Research Article

Formulation and Evaluation of Glicazide Mouth Dissolving Tablets

Vishakha S. Hastak*, Yogyata S. Pathare, Kiran C. Mahajan
Department of Pharmaceutics, Shree Chanakya Education Society's Indira college of Pharmacy, Tathawade, Pune, Maharashtra, India.
***Corresponding author's E-mail:** vishakha.hastak@indiraicp.edu.in

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ABSTRACT

Mouth disintegrating tablet (MDT) emerged as an alternative to the conventional oral dosage forms to improve the patient compliance. As the two extreme end age group (paediatric and geriatric) complain about the swallowing of conventional oral solid dosage forms. MDTs are solid dosage form containing medicinal substances or active ingredients which disintegrates rapidly within a few seconds when placed up on tongue. In this article the Gliclazide MDT were prepared using cross carmellose and sodium starch glycolate as superdisintegrant separately and then in combination by direct compression method. Gliclazide, second generation sulphonylurea, is an oral antihypereglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus. The prepared MDT's were evaluated for various parameters like disintegration time, wetting time, drug content, *in vitro* drug release study etc. From the result it was observed that among two superdisintegrants used, crosscarmellose sodium showed better result in disintegration time, *in vitro* drug release. The formulation of F-4 containing cross carmellose sodium (5%) showed better result in disintegration time 11 sec. and maximum *in vitro* drug release of 99.89 % at the end of 20 minutes.

Keywords: MDT, Gliclazide, crosscarmellose, sodium starch glycolate.

INTRODUCTION

The tablet is the most widely used dosage form existing today because of its convenience in terms of self administration, compactness and ease in manufacturing. However geriatric, pediatric and mentally ill patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance.[1] To overcome these problems, scientists have developed innovative drug delivery system know as mouth dissolving/disintegrating tablets (MDTs). The time for disintegration of orally disintegrating tablets are generally considered less than 1 minute.[2]

According to European Pharmacopoeia; these MDTs should dissolve/disintegrate in less than three minutes. Mouth dissolving tablets are also called as orodispersible tablets, fast disintegrating tablets, orally disintegrating tablets, quick disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, quick melt tablets and rapid melt tablet. However, of all the above terms United States Pharmacopoeia (USP) approved these dosage forms as MDTs.

United States Food and Drug Administration (FDA) defined MDTs as "A solid dosage form containing medicinal substances or active ingredients which disintegrates rapidly within a few seconds when placed up on tongue"[3, 4]. Mouth dissolving tablets are formulated by using superdisintegrants like crosscarmellose sodium, cross povidone and sodium starch glycolate. The various technologies used for manufacturing of MDTs are Freeze drying, Spray drying, Molding, Mass extrusion, Melt granulation, Sublimation and Direct compression.[5]

Gliclazide is an oral Antihypereglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus (NIDDM). Gliclazide is a second generation sulphonylurea which acts as a hypoglycemic agent. It stimulates β cells of the islet of Langerhans in the pancreas to release insulin. It also enhances peripheral insulin sensitivity.[6]

MATERIALS AND METHOD

Gliclazide were obtained as a gift sample from Jai Radhe Sales, Gujarat. Croscarmellose sodium, sodium starch glycolate and all other ingredients used were of laboratory grade.

Formulation of mouth dissolving tablets of gliclazide

The mouth dissolving tablets of Gliclazide were prepared by using superdisintegrants- cross carmellose sodium and sodium starch glycolate at different concentrations alone and in combination by direct compression method as shown in Table 1.

Gliclazide, superdisintegrants, microcrystalline cellulose, mannitol, magnesium stearate and talc were accurately weighed. All the materials were passed through 60 # screen prior to mixing and transferred to glass mortar and triturated till it was mixed uniformly. The mixture is then evaluated for precompression parameters. After this the powder mixture was compressed into tablets by using 9 mm diameter punch in a rotary tablet machine.[7]

Precompression evaluation of powder blend [8-10]

1) Bulk Density

Apparent bulk density (ρb) was determined by pouring blend into a graduated cylinder. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the following formula

$$\rho b = M/Vb$$

2) Tapped Density

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight (M) of the blend as measured. The tapped density (ρt) was calculated using the following formula

$\rho t = M/Vt$

3) 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 angle of repose was calculated using following formula

$\theta = \tan^{-1} (h / r)$

Where, θ is angle of repose

h is height of pile

r is the radius of the base pile.

4) Hausner ratio:

Hausner ratio is an in direct index of ease of powder flow. It is calculated by the following formula

Hausner ratio = ρt/ρb

Where ρt is tapped density

ρb is bulk density.

Lower Hausner ratio (< 1.25) indicate better flow properties.

