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Research Article

DEVELOPMENT AND INVITRO EVALUATION OF FAST DISSOLVING TABLETS OF GLIPIZIDE

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ABSTRACT

In the present work, fast dissolving tablets of glipizide were prepared by direct compression method with a view to enhance patient compliance. Two superdisintegrants viz, crospovidone and croscarmellose sodium (4%, 5%, 6%) with different binders viz, pvp k-30 and pregelatinized starch (3%) were used. The prepared batches of tablets were evaluated for hardness, friability, weight variation, disintegration, wetting time, drug content and in vitro dissolution studies. Based on evaluating parameters, Formulation prepared by using 5% croscarmellose sodium with 3% PVP K30 was selected as optimized formulation. Finally, the optimized formulation was compared with marketed conventional formulation. Stability studies were carried out at 25ºC / 60% RH and 40ºC / 75% RH for optimized formulation for 2 months. Stability studies on the optimized formulation indicated that there was no significant change found in physical appearance, disintegration time and wetting time of the tablets.

Keywords: Fast Dissolving Tablets, Glipizide, Superdisintegrants, Direct Compression.

INTRODUCTION

Many patients express difficulty in swallowing tablets and hard gelatine capsules, resulting in non-compliance and ineffective therapy[1]. Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach led to development of fast dissolving tablets[2-4]. Advantages of this drug delivery system include administration without water, convenience of administration and accurate dosing as compare to liquids, easy portability, ability to provide advantages of liquid medication in the form of solid preparation, ideal for paediatric and geriatric patients and rapid dissolution/absorption of the drug, which may produce rapid onset of action. Some drugs are absorbed from mouth, pharynx and oesophagus as the saliva passes down in to stomach and in such cases bioavailability of drug is increased, pre-gastric absorption can result in improved bioavailability and as result of reduced dosage form, improved clinical performance through a reduction of unwanted effects. Glipizide is a second-generation oral sulfonylurea hypoglycemic agent to lower the blood sugar in patients with non- insulin dependent diabetes dependent diabetes mellitus. Mechanism of action is produced by blocking potassium K^+ channels in beta cells of islets of Langerhans. The increase in calcium will initiate more insulin release from each beta cell. It increases the concentration of insulin in the pancreatic vein. By this, it decreases glucose concentration[5].

MATERIALS AND METHODS

Materials

All the materials including superdisintegrants were obtained from Lincoln pharmaceuticals Ltd, Ahmedabad. All other reagents were of analytical grade.

Methods

Formulation of fast dissolving tablets by direct compression method[6]

All the ingredients were weighed and passed through #60 mesh separately. Then the ingredients were mixed and compressed in to tablet using 6.5mm flat-faced punches on 16 station rotary tablet machine (Lincoln Pharmaceuticals Ltd, Ahmedabad.) The blend was compressed into tablets. Formulations of Glipizide FDTs by direct compression method are shown in Table 1.

Table 1: Formulation of Glipizide FDTs by direct compression method

INGREDIENTS	FD_1 (mg)	FD_2 (mg)	FD_3 (mg)	FD_4 (mg)	FD_5 (mg)	FD_6 (mg)	FD_7 (mg)	FD_8 (mg)	FD_9 (mg)	FD_{10} (mg)
Glipizide	5	5	5	5	5	5	5	**5**	5	5
MCC	-	-	-	-	-	-	85	**85**	85	85
DCP	86	85	84	86	85	84	-	**-**	-	-
Crospovidone	4	5	6	-	-	-	5	**-**	5	-
Croscarmellose sodium	-	-	-	4	5	6	-	**5**	-	5
PVP K-30	3	3	3	3	3	3	3	**3**	-	-
Pregelatinized starch	-	-	-	-	-	-	-	**-**	3	3
Aerosil	1	1	1	1	1	1	1	**1**	1	1
Mg. stearate	1	1	1	1	1	1	1	**1**	1	1

Evaluation parameters of fast dissolving tablets:

Hardness [7]

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Friability [7]

The friability of a sample of 20 tablets was measured using Roche friabilator (Electrolab, Mumbai, India). Twenty tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated. Friability below 1% was considered acceptable.

