2, 3 months and evaluated for hardness, friability, disintegration time, drug content and *in-vitro* dissolution study.

RESULTS & DISCUSSION

Table 2: Formulation of Fast dissolving tablets of Clobazam

Ingredients(mg)	FLY1	FLY2	FLY3	FLU1	FLU2	FLU3
Clobazam + HP β-CD (1:2) (KF4)(containing Clobazam 10mg)	30	30	30	30	30	30
Lycoat RS 720 (mg)	5	10	15	-	-	-
Ludiflash (mg)	-	-	-	5	10	15
Mannitol (mg)	156	151	146	156	151	146
Saccharin (mg)	2	2	2	2	2	2
Magnesium stearate (mg)	4	4	4	4	4	4
Vanilla Flavour	1	1	1	1	1	1
Talc	2	2	2	2	2	2
Total (mg)	200	200	200	200	200	200

Table 3: Drug content of prepared inclusion complexes

Form. Code	Kneading method (Drug content %) (Mean± SD)	Form. Code	Physical Mixture (Drug content %) (Mean± SD)
KF1	78.89±0.18	PF1	75.12±0.29
KF2	83.23±0.22	PF2	79.09±0.32
KF3	85.34±0.16	PF3	81.85±0.42
KF4	88.91±0.34	PF4	83.60±0.32
KF5	80.23±0.28	PF5	84.46±0.28
KF6	79.64±0.36	PF6	82.01±0.26

Table 4: *In-vitro* dissolution study of kneading method inclusion complexes

Time (mins)	% Drug dissolved (Mean± SD)					
	KF1	KF2	KF3	KF4	KF5	KF6
0	0	0	0	0	0	0
5	6.47±0.26	9.22±0.24	14.46±0.12	18.86±0.26	12.58±0.26	7.62±0.18
10	11.22±0.18	16.88±0.16	20.22±0.36	26.54±0.18	21.62±0.32	12.84±0.36
15	16.68±0.13	21.54±0.02	26.84±0.24	31.58±0.24	28.54±0.46	18.46±0.28
20	24.54±0.02	28.14±0.18	32.14±0.48	37.22±0.38	37.48±0.42	23.22±0.22
25	29.62±0.08	32.29±0.06	39.48±0.02	43.87±0.42	44.68±0.32	31.54±0.48
30	36.24±0.01	39.86±0.04	46.82±0.18	50.64±0.24	52.82±0.26	39.62±0.64
35	40.58±0.12	47.68±0.16	51.74±0.16	58.62±0.32	58.54±0.28	46.21±0.22
40	47.74±0.19	52.28±0.08	59.62±0.22	64.28±0.16	63.75±0.48	51.94±0.24
45	54.22±0.24	58.92±0.12	63.86±0.08	72.15±0.02	70.86±0.22	58.62±0.36
50	60.18±0.16	64.48±0.18	70.24±0.19	78.22±0.48	74.32±0.18	63.22±0.18
55	67.26±0.04	72.22±0.14	79.86±0.26	83.64±0.22	79.68±0.02	68.56±0.02
60	72.89±0.014	80.64±0.06	84.22±0.34	89.26±0.18	82.18±0.06	74.68±0.36

Table 5: *In-vitro* dissolution study of physical mixture method inclusion complexes

Time (mins)	% Drug dissolved (Mean± SD)					
	PF1	PF2	PF3	PF4	PF5	PF6
0	0	0	0	0	0	0
5	7.47±0.16	9.34±0.12	12.96±0.02	15.26±0.36	10.36±0.02	7.28±0.12
10	12.64±0.22	16.22±0.36	18.54±0.45	21.84±0.28	16.92±0.18	11.68±0.26
15	18.58±0.36	22.16±0.24	25.86±0.36	28.62±0.34	23.58±0.36	18.96±0.46
20	27.16±0.54	28.06±0.02	31.49±0.28	34.26±0.48	31.86±0.18	24.22±0.54
25	30.48±0.36	31.84±0.18	37.38±0.22	40.84±0.18	38.54±0.12	32.68±0.38
30	38.29±0.54	40.26±0.06	42.58±0.18	48.39±0.36	45.23±0.18	41.29±0.52
35	44.29±0.26	48.69±0.18	50.26±0.16	56.21±0.18	51.26±0.21	50.62±0.29
40	50.12±0.34	54.22±0.29	57.62±0.02	61.34±0.14	59.38±0.64	57.69±0.22
45	56.22±0.12	60.24±0.28	62.06±0.42	68.29±0.02	65.46±0.28	62.84±0.12
50	61.84±0.18	66.26±0.36	68.22±0.56	75.24±0.16	70.32±0.54	69.36±0.02
55	67.39±0.26	72.22±0.37	74.26±0.58	79.22±0.24	74.88±0.26	73.26±0.42
60	71.24±0.64	76.09±0.54	80.34±0.22	82.64±0.36	79.62±0.24	76.88±0.36