5) Carr's compressibility index:

The simplex way of measurement of the free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index of the granules was determined by Carr's compressibility index (I) which is calculated by using the following formula

$I = \{(\rho b - \rho t) / \rho t \} X 100$

Evaluation of gliclazide mouth dissolving tablets

1. Tablet hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester.[11]

2. Tablet thickness

Tablet thickness can be measured using a simple procedure. The thickness was measured by placing tablet between two arms of the Vernier calipers.[11]

3. Friability

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. A pre weighed tablet was placed in the friabilator. Friabilator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as;[12]

%Friability = loss in weight / Initial weight x 100

4. Uniformity of weight

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of the tablet was determined from the collective weight.[12]

5. *In vitro* disintegration Time

The test was carried out on six tablets using distilled water at 37ºC ± 2ºC was used as disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.[12]

6. Wetting time

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml purified water. A tablet was put on the paper and the time required for water to reach upper surface of the tablet is noted as a wetting time.

7. Water absorption ratio

A piece of tissue paper folded twice was kept in a Petri dish (internal diameter 5.5cm) containing 6ml of purified water. The tablet was placed on the tissue paper and allowed to wet completely. The wetted tablet was removed and reweighted. Water absorption ratio, R was determined according to the following equation:[13]

R = 100 (Wa – Wb)/Wa

Where Wb and Wa are the weight before and after water absorption, respectively.

8. Content uniformity test

Weight of powder 10 mg of equivalent to 10 mg of Gliclazide was weighed and dissolved in suitable quantity of buffer, the solution was filtered suitably diluted and the drug content was analyzed using UV spectrometer at 226 nm.[14]

9. *In vitro* drug release study

Drug release study was performed for all the formulation using USP type-II apparatus. The dissolution test was performed using 900 ml of phosphate buffer (PH 6.8) was taken as the dissolution medium at 100 rpm and $37^0C \pm 0.5^0C$. Five millilitres of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed spectrophotometrically at 226 nm and % dug release were calculated.[14]

Table 1: Formulation of Gliclazide mouth dissolving tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Gliclazide (mg)	80	80	80	80	80	80	80	80
Sodium starch Glycolate (mg)	10	15	--	--	10	10	15	15
Crosscarmellose sodium (mg)	--	--	10	12.5	10	12.5	10	12.5
Microcrystalline cellulose (mg)	119.75	114.75	119.75	117.25	109.75	107.25	104.75	102.25
Mannitol (mg)	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5
Magnesium Stearate (mg)	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625
Talc (mg)	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625
Sodium Saccharin (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total (mg)	250	250	250	250	250	250	250	250

Table 2: Evaluation of mixed blend of drug and excipients

Formulation code	Angle of repose (θ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Hausner's ratio	Carr's compressibility index (%)
F1	28.02	0.56	0.67	1.196	16.417
F2	26.55	0.55	0.67	1.218	17.910
F3	26.81	0.60	0.73	1.216	17.808
F4	27.71	0.60	0.71	1.183	15.492
F5	26.29	0.58	0.68	1.188	15.046
F6	27.10	0.57	0.68	1.192	16.176
F7	26.96	0.59	0.70	1.185	15.642
F8	27.84	0.59	0.69	1.169	14.492

Table 3: Evaluation of Mouth dissolving tablets of Gliclazide

Formulation code	Hardness (kg/cm2)*	Thickness (mm)*	Disintegration time (sec.)	Friability (%)	Average Weight (mg)
F1	3.53±0.057	3.06±0.115	20±0.577	0.40±0.010	249±1.154
F2	3.46±0.115	2.83±0.577	21±1.154	0.40±0.005	250±1.000
F3	3.50±0.100	3.03±0.100	16±1.527	0.80±0.228	249±1.000
F4	3.60±0.200	2.76±0.152	11±1.000	0.53±0.233	250±1.527
F5	3.60±0.200	2.93±0.152	25±1.154	0.67±0.225	249±1.732.
F6	3.56±0.057	3.03±0.458	18±1.527	0.39±0.005	251±1.000
F7	3.43±0.057	2.73±0.208	25±0.577	0.53±0.231	249± 1.154
F8	3.30±0.264	2.83±0.152	22±1.000	0.80±0.005	250±1.527

mean ± S.D., *- n=3 (all the values are the average of three determinations)