Weight variation test [7]

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight.

In vitro disintegration time[7]

The disintegration time of the tablet was measured in water (37±2°C) according to disintegration test apparatus with disk. The time in seconds taken for the complete disintegration of the tablet with no palpable mass in the apparatus was measured in seconds. Three tablets from each batch (formulation) were tested for the disintegration time calculations.

Wetting time[8]

A piece of tissue paper folded twice was placed in a small petridish (ID= 6.5 cm) containing 6 ml of simulated saliva pH 6.8, a tablet was put on the paper, and the time for complete wetting was measured.

In vitro dissolution profile[9]

Dissolution studies were carried out by USP paddle method at 37 ± 0.5^0 c, taking 900ml of

phosphate buffer pH 6.8 as a dissolution medium. Speed of rotation of paddle was set at 50 rpm. Absorbance of sample was measured at 276 nm by spectrometrically.

Stability studies[10]

Stability studies were carried out at 25^0c/60% RH and 40^0c/75% RH for 60 days for optimized formulation FD_8 according to ICH guidelines.

RESULT AND DISCUSSION

The present investigation was undertaken to formulate and evaluate fast dissolving tablets of glipizide by direct compression method using Croscarmellose sodium and crospovidone as a superdisintegrants. Superdisintegrants are generally used by formulation scientists for developing FDTs or for improvement of solubility for drugs. The primary requirement for both dosage forms is quicker disintegration. The amount of Superdisintegrants was optimized in the formulation of FDTs. The total 10 were formulation (FD_1-FD_{10}) prepared using different concentration of Croscarmellose sodium and crospovidone to study its effect on disintegration time.

The results for evaluation of different batches of Glipizide FDTs by direct compression method are shown in Table 2.

Table 2: Evaluation of direct compressible fast dissolving tablets

Formulation	Hardness (Kg/cm^2)	Friability (%)	Weight Variation (%)	W.T. in Sec	D.T. in sec
FD_1	3.6	0.40	±4.5	38.00	20.16
FD_2	3.8	0.42	±4.8	36.46	18.48
FD_3	3.7	0.48	±5.6	41.11	20.11
FD_4	3.6	0.43	±5.9	34.50	20.12
FD_5	3.8	0.44	±6.0	37.30	18.32
FD_6	3.6	0.47	±4.6	42.07	19.48
FD_7	3.5	0.56	±4.9	18.19	12.12
FD_8	**3.5**	**0.58**	**±4.1**	**16.40**	**11.42**
FD_9	3.6	0.44	±5.8	28.38	16.52
FD_{10}	3.6	0.43	±5.5	24.44	16.00

Percent weight variation was observed between 4.1 and 6.0 which were well within the acceptable limit for uncoated tablets as per United States Pharmacopoeia. It is well known to formulation scientists that the tablets with more hardness show longer disintegration time. Since mechanical integrity is of paramount importance in successful formulation of FDTs, hence the hardness of tablets was determined and was found to be in the range of 3.5 to 3.8 Kg/cm^2. Friability was observed between 0.40 and 0.58%, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets. The disintegration time for all formulations was found to be 11-21 seconds and wetting time was 16-43 seconds.

The In vitro dissolution study was performed for all formulations and the results are shown in Table 3.

Table 3: Dissolution parameters of directly compressible fast dissolving tablets

Formulation	% Release after 2.5min	% Release after 5min	% Release after 10min	% Release after 15min	% Release after 20min
FD_1	40.11	58.95	82.93	92.81	96.21
FD_2	39.37	56.19	81.26	91.26	95.37
FD_3	39.93	57.43	81.74	91.43	95.11
FD_4	43.54	58.68	83.37	93.51	97.47
FD_5	41.13	56.70	80.24	90.67	94.58
FD_6	42.39	58.41	83.98	93.23	94.69
FD_7	46.75	59.96	88.02	98.89	99.00
FD_8	**51.35**	**62.70**	**89.74**	**99.28**	**99.89**
FD_9	49.96	59.67	85.78	96.68	98.00
FD_{10}	49.76	58.78	84.91	97.41	98.79