Table 6: Taste evaluation results by taste panel

Form.Code	Volunteers Scores						Avg
	A	B	C	D	E	F	
KF1	3	3	3	3	3	3	3
KF2	1	2	2	2	2	1	1.6
KF3	1	1	1	2	1	1	1.1
KF4	0	0	1	1	1	1	0.6
KF5	0	1	0	0	1	1	0.5
KF6	0	0	0	1	1	1	0.5

Table 7: Results of flow properties of powder blend

Parameters	Formulation Code					
	FLY1	FLY2	FLY3	FLU1	FLU2	FLU3
Angle of repose (^{0}) (Mean± SD)	22.13±0.18	22.56±0.26	23.02±0.02	22.47±0.16	25.05±0.28	24.32±0.12
Bulk density (g/ml) (Mean± SD)	0.254±0.23	0.261±0.10	0.250±0.30	0.264±0.41	0.258±0.12	0.267±0.09
Tapped density (g/ml) (Mean± SD)	0.309±0.09	0.316±0.23	0.311±0.42	0.307±0.26	0.301±0.39	0.320±0.17
Carr's Index (Mean± SD)	17.79±0.12	17.40±0.21	19.61±0.08	14.0±0.05	14.28±0.19	16.56±0.27
Hausner's ratio (Mean± SD)	1.21±0.25	1.21±0.13	1.24±0.22	1.16±0.18	1.16±0.02	1.19±0.07

Table 8: Results of different parameters of prepared fast dissolving tablets

Parameters	Formulation Code					
	FLY1	FLY2	FLY3	FLU1	FLU2	FLU3
Thickness (mm) (Mean± SD)	2.74±0.01	2.78±0.16	2.89±0.28	2.70±0.11	2.77±0.08	2.85±0.19
Hardness(kg/cm^2) (Mean± SD)	3.12±0.05	3.15±0.10	3.19±0.22	3.45±0.16	3.52±0.07	3.60±0.21
Weight variation (%) (Mean±SD)	199.13±0.45	198.69±0.51	199.97±0.23	199.02±0.09	198.36±0.22	199.13±0.31
Drug content (%) (Mean± SD)	96.47±0.74	97.16±0.88	99.79±0.08	95.14±0.44	96.02±0.03	98.70±0.69
Friability (% loss) (Mean± SD)	0.46±0.14	0.29±0.51	0.17±0.10	0.74±0.63	0.67±0.22	0.70±0.66
Disintegration time(sec) (Mean± SD)	75.45±0.13	52.01±0.22	21.33±0.97	81.89±0.24	58.19±0.64	28.60±0.15
Wetting time (sec)(Mean± SD)	45.30±0.78	36.07±0.33	18.55±0.98	63.74±0.77	33.03±0.02	40.41±0.14

Table 9: Results of *In-vitro* dissolution test of different tablets

Time (min)	% Drug dissolved (Mean± SD)			% Drug dissolved(Mean± SD)		
	FLY1	FLY2	FLY3	FLU1	FLU2	FLU3
0	0	0	0	0	0	0
2	33.40±0.15	37.40±0.19	43.48±0.04	30.47±0.11	34.77±0.10	39.08±0.18
4	51.57±0.96	55.56±0.07	60.77±0.25	48.69±0.49	51.58±0.01	54.90±0.36
6	70.12±0.87 12±0.65	74.60±0.40	79.58±0.09	66.30±0.77	70.15±0.48	73.78±0.45
8	82.25±0.33	84.23±0.56	87.14±0.71	75.51±0.26	79.98±0.69	82.69±0.22
10	95.06±0.08	97.76±0.77	99.03±0.85	87.29±0.09	90.04±0.45	96.74±0.50

Table 10: Stability data for the selected best formulationFLY3

Name of the parameter	Time interval(months) after storage for			
	Initial	1	2	3
Disintegration Time(Sec) (Mean± SD)	21.33±0.97	23.31±0.22	22.12±0.32	24.23±0.27
Hardness(kg/cm^{2}) (Mean± SD)	3.19±0.22	3.13±0.11	3.15±0.14	3.12±0.16
Friability (% loss) (Mean± SD)	0.17±0.10	0.20±0.31	0.22±0.12	0.28±0.23
Drug content(%) (Mean± SD)	99.72±0.58	99.12±0.51	98.94±0.28	98.32±0.38
% drug dissolved in 10 mts (Mean± SD)	99.03±0.42	99.68±0.46	99.42±0.29	99.12±0.36

