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FORMULATION AND EVALUATION OF METFORMIN MOUTH DISSOLVING TABLETS – A REVIEW

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ABSTRACT
Mouth dissolving tablets used as an alternative of conventional oral dosage form to improve the patient compliance. Many patient groups, such as the elderly, children, mentally retarded, uncooperative or nauseated, have difficulty in swallowing conventional dosage forms, like tablets. Swallowing conventional tablets will be further hindered by conditions such as unavailability of water, allergic reactions and episodes of coughing. These problems can be solved by developing rapidly disintegrating and dissolving tablet dosage forms for oral administration, because they dissolve in saliva and does not require water for swallowing. Upon ingestion, the saliva serves to rapidly dissolve the dosage form. The popularity and usefulness of the formulation resulted in development of several mouth dissolving tablet technologies for preparation. This article provides a brief overview on the use of Metformin mouth dissolving tablets which recommended for the treatment of diabetes type II.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, decreaseing glucose absorption and increasing insulin mediated glucose uptake.

KEYWORDS:Mouth dissolving tablets,Metformin HCL, NIDDM,Superdisintegrants,Diabetes mellitus,Hypoglycaemia,Insulin,SSG,Crosscarmellose sodium,Mannitol.

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 geriatrics and mentally ill patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome these problems, scientists have developed innovative drug delivery system known as mouth dissolving/disintegrating tablets (MDTs). The time for disintegration of orally disintegrating tablets are generally considered less than 1 minute.[1]

Mouth dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need of water .They are beneficial to swallowing tablets and capsules.Metformin HCL is an oral antihyperglycemic agent that improves glucose tolerance in patients with NIDDM,lowering both basal and postprandial plasma glucose. The poor water solubility of the drug gives to 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.[2]

Metformin is considered to be the initial drug of choice for type II diabetes mellitus, particularly in overweight patients. This is based on its effectiveness in achieving glycaemic control, its favourable effects on weight, its low risk of causing hypoglycaemia and its reasonable cost. More importantly, Metformin has also been consistently shown to have a favourable effect on cardiovascular risk factors, and to improve cardiovascular outcomes. It can be combined with other oral hypoglycaemic agents, as well as insulin, allowing for a beneficial additive effect.

The mechanism of action of Metformin, e.g. Glucophage®, of which several generic formulations are available, has been well established as the first-line treatment option in the management of type II diabetes. It exerts its effect on blood glucose levels by:

- Inhibiting hepatic glucose production (gluconeogenesis)
- Enhancing glucose uptake by peripheral tissue

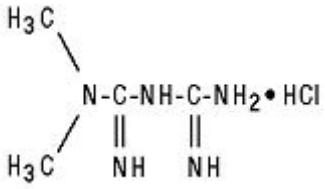
- Reducing intestinal glucose absorption, thus leading to reduced postprandial hyperglycaemia.

Collectively, these actions result in a reduction in the glycosylated HbA1c level, the lowering of low-density lipoprotein and an increase in high-density lipoprotein cholesterol[3].

MATERIALS AND METHODS

Drug Profile

Metformin hydrochloride (*N*, *N*-dimethylimidodicarbonimidic diamide hydrochloride) is not chemically or pharmacologically related to any other classes of oral antihyperglycemic agents.
The structural formula is as shown:



Metformin hydrochloride is a white to off-white crystalline compound with a molecular formula of C4H11N5 • HCl and a molecular weight of 165.63. Metformin hydrochloride is freely soluble in water and is practically insoluble in acetone, ether, and chloroform. The pKa of metformin is 12.4. The pH of a 1% aqueous solution of metformin hydrochloride is 6.68.

Preparation of Mouth Dissolving Tablets of Metformin HCl

All the materials were passed through 60 # screens prior to mixing. Metformin HCl, Croscarmellose sodium, Sodium Starch Glycolate, and Mannitol were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets on a 8-station rotary tablet machine.[5]

EVALUATION PARAMETERS

Precompression parameters: Evaluation of blend for the following parameters to be carried out before compression of MDT's

Bulk Density (Db):-

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 was calculated according to the formula mentioned below. It is expressed in g/ml and is given by:

Db = M / Vb

Where, M- is the mass of powder
Vb - is the bulk volume of the powder (ml).

Tapped Density (Dt)

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:

Dt = M / Vt

Where, M- is the mass of powder (gm).
Vt - is the tapped volume of the powder.[6]

Angle of repose (θ)

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. The angle of repose was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of a funnel was adjusted in such a way that its tip just touches the apex of the heap of the powder. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder heap was measured and angle of repose was calculated using following equation,

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

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

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.[7]

Table: 1 Angle of repose as an indication of powder flow properties

S.No.	Angle of repose(°)	Type of flow
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very poor

Hausner Ratio: Indirect index of powder flow can be determined from hausner ratio calculation

Haunser Ratio = **Pt/Pd**

Pt = tapped density, Pd = bulk density

Carr's Compressibility Index: To determine the flow ability of the powder blend for compression was determined by using:

