



FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF GLIMIPRIDE

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Article Received on
27 June 2015,

Revised on 18 July 2015,
Accepted on 09 Aug 2015

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ABSTRACT

In the present work, fast dissolving tablets of glimipride 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 25°C / 60% RH and 40°C / 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, Glimipride, 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. Glimipride 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

All the ingredients were weighed and passed #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 Glimipride FDTs by direct compression method are shown in Table 1.

Table 1: Formulation of Glimipride FDTs by direct compression method.

INGREDIENTS	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9	FD10
	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)
Glimipride	5	5	5	5	5	5	5	5	5	5
MCC	-	-	-	-	-	-	-	85	85	85
DCP	86	85	84	86	85	84	-	-	-	-
Crospovidone	4	5	6	-	-	-	5	-	5	-
Croscarmellose	-	-	-	4	5	6	-	5	-	5
Sodium										
PVP K-30	3	3	3	3	3	3	3	3	-	-
Aerosil	1	1	1	1	1	1	1	1	1	1
Pregelatinized starch	-	-	-	-	-	-	-	-	-	3
Mg. stearate	1	1	1	1	1	1	1	1	1	1

Evaluation parameters of fast dissolving tablets:***Hardness***

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^[7].

Friability

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^[7].

Weight variation test

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight^[7].

In vitro disintegration time

The disintegration time of the tablet was measured in water ($37\pm 2^\circ\text{C}$) 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^[7].

Wetting time

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^[8].

In vitro dissolution profile

Dissolution studies were carried out by USP paddle method at $37\pm 0.50^\circ\text{C}$, 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^[9].

Stability studies

Stability studies were carried out at $25^\circ\text{C}/60\% \text{RH}$ and $40^\circ\text{C}/75\% \text{RH}$ for 60 days for optimized formulation FD8 according to ICH guidelines^[10].

RESULT AND DISCUSSION

The present investigation was undertaken to formulate and evaluate fast dissolving tablets of glimepiride 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 (FD1-FD10) prepared using different concentration of Croscarmellose sodium and crospovidone to study its effect on disintegration time. The results for evaluation of different batches of Glimipride FDTs by direct compression method are shown in Table 2. 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/cm². 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 2: Evaluation of direct compressible fast dissolving tablets

Formulation	Hardness (Kg/cm ²)	Friability (%)	Weight Variation (%)	W.T. in Sec	D.T. in sec
FD1	3.5	0.40	+4.4	38.00	21.00
FD2	3.8	0.41	+4.9	36.46	18.48
FD3	3.6	0.46	+5.7	41.11	20.15
FD4	3.7	0.42	+5.8	34.50	20.21
FD5	3.8	0.46	+6.0	37.30	16.23
FD6	3.5	0.47	+4.6	42.07	16.48
FD7	3.6	0.56	+4.9	18.19	14.12
FD8	3.5	0.58	0.58	+4.1	16.40
11.42					
FD9	3.6	0.41	+5.9	28.38	15.52
FD10	3.5	0.46	+5.6	24.44	18.00

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
FD1	40.11	58.95	82.93	92.81	96.21
FD2	39.37	56.19	81.26	91.26	95.37
FD3	39.93	57.43	81.74	91.43	95.11
FD4	43.54	58.68	83.37	93.51	97.47
FD5	41.13	56.70	80.24	90.67	94.58
FD6	42.39	58.41	83.98	93.23	94.69
FD7	46.75	59.96	88.02	98.89	99.00
FD8	51.35	62.70	89.74	99.28	99.89
FD9	49.96	59.67	85.78	96.68	98.00
FD10	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 FD8 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 FD8 was compared with marketed tablet (Axylim 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 FD8 with marketed tablet (Axylim 5mg)

Time (min)	% release of FD8	% 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

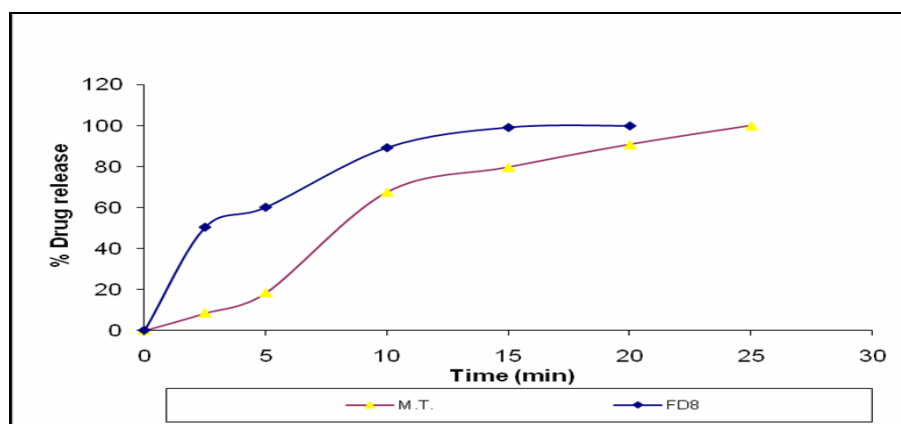


Fig. 1: Comparison of dissolution profiles of Optimized formulation FD8 with marketed tablet (Axylim 5mg)

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 FD8 was carried out at 25°C/60% RH and at 40°C/75% RH and the results are shown in Table 5.

Table 5: Stability studies parameters for Optimized formulation FD8

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

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

CONCLUSION

Fast dissolving tablets of Glimipride 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 without need of water for swallowing or administration. Be concluded that the superdisintegrant based fast dissolving tablets of Glimipride would providing quick onset of action Further investigations are needed to confirm the in vivo efficiency.

ACKNOWLEDGEMENTS

The authors wish to thank Dr. Sunil prajapati (H.O.D.) and Lincoln Pharmaceuticals Ltd., Ahmedabad for providing most of the utilized materials and reagent to carry out the research work.

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