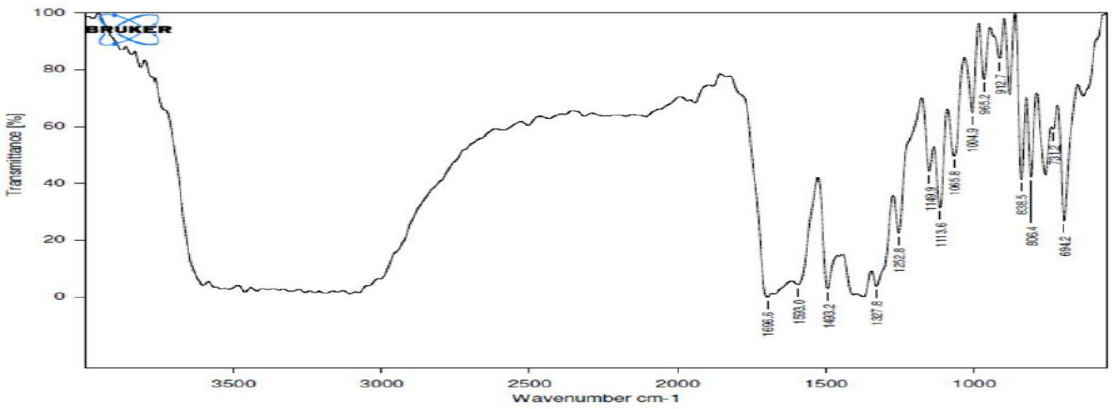

Figure I: FTIR spectrum of Clobazam

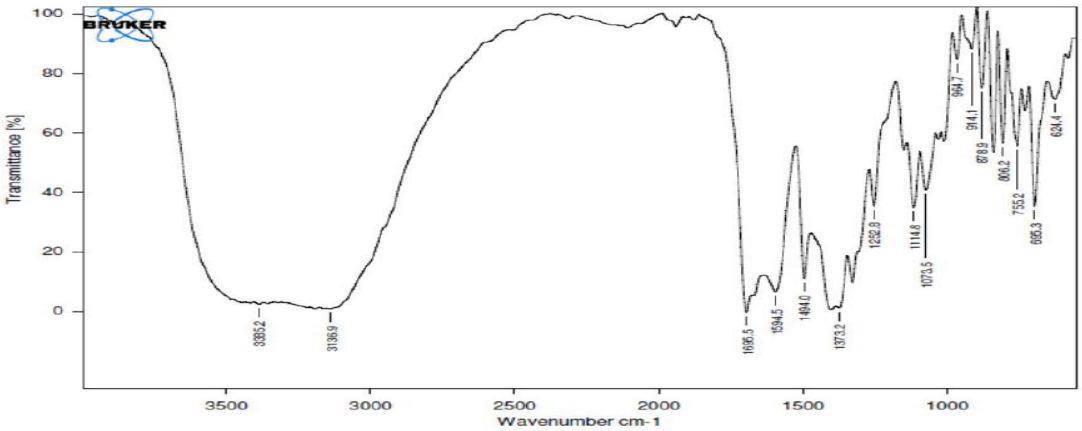

Figure II: FTIR spectrum of Clobazam selected best formulation (FLY3)

RESULTS AND DISCUSSION

Clobazam, HP-β-Cyclodextrin inclusion complexes were prepared in different ratios by kneading and physical mixing methods (table 1). Then the complexes were evaluated for drug content and taste. KF4 prepared by kneading method was found to have more drug content, drug dissolution and good taste (table 3,4,5& 6).Then, tablets were prepared using KF4 with different concentrations of two superdisintegrants (table 2).The final blend of tablets was evaluated for flow properties and was found that the flow property of prepared blends was good(table 7). The blends were directly compressed to obtain tablets. The tablets were evaluated for different parameters and results are shown in table 8.

As the ratio of complexing agent increased, the % drug content was also increased upto 1:1 to 1:2.5 ratio. But further increase in ratio of complexing agent, the % drug content was decreased due to saturation capability of complex.

The weight variation, hardness, friability and drug content of all tablet formulation were found to be satisfactory as shown in table 8. All the formulated tablets were of uniform weight with acceptable weight variation. Hardness of all formulations was 3-3.6 kg/cm^{2} , % loss in friability was found to be between 0.17 -0.74% , and drug content was found to be high (>95.14%).

