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Original Research Article

Development and Evaluation of Fast Dissolving Tablets of Metformin HCl using different crosslinked cellulose

Deepshikha Gunwan*, Prabhakar Budholiya, Hemant Kumar Sharma

Sri Satya Sai University of Technology & Medical Sciences, Sehore (M.P.)

***Correspondence Info:**

Deepshikha Gunwan

Sri Satya Sai University of Technology & Medical Sciences, Sehore (M.P.)

Email: Deepshikhagunwan@gmail.com

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ABSTRACT

In the current research work was to developed immidiate release tablets of metformin HCl with improved dissolution rate and faster disintegration and dissolution characteristics with increased bioavailability. The fast dissolving tablets of metformin HCl were prepared by direct compression methods and blend was evaluated for the pre-compression parameters such as bulk density, compressibility, angle of repose etc. The tablets were prepared by using cross-carmellose sodium and primallose as superdisintegrants in various concentration along with lubricant and glidant. Six different formulations were prepared and evaluated different parameters as per IP. *In-vitro* dissolution studies are accomplished by utilizing phosphate buffer pH 6.8 at 75 rpm by paddle dissolution method. Among the all formulation F5containing of croscarmellose sodium was found to be appropriate and has shown a disintegration time 25 sec. The stability studies were performed for three months (accelerated studies) as per ICH guidelines. The optimized formulation (F5) indicates no variations for the parameters of tablets and it was stable for the specific time period.

Key words: Metformin HCl, Fast dissolving tablets, Direct compression, Superdisintegrants.

INTRODUCTION

Rapidly dissolving or quick dissolving dosage forms have capture great importance in the pharmaceutical industry due to their unique properties and advantages (Liang and Chen, 2001; Borsadia *et al*., 2003). Above all the dosage forms administered orally, the tablet is one of the most preferred dosage forms. Disintegrates are agents unified to tablet and other encapsulated preparation to advertize the difference of the tablet and capsule punch into more small pieces in an aqueous environment thereby incrementing the accessible surface area and advertise a more rapid release of the drug particle. They may promote moisture penetration and dispersion of the tablet matrix. Tablet disintegration has taken considerable attention as an important step in obtaining fast drug release. The emphasis at the availability of drug and importance of the comparatively rapid disintegration of a tablet as a approximately for make sure uninhibited drug dissolution charecteristics. The various factors affected the disintegration of tablets. The disintegrant have the major charecteristics to oppose the efficiency of the tablet binder and the physical forces that act below compression to the

tablet. The powerful binder, the more efficacious might be the disintegrating agents in sequence for the tablet to release its medication. Basically, it should create the tablet to disrupt, not only into the granules from which it was compressed, but additionally into powder particles from which the granulation. Combination of swelling and/or wicking and/or deformation is the mechanisms of disintegrant action. A disintegrant utilized in granulated formulation development can be more productive if used both intra-granularly and extra-granularly, thereby substituting to break the tablet up into granules and may be the granules further disintegrate to release the drug substance. (Ansel et al., 1998; Jain and Sharma, 1998). 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 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 fast dissolving tablets of metformin HCl using superdisintegrants in different concentrations (Seager, 1998; Bradoo et al., 2001).

Materials and methods

Materials

Metformin hydrochloride was a gift sample from Hetero Drugs Ltd., (Hyderabad, India). Crospovidone and Sodium croscarmellose was obtained from Hi-Media Laboratories Pvt. Ltd., Mumbai, India. Lactose, talc, mannitol and magnesium stearate was procured from Central Drug House (P) Ltd. New Delhi. All other solvents and chemicals used were of analytical grade.

Methods

Drug-excipient compatibility study

The spectra of FTIR of standard drugs and polymers powder were on KBr disk method (Brukers Alpha Spectrophotometer) with IR solution software to showed the compatibility between drug and excipients. The powder sample become thoroughly combined by triturating with potassium bromide in a pitcher mortar with pestle and compressed into disks in a hydraulic press (Techno search Instruments, India). FTIR spectra of all the samples were recorded over a spectral region from 4700 to 400 cm-1 using 20 scans with 4 cm-1 resolutions.

Preparation of tablets of metformin HCl

Fast dissolving tablets of metformin HCl were prepared by direct compression (Kuchekar et al., 2004) according to the formulae given in Table 1. All the ingredients were passed through # 60 meshes separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 600 mg using 8 mm round flat punches on 10-station rotary tablet machine.