Table 4: Evaluation of Mouth dissolving tablets of Gliclazide

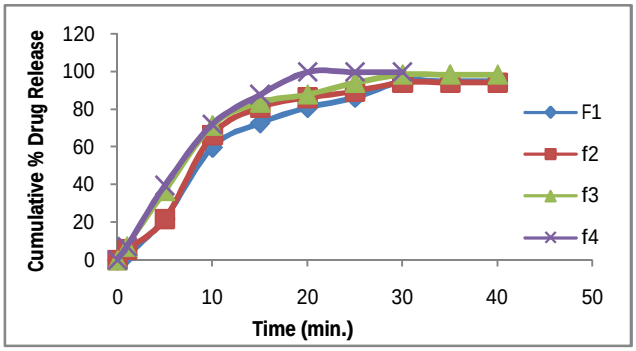
Formulation code	Wetting time (sec.)*	Water absorption ratio*	Drug content (%)	Drug release (%)
F1	23±1.000	56.64±0.433	95.53±0.894	94.89
F2	21±1.154	58.46±0.230	94.24±0.438	94.12
F3	19±1.527	57.77±0.498	98.65±0.502	98.35
F4	14±1.000	58.22±0.562	99.67±0.386	99.89
F5	24±1.154	57.61±0.720	97.84±0.444	97.29
F6	17±1.000	57.04±0.792	99.16±0.772	99.02
F7	23±0.577	58.14±0.698	99.38±0.889	99.21
F8	22±0.577	58.09±0.409	98.10±0.444	97.87

mean ± S.D.,* - n=3 (all the values are the average of three determinations)

RESULTS AND DISCUSSION

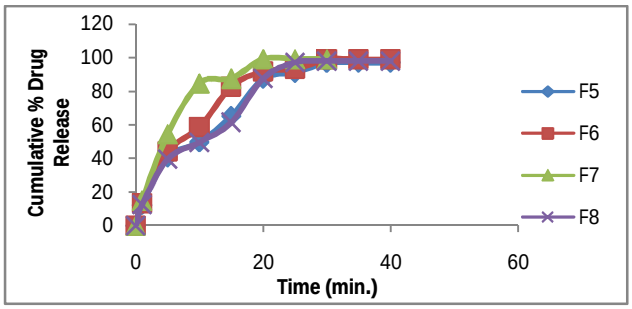
The mouth dissolving tablets of Gliclazide were prepared by using superdisintegrants- cross carmellose sodium and sodium starch glycolate at different concentrations alone and in combination by direct compression method. The powder blend was evaluated for preformulation parameters and results are shown in table no. 2. The angle of repose was in the range of 26.29°-28.02 ° indicating the good flow properties. Bulk density was found in the range of 0.55-0.60 g/cm^3 and the tapped density between 0.67-0.73 g/cm^3. Hausner's ratio was in the range of 1.169-1.218 indicating good flowability. The Carr's compressibility index was found to be between 14.492-17.910 %. Hence the prepared blends possessed good flow properties.

The powder blend containing drug was compressed by using direct compression technique and Glicazide MDT's were prepared. The compressed tablets were evaluated for physical properties and the results are tabulated in table no. 3 and 4. The hardness was in the range of 3.30±0.264 to 3.3.60±0.200 kg/cm^2. The thickness varies between 2.73±0.18 to 3.06±0.115 mm. Uniformity of weight of prepared tablets was found within specifications of Indian Pharmacopoeia. Uniformity of weight was found to be in the range of 249.± 1.000 to 251±1.000 mg. The friability of all formulations was found to be less than 1.0 % and was in the range of 0.39± 0.005 to 0.80 ± 0.005 % indicating a good mechanical resistance of tablets. The wetting time for all the formulated tablets was in the range of 14 ± 1.000 to 24 ± 1.154 sec. The disintegration time of all the formulated tablets was found to be in the range of 11 ± 1.000 to 25± 1.154 sec. The formulation F4 shows lowest disintegration time i.e. 11 sec. Water absorption ratio ranged from 056.64± 0.433 to 58.46 ± 0.230 %.The Percentage drug content was found in between 94.24± 0.438 to 99.38 ± 0.889 %. All the formulations *In vitro* drug release results were mentioned in the Table no.4. *In vitro* drug release of the prepared mouth dissolving tablets was performed in pH 6.8 using USP dissolution apparatus type 2. The result of *in vitro drug* release was shown in Table no.4.



Graph 1: *In-Vitro* drug release Profile of formulation F1, F2, F3 and F4

The drug release profiles of all the batches are shown in Graph 1 and 2. The cumulative percentage of dug release of all the formulation was found in the range of 94.12% to 99.21 %. The results are shows that the increase in proportion of superdisintegrants was associated with change in the overall cumulative drug release rate. Release profile of F-4 was found to have maximum release of 99.89 % at the end of 20 minutes.



Graph 2: *In-Vitro* drug release Profile of formulation F5, F6, F7 and F8

CONCLUSION

From the result it was concluded that mouth dissolving tablets of Gliclazide can be successfully prepared by direct compression techniques using different concentrations of superdisintegrants crosscarmellose sodium and sodium starch glycolate alone and in combinations. The prepared MDT's were evaluated for various parameters like disintegration time, wetting time, drug content , *in vitro* drug release study etc. And shows the satisfactory result. Among two superdisintegrants used, crosscarmellose sodium showed better result in disintegration time and *in vitro* drug release when compared to sodium starch glycolate. The formulation of F-4 containing cross carmellose sodium (5%) showed better result in disintegration time 11 sec. and maximum *in vitro* drug release of 99.89 % at the end of 20 minutes.

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