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ISSN 2230 – 8407 Research Article

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF METFORMIN HYDROCHLORIDE

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Article Received on: 17/04/12 Revised on: 20/05/12 Approved for publication: 06/06/12

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ABSTRACT

Metformin HCl is a biguanide antihyperglycemic agent used for treating non-insulin-dependent diabetes mellitus (NIDDM). It improves glycemic control by decreasing hepatic glucose production, decreasing glucose absorption and increasing insulin-mediated glucose uptake. In the present study an attempt has been made to prepare fast dissolving tablets of Metformin HCl in the oral cavity with enhanced dissolution rate. The tablets were prepared with three superdisintegrants e.g., Croscarmellose sodium, Sodium starch glycolate and Crospovidone. The blend was examined for angle of repose, bulk density, tapped density, compressibility index and hausners ratio. The tablets were evaluated for hardenss, friability, disintegration time, dissolution rate, drug content, and were found to be within 1 min. It was concluded that the mouth dissolving tablets with proper hardness, rapidly disintegrating with enhanced dissolution can be made using selected superdisintegrants.

Key Words: Fast dissolving tablets, Metformin HCl, Superdisintegrants, Crospovidone, Sodium starch glycolate, Croscarmellose sodium

INTRODUCTION

Mouth dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need for water. They are beneficial to swallowing tablets and capsules. Thus difficulty is particularly experienced by pediatric and geriatric patients. Various techniques such as freeze drying, sublimation, spray drying, molding, mass extrusion and direct compression method have been reported for preparation of mouth tablets. Metformin HCl is an oral dissolving antihyperglycemic agent that improves glucose tolerance in patients with NIDDM, lowering both basal and postprandial plasma glucose. The poor water solubility of the drug give rise to difficulties in the formulation of dosage form leading to variable dissolution rate. Hence it was selected as a model drug. In the present work an attempt has been made to prepare MDTs of Metformin HCl using superdisintegrants in different concentrations.^{1,2}

MATERIALS AND METHODS

Metformin HCl was received as a gift sample from Aventis Pharmaceuticals Pvt. Ltd., crosspovidone, croscarmellose, sodium starch glycolate and all other excipients were gift samples from New Neeta Chemicals,Pune.

Preparation of Metformin HCl tablets using direct compression

Weighed the Metformin HCl, superdisintegrants, microcrystalline cellulose, mannitol, magnesium stearate, and talc accurately. All the materials were passed through 60 # screen prior to mixing and transferred to glass mortar and triturated till it was mixed uniformly. The resulting powder mixture was compressed into tablets using single punch tablet machine.^{3,4}

Evaluation of powder blend Bulk density (D_b)^{5,6}

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by:

$$D_b = M/V_b$$

Where, M is the mass of powder

 V_b is the bulk volume of the powder.

Tapped density $(D_t)^{7,8}$

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by:

$$D_t = M / V_t$$

Where, M is the mass of powder V_t is the tapped volume of the powder.

Angle of repose $(\theta)^9$

The friction forces in a loose powder can be measured by the angle of repose (θ) . It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan (\theta) = h / r$$

$$\theta = \tan(h / r)$$

Where, θ is the angle of repose.

'h' is the height in cms

'r' is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel.

Carr's index (or) % compressibility^{10,11}

It indicates powder flow properties. It is expressed in percentage and is given by

$$I = \frac{Dt - Db}{Dt}$$

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder.

Hausner ratio

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

Where, Dt is the tapped density.

Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P

Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm2.

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{\text{Winitial} - \text{Wfinal}}{\text{Winitial}}$$

In vitro disintegration time

The in-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Table 1: Formulation composition of Mettromin HCI mouth dissolving tablets							
Sr.No.	Ingrediants	F1	F2	F3	F4	F5	F6
1	Metformin HCl	250	250	250	250	250	250
2	Croscarmellose Sodium	-	-	20	25	20	-
3	Crospovidone	10	15	-	20	-	25
4	Sodium starch glycolate	18	22.5	-	-	18	31.5
5	Microcrystalline cellulose	-	-	45	67.5	-	-
6	Magnesium stearate	5.4	5.4	5.4	5.4	5.4	5.4
7	Talc	3.1	3.1	3.1	3.1	3.1	3.1
8	Mannitol upto	213.5	204	176.5	124	203.5	185
9	Total weight	500	500	500	500	500	500

Table 1: Formulation composition of Metfromin HCl mouth dissolving tablets

Wetting time^{5,8,10}

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

$$dl/dt = r \Upsilon \cos\theta/(4\eta l)$$

Where l is the length of penetration, r is the capillary radius, Υ is the surface tension, η is the liquid viscosity, t is the time, and θ is the contact angle.