Disintegration time of tablet was decreased with increase in concentration of lycoat and ludiflash. Tablet showing lower disintegration time has shown fast drug dissolution. The *In-vitro* disintegration time of tablets was found to be between 21 and 82 sec. The wetting time of tablets was found to be between 18 and 64sec. Formulation FLY3 has

shown less disintegration time i.e. 21 sec and high drug dissolution i.e. 99.03% within 10 min. From the above results FLY3 formulation was found to be the best and used for further compatibility and stability study.

The FTIR spectra of Clobazam pure drug and the best formulation FLY3 are shown in Figure 1 & 2 respectively. Pure Clobazam displays a peak characteristic of C=O stretching vibration at 1694 cm^{-1}, aromatic CH stretching at 3075 cm^{-1} , C-C stretching at 1493 cm^{-1}, C-N stretching at 1100-1200 cm^{-1} , C-H bending at 600-900 cm^{-1}, CH_3 bending at 1371 cm^{-1} , the spectra of best formulation showed all characteristic peaks of pure drug indicating that the drug is compatible with excipients.

Stability study was performed on the best selected on FLY3 formulation as per ICH guidelines. The study confirmed that no remarkable changes in the physical properties of tablets, no significant variation in the disintegration time, hardness, friability and drug release on storage at accelerated conditions for 3 months.

CONCLUSION

Clobazam could be successfully taste masked using HP-β-Cyclodextrin by complexation method. The taste masked complex was incorporated to prepared into fast dissolving tablets. Tablets were formulated using two superdisintegrants Lycoat, Ludiflash in three % (2.5%,5%,7.5%). Among all FLY3 showed fast disintegration and drug release. The prepared formulation offered significant results in terms of improving taste and fast dissolution.

REFERENCES

1. Fu Y, Yang S, Jeong SH, Therapeutic drug carrier systems, orally fast disintegrating tablets: developments, technologies, taste-masking and clinical studies, Crit reviews, 21(6), 2014, 433-475.
2. Chein. Yw. Oral Drug Delivery and Delivery System. 2nd ed. New York: Marcel Dekker: 1992.
3. Inayat Bashir Pathan, Praksash Ram Shingare, Formulation design and optimization of novel mouth dissolving tablets for venlaflaxine hydrochloride using sublimation technique, Journal of Pharmacy Research, 6, 2013, 593-598.
4. Mallikarjuna settey C, Prassad D.V.K, Gupta V.R.M, Development of fast dispersible Aceclofenac Tablets: Effect of functionality of super disintegrants, Indian journal of pharmaceutical Sciences, 70(2), 2008, 180-185.
5. Rajeshwari R A, Chhalla V J, Pharmaceutical Applications of Cyclodextrins II: in-vivo Drug Delivery, J Pharm Sci, 85, 1996, 1142-1169.
6. Freudenberg K, Cramer F, Plieninger H, Inclusion compounds of physiologically Active Organic Compounds, Germen patent 895769:1953.
7. Szejtli J, Szente L, Elimination of Bitter, Disgusting taste of Drugs and Foods by Cyclodextrins. Eur J Pharm Biopharm, 61, 2005, 115-125.
8. Patel AR, Vavia PR. Preparation and Evaluation of Taste Masked Famotidine Formulation using Drug/ β-Cyclodextrin/Polymer ternary Complexation approach. AAPS PharmSciTech, 9(2), 2008, 544-550.
9. Ahmed Abd Elbary, Mohammed Ahmed. Formulation and Evaluation of taste masked orally disintegrating tablets of nicergoline based on β-cyclodextrin inclusion complexation, international journal of drug delivery, 5, 2013, 110-120.
10. Lachman L, Lieberman A, King JL. The Theory and Practice of Industrial Pharmacy. Varghese Publishing House, 1991, 67-68.
11. Indian Pharmacopeia. 4th ed. Vol 2. New Delhi: Controller of Publication, Govt of India, 1996, 736.
12. Battue SK, Repay MA, Maunder S, Rio MY, Formulation and Evaluation of rapidly disintegrating tablet fenoverine tablets: effect of superdisintegrants, Drug Dev Ind Pharm, 33, 2007, 1225-1232.
13. Swarbrick James. Encyclopaedia of Pharmaceutical Technology. 3rd ed. vol 6, 1998, 2614-2629.
14. Singh J, Philip AK, Pathak K, Optimization studies on design and evaluation of orodispersible paediatric formulation of Indomethacin, AAPS Pharm Sci Tech, 9,2008,60-66.

Source of Support: Nil, **Conflict of Interest:** None.