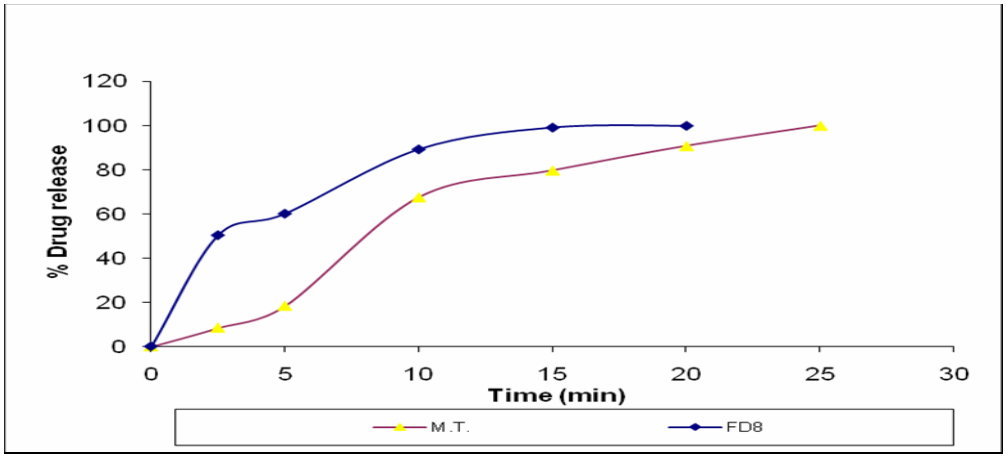
In vitro dissolution studies showed that more than 50% of the drug was released from the all formulations within 5 minutes. The FD_8 formulation containing croscarmellose sodium in concentration of 5% showed minimum disintegration time of 11.42 seconds, wetting time of 16.40 seconds and 51.35% drug and 99.89% drug was released within 2.5 and 20 minutes respectively.

The optimized formulation of FD_8 was compared with marketed tablet (Glucotrol 5mg) and the dissolution parameters of both formulations are shown in Table 4 and Fig 1.

Table 4: Comparison of dissolution profiles of Optimized formulation FD_8 with marketed tablet (Glucotrol 5mg)

Time (min)	% release of FD_8	% release of M.T.
2.5	50.32	8.47
5	60.08	18.36
10	89.16	67.50
15	99.01	79.61
20	99.78	90.68
25	-	99.87

Fig. 1: Comparison of dissolution profiles of Optimized formulation FD_8 with marketed tablet (Glucotrol 5mg)



From the dissolution studies, it was confirmed that the more than 99% drug release for optimized formulation was within 15 minutes, where as the marketed tablet showed the maximum release at 25 minutes.

Stability studies for optimized formulation FD_8 was carried out at 25^0c/60% RH and at 40^0c/75% RH and the results are shown in Table 5.

Table 5: Stability studies parameters for Optimized formulation FD_8

Time in Days	At 25ºC / 60% RH		At 40ºC / 75% RH	
	DT	WT	DT	WT
0	11.42	16.40	11.42	16.40
15	11.40	16.12	11.55	16.02
30	11.56	16.21	11.40	16.04
45	11.35	16.15	11.29	16.12
60	11.58	16.14	11.38	16.19

There was no significant variation found in physical appearance, disintegration time and wetting time of the tablets.

CONCLUSION

Fast dissolving tablets of Glipizide were prepared by direct compression method using Croscarmellose sodium and crospovidone as a superdisintegrants. The tablets disintegrated rapidly in oral cavity and had acceptable hardness and friability. In vitro drug release from the tablets shows significantly improved drug dissolution. It was concluded that in direct compression method, croscarmellose sodium was best superdisintegrant with pvpk-30 as binding agent. Hence it could be concluded that the superdisintegrant based fast dissolving tablets of Glipizide would providing quick onset of action without need of water for swallowing or administration. Further investigations are needed to confirm the in vivo efficiency.

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