Table 1 Composition of metformin HCl fast dissolving tablets

Ingredients (mg)	Formulation code					
	F1	F2	F3	F4	F5	F6
Metformin HCl	500	500	500	500	500	500
Croscarmellose sodium	-	-	-	30	40	50
Primellose	30	40	50	-	-	-
Mannitol	10	10	10	10	10	10
Lactose	40	30	20	40	30	20
Talc	10	10	10	10	10	10
Magnesium stearate	10	10	10	10	10	10
Total weight	600	600	600	600	600	600

Evaluation of fast dissolving tablets of metformin HCl

Precompression parameters

Angle of repose (ϑ)

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

$$\text{Tan } \theta = h/r$$

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

Where, θ is the angle of repose, h is the height, r is the radius.

The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas.

LBD (Loose Bulk Density) = Mass of Powder/Volume of Packing

TBD (Tapped Bulk Density) = Mass of Powder/Tapped Volume of Packing

Compressibility index

The compressibility index of the granules was determined by Carr's compressibility index**.**

$$\text{Carr's index (\%)} = [(TBD - LBD)/TBD] \times 100.$$

Hausner's ratio

Hausner's ratio is an indirect index of ease of measuring the powder flow. It was calculated by the following formula (Subramanyam, 2001).

Hausner's ratio = Tapped density/Bulk density.

Evaluation of Tablets

Thickness

Twenty tablets from the representative sample were randomly taken and individual tablet thickness was measured by using digital vernier caliper (Salsa et al., 1997).

Hardness

Tablet hardness was measured by using Monsanto hardness tester. From each batch six

tablets were measured for the hardness and average of six values was noted along with standard deviations.

Friability Test

From each batch, ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25 rpm for 4 minutes and tablets were observed while rotating. The tablets were then taken after 100 rotations, de dusted and reweighed. The friability was calculated as the percentage weight loss.

% friability was calculated as follows

$$\% \text{ Friability} = (W1 - W2) \times 100/W1$$

Where W1 = Initial weight of the 10 tablets, W2 = Final weight of the 10 tablets after testing.

Friability values below 0.5-1% are generally acceptable.

Weight Variation Test

To study weight variation individual weights (WI) of 20 tablets from each formulation were noted using electronic balance. Their average weight (WA) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets along with standard deviation values were calculated.

Drug content

Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered and Drug equivalent to 25 mg of drug dissolved in 10 ml phosphate buffer pH 6.8 sonicate it for 20 minutes, till the entire drug leached out from complex, then the solution was filtered through whatman filter paper No. 41. From this solution take 1 ml and diluted up to 100 ml with phosphate buffer pH 6.8 and the drug content was determined spectrophotometrically at 234 nm.

Wetting time

The wetting time and capillarity of the oral dispersible tablets were measured by a conventional method. The tablet was placed in a Petridis of 6.5 cm diameter containing 10 ml water at room temperature and the times for complete wetting of tablets were recorded.

In vitro disintegration time

The disintegration test was performed using an USP disintegration apparatus, with 0.1N HCl for 2 h and then in phosphate buffer pH 6.8 maintaining the temperature at 37 ± 2°C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.

Dissolution rate studies

The prepared tablets were evaluated for *in vitro* drug release. The drug release studies were carried out using a dissolution test apparatus (E.I. Instrument, Hariyana, India). The USP Type II (paddle type) method was selected to perform the dissolution profile of metformin hydrochloride 0.1N HCl first two hours and then media was changed into phosphate buffer pH 6.8 for remaining 6 hours. The temperature was maintained at 37 ± 0.5°C and a constant paddle rotation speed of 50 rpm. Samples (10 ml) were withdrawn at regular intervals and filtered through membrane filter (pore size 0.22μm). Concentration of metformin was determined spectrophotometrically at 234 nm (Systronics 1700 UV-Vis Spectrophotometer). Actual

amount of released drug was determined from the calibration curve (Khan et al., 2019; Gautam et al., 2013).