I = Vb-Vt/Vb x100

Vb = freely settled volume of a given mass of powder, Vt = tapped volume of the same mass of the powder.[8]

Table: 2 Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5-12	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor
33-38	Very poor
<40	Very very poor

Porosity: Percent relative porosity (ε) was obtained using the relationship between apparent density (ρapp) and true density (ρtrue) which is calculated by following formula.[9]

ε = (1 - ρapp / ρtrue) ×100

Moisture content

The moisture content of the powder blend was determined by placing a specific quantity (5 gm) of the powder blend in the moisture analyzer at 105°C.[10]

EVALUATION OF METFORMINE HCL MDT

1. 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. is shown in table.[11]

Average Weight of Tablets	%Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

2. Dissolution test

The dissolution study is perfortmed by use of USP 2 (paddle speed of 50 rpm) apparatus which is most suitable for MDTs.The USP 1 (basket) apparatus may have certain application for such tablets but is used less frequently due to specific physical properties of tablets.

3. Hardness (Crushing strength)

Tablet hardness is measured with hardness testers like Monsanto. A tablet is placed in the hardness tester and load required to crush the tablet is measured. The hardness of MDTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. A good compromise between mechanical strength and disintegration time is achieved for a satisfactory mouth dissolving formulation.[12]

4. Compatibility studies

Compatibility between the drug and the excipients were studied using Fourier Transform Infrared (FTIR) spectrophotometer (Shimadzu) using KBr disc method.

5. Wetting time

This parameter is very much useful in predicting the disintegration time of the tablet. Here the tablet was placed on a filter paper that placed in a petridish containing 10 ml of water. The time taken for complete wetting of the tablet was noted and recorded.[13]

6. Friability

The friability of tablets using 10 tablets as a sample is measured using a Roche Friabilator. Tablets are rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets are then taken out, dedusted and reweighted. The percentage friability is calculated from the loss in weight as given in equation below. The weight loss should not more than 1%.

%Friability = (initial weight- final weight) x 100/ (initial weight)

7. Drug Content

Ten randomly selected tablets from each formulation are finely powdered and fixed amount of powder is accurately weighed and transferred to 100 ml volumetric flasks containing 50 ml of phosphate buffer(pH 6.8) or 0.1 N HCl solution. The flasks are shaken to mix the contents thoroughly and filtered. One ml of the filtrate is suitably diluted and drug content is estimated at 216.0 nm using a double beam UV-visible spectrophotometer. This procedure is repeated thrice and the average value is calculated.[14]

8. Stability studies

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions, re-test periods and shelf lives to be established. ICH specifies the length of study and storage conditions: Long term testing 25˚C±2˚C /60% RH 5% for 12 months. Accelerated testing 40˚C±2˚C / 75% RH 5% for 6 months. In the present study, stability studies were carried out at 25˚C/60% RH and 40˚C/75% RH for a specific time period up to 30 days for selected formulations.

9. In vitro disintegration time

The process of breakdown of a tablet into smaller particles is called as disintegration. The invitro disintegration time of a tablet was determined using disintegration test apparatus as per I.P.specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.4 (simulated saliva fluid) maintained at 37±0.2 ˚C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in pH 6.4 maintained at 37±0.2 ˚C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded[15].

10. Uniformity of weight

20 tablets are weighed collectively and individually.From the collective weight, average weight is calculated.Each tablet weight is then compared with average weight to ascertain whether it was within permissible limits or not[16].

11. Shape of Tablets

The compressed tablets were examined under the magnifying lens for the shape of the tablet.

12. Tablet Dimensions

Thickness and diameter were measured using a Vernier Callipers[17].

13. In-vitro dispersion time

In-vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation was randomly selected and in-vitro dispersion time was performed.

14. Water Absorption Ratio

A small piece of tissue paper folded twice was placed in a small petridish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then reweighed. Water absorption ratio, R was determined by using following formula given:

R= 100 x Wa-Wb / Wb

Wb is the weight of tablet before water absorption
Wa is the weight of tablet after water absorption[18].

RESULT AND DISCUSSION

This study is undertaking to formulate and evaluate Mouth dissolving tablets of Metformin HCL by direct compression method using different superdisintegrants. Superdisintegrants are generally used for developing disintegration rate of Mouth dissolving tablets or for improvement solubility of drugs. We are preparing the tablet containing Metformin HCl with different superdisintegrants.All ingredients are blend and compress by direct compression method. Precompression and postcompression evaluation is carried out. The compressed tablets is evaluated for weight variation, thickness, friability, hardness, drug content, wetting time, disintegration time and dissolution studies as per official Pharmacopoeia.