It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place.

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 370. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

In vitro drug release

Release of the drug in vitro, was determined by estimating the dissolution profile.

Dissolution test

USP II Paddle apparatus was used and paddle was allowed to rotate at 50 rpm. 0.1 N HCl (900 ml) was used as a dissolution medium. Determination of amount of drug dissolved from tablets was carried out by UV 1601 spectrophotometer at 234 nm.

RESULT AND DISCUSSION

Evaluation of blend

Formulation	Bulk	Tapped	Carr's	Hausner's
code	density	density	index	ratio
F1	0.47	0.52	17.23	1.29
F2	0.46	0.53	16.78	1.17
F3	0.48	0.56	16.99	1.09
F4	0.38	0.48	17.54	1.26
F5	0.49	0.55	17.28	1.36
F6	0.42	0.53	16.36	1.22

Table 2: Evaluation of the physical parameters of blend of Metformin

nci								
Formulation code	Hardness (kg/cm ³)	Weight variation	Friability (%)	Disintegration time (sec)				
F1	2.8±0.1	4.5	0.457	21				
F2	2.6±0.12	4.1	0.524	17.5				
F3	3.2±0.10	5.5	0.435	33.5				
F4	3.8±0.23	4.9	0.463	27				
F5	3.8±0.14	4.7	0.511	25				
F6	2.8±0.8	4.4	0.455	18.5				

Table 3: Evaluation of Physical Parameters of MDTs of Metformin HCl In vitro drug release



Figure 1: In vitro drug release profile for MDTs of Metformin HCl

From Figure 1, in vitro dissolution studies showed that more than 50% of drug was released from within 5 minutes. The fast dissolving tablet of F2 formulation containing 3% Crosspovidone and 5% Sodium Starch Glycolate disintegrated in 17.5seconds. 62.74% drug was released in 5 minutes and 99.0% drug was released in 25 minutes.

The present investigation was undertaken to formulate and evaluate fast dissolving tablets of Metformine hydrochloride by direct compression method using Croscarmellose Sodium, Crospovidone and Sodium Starch Glycolate as а superdisintegrants. Superdisintegrants are generally used by formulation scientists for developing fast dissolving tablets or for improvement of solubility for drugs. The amount of Superdisintegrants was optimized in the formulation of fast dissolving tablets. The ten formulations were prepared using different concentration of Croscarmellose Sodium. Crospovidone and Sodium Starch Glycolate to study its effect on Disintegration Time.^{2,4,7}

Percent weight variation was found to be between 4.1 and 5.6, well within the acceptable limit for uncoated tablets as per Indian 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 formulations of fast dissolving tablets, hence hardness of tablet was determined and was found to be in the range of 2.6 to 3.8 Kg/cm² (9,10,11)

Friability was found between 0.43 and 0.52%, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets.

The Disintegration time for formulation was found to be 17-34 seconds.

CONCLUSION

Fast dissolving tablets of Metformin Hydrochloride were prepared by direct compression method using Croscarmellose Sodium, Crospovidone and Sodium Starch Glycolate as superdisintegrants. The tablets disintegrate rapidly in oral cavity and had acceptable hardness and friability. In vitro drug release from the tablets shows significantly improved drug dissolution. The Crosspovidone was taken 3% and Sodium Starch Glucolate was taken 5% showed minimum disintegration time of 17.5 seconds and the 62.74% drug was released in 5 minutes and 99.0% drug was released in 25 minutes.^{12,13}

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Source of support: Nil, Conflict of interest: None Declared