CONCLUSION

Mouth dissolving tablets are the general forms of tablets which rapidly or instantly disintegrate in the oral cavity and it's also proves significance for enhancing the bioavailability of water insoluble drug by increasing its dissolution and solubility. Metformin mouth dissolving tablet used for the treatment of diabetes mellitus II. Mouth dissolving tablets have better patient compliance and acceptance because mostly geriatric and pediatric patient facing the problem of swallowing so it's a better option.These formulation is prepared by various methods but direct compression is the easiest method for it.It can prepare by using drug with superdisintegrants such as; Crosspovidone, sodium starch glycolate (SSG).After direct compression, Values for angle of repose , loose bulk and tapped density , carr's index and hausner's ratio can be found. Hence it could be concluded that the mouth dissolving tablets of metformin hydrochloride would provide quick onset of action without need of water for swallowing or administration in the case of diabetes mellitus type II.

REFERENCES

1. Hastak, V.S. and Pathare, Y.S., 2013. *International Journal of Pharmaceutical Sciences Review and Research*, Formulation and evaluation of gliclazide mouth dissolving tablets. Vol. 21, Issue 2, pp. 325-329.
2. Sheikh, T.H. and Bhise, S.D., 2012. *International Research Journal of Pharmacy*, Formulation and evaluation of mouth dissolving tablets of metformin HCL. Vol. 3, Issue 6, pp. 96-98.
3. Mkele, G., 2013. *CPD article*, A review of metformin and its place in the diabetes guidelines. Vol. 55, Issue 6, pp. 504-506.
4. Laxmi, P.S.P. and Reddy, M.N., 2014. *International Journal of Innovative Pharmaceutical Sciences and Research*, Formulation and evaluation of metformin hydrochloride and hydrochlorothiazide bilayer tablets. Vol. 2, Issue 8, pp. 1824-1836.
5. Jadhav, A. and Pathan, J., 2014 *Journal of Current Pharma Research*, Formulation and evaluation of mouth dissolving tablets of metformin HCL by direct compression technique. Vol. 4, Issue 4: pp. 1271-1273.
6. Shah, D. and Shah, T. and Patel, M., 2013. *Asian Journal of Pharmaceutical Sciences and Research*, Formulation and evaluation of mouth dissolving tablets of tacrine hydrochloride using novel sweetener: a user friendly oral solid dosage form for geriatric patients.Vol. 3, Issue 2, pp. 18-30.
7. Bera, A. and Mukherjee, A., 2013. *Acta Chimica & Pharmaceutica Indica*, A detailed study of mouth

dissolving drug delivery system. Vol. 3, Issue 1, pp. 65-93.

8. Moris, S. and Pananchery, J. and Jain, A., 2015. *International Journal of Pharma Sciences and Research*, Formulation and evaluation of metformin HCL mouth dissolving tablet using sublimating agent. Vol. 6, Issue 7, pp. 1050-1055.
9. Ashish, P. and Harsoliya, M.S. and Pathan, Y.S., 2011. *International Journal of Pharmaceutical and Clinical Sciences*, A Review-Formulation of mouth dissolving tablets. Vol. 1, Issue 1, pp. 1-8.
10. Nazir, S.U.R. and Amer, M., 2013. *International Journal of Pharmaceutical Sciences Review and Research*, Formulation development of metfrmin tablet and its comparative in vitro study with different brands in Pakistan. Vol. 19, Issue 2, pp. 12-17.
11. Reddy, V. and Kumar, V., 2015. *Asian Journal of Chemical and Pharmaceutical Research*, Formulation and evaluation of mouth dissolving tablets of mosapride citrate. Vol. 3, Issue 1, pp. 220-225.
12. Patil, M.R. and Gujarathi, N.A. and Rane, B.R., 2014. *An International Journal of Pharmaceutical Sciences*, Formulation and evaluation of mouth dissolving tablet:review article. Vol. 5, Issue 2, pp. 7-20.
13. Anisree, G. S and Anu, V. and Rauof, P., 2014. *Scholars Academic Journal of Pharmacy*, Design and evaluation of mouth dissolving tablet of levocetrizine hydrochloride. Vol. 3, Issue 1, pp. 45-49.
14. Nasreen, W. and Chowdhury, Z.S. and Jhankar, Y.M. and Kadir, M.F., 2013. *IOSR Journal of Pharmacy and Biological Sciences*, Mouth dissolving tablets-A unique dosage form curtailed for special purpose: a review. Vol. 6, Issue 5, pp.53-61.
15. Arjun, G. and Prasad, M.S. and Santhosha, D., 2010. *International Journal of Pharma and Bio Sciences*, Formulation and evaluation of rosiglitazone mouth dissolving tablet. Vol. 1, Issue 1, pp. 1-9.
16. Srivastava, S. and Bala, R., 2012. *International Research Journal of Pharmacy*, Mouth dissolving tablets: a future compaction. Vol.3, Issue 8, pp. 98-109.
17. Shankr, M. and Sowmya, T. and Saikiran, Y., 2012. *International Journal of Pharmacy Practice & Drug Research*, Design and in-vitro evaluation of mouth dissolving tablets of pioglitazone hydrochloride by using novel coprocessed superdisintegrants. Vol. 2, Issue 2, pp. 68-75.
18. Gandhi, A., 2012. *The Pharma Innovation*, Mouth dissolving tablets: A new venture in modern formulation technology. Vol. 1, Issue 8, pp. 14-31.