Results and Discussion

The λ_{max} of metformin HCl was found to be 234 nm by using U.V. spectrophotometer (Systronics 1700 UV-Vis) in linearity range 2-10 µg/ml. Tablet powder blend was subjected to various pre-compression parameters Table 2. The angle of repose values indicates that the powder blend has good flow properties. The bulk density, tapped density, compressibility index and hauser's ratio of all the formulations was found to be within the range and showing that the powder has well flow properties. The results of post-compression parameters such as the uniformity of weight, hardness, thickness, friability and drug content of the tablets are given in Table 3. All the tablets of different batches complied with the official requirements of uniformity of weight. The hardness of the tablets ranged from 4.0 to 5.5 kg/cm^2 and the friability values were less than 0.98% indicating that the tablets were compact and hard. The wetting time of the tablets ranged from 11 to 20 sec. All the formulations satisfied the content of the drug as they contained 94.8to 99.8 % of metformin HCl and good uniformity in drug content was observed. Thus all the physical attributes of the prepared tablets were found be practically within control. The result in vitro disintegration were within the prescribe limit and comply with the criteria for orally disintegrating tablets. The tablets were evaluated for in vitro dissolution studies in0.1N HCl and phosphate buffer pH 6.8 for 15 min. The results of the optimized formulation F5 showed maximum drug release i.e. 98.2±0.007% at the end of 6 min. The results of release studies of all formulations were shown in Table 4.

Table 2 Results of pre-compression parameters of metformin HCl

Formulation code	Parameters			
	Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	4.2	0.54	17.24	1.29
F2	4.5	0.53	16.60	1.28
F3	4.8	0.52	17.63	1.27
F4	4.5	0.53	16.95	1.09
F5	4.9	0.54	17.54	1.26
F6	4.8	0.51	17.12	1.14

Table 3 Results of Post-Compression parameters of all formulations

F. Code	Hardness (kg/cm^2)*	Friability (%)*	Weight variation (%)*	Wetting time (Sec)	Drug content (%)*	Disintegration Time (sec.)*
F1	4.5	0.65	596.3	11	97.3	65
F2	5.0	0.95	602.3	14	99.8	45
F3	4.0	0.58	612.5	15	95.7	50
F4	5.5	0.98	610.0	17	97.8	35
F5	5.0	0.54	607.4	20	94.8	25
F6	4.1	0.75	608.2	15	96.5	45

***Average of three determinations (n=3)**

Table 4 *In-vitro* drug release data for all formulation

F. Code	2min	4min	6min	8min	10min	12min	15min
F1	35.59±0.120	74.07 ±0.02	85.47±0.070	90.82±0.0.120	91.88 ±1.050	99.08±0.070	-
F2	38.93±0.101	74.07 ±1.00	79.76 ±0.101	85.57 ± 0.020	88.76 ±1.00	91.88 ±0.105	99.96 ±0.95
F3	38.32±0.007	79.78±0.07	84.04±0.007	89.02 ± 0.010	92.99±0.007	98.99 ±0.950	-
F4	34.39 ±0.010	70.28 ±0.02	75.34± 0.10	79.21 ± 0.024	82.67 ±0.105	87.93± 0.10	96.95 ±1.05
F5	41.93 ±0.030	77.05 ±0.105	98.2±0.007	-	-	-	-
F6	37.75±0.007	78.05 ±0.03	83.07±0.007	91.78 ±0.007	99.00 ±0.024	-	-

Conclusion

Thus from the whole research work it can be concluded that, the oral fast dissolving tablet of metformin HCl were formulated and evaluated for various parameters. From the compatibility studies by IR of drug it was found to be compatible with other formulation excipients. All evaluation parameters were within specification. The croscarmellose sodium shown faster drug release than crospovidone. Formulation F5 release maximum drug within the 6 mins.ie. 98.2±0.007% and shown minimum disintegration time i.e. 25sec than other formulation and hence considered best formulation.

References

1. Liang, A.C., Chen, L.H. (2001). Fast-dissolving intraoral drug delivery systems. Exp Opin Ther Patents, 11: 981–986.
2. Borsadia, S., O'Halloran, D., Osborne, J.L. (2003). Quick dissolving films-A novel approach to drug delivery. Drug Deliv Technol. 3:63-6.
3. Ansel, H.C., Popvich, N.G., Allen, L.V. (1998). Pharmaceutical Dosage Forms and Drug Delivery System, 1st edition.
4. Jain N.K., Sharma S.N. (1998). A Text Book of Professional Pharmacy, 4th edition.

5. Seager, H. (1998) Drug-delivery Products and the Zydis Fast-dissolving Dosage Form. J Pharm Pharmacol, 50:375-382.
6. Bradoo, R., Shahani, S., Poojary, S., Deewan, B., Sudarshan, S. (2001) Fast Dissolving Drug Delivery Systems. JAMA India, 4(10): 27-31.
7. Kuchekar, B.S., Badhan, A.C., Mahajan H.S. (2004). Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Indian Drugs, 41:592-8.
8. Subramanyam, C.V.S. (2001). Textbook of Physical Pharmaceutics. 3rd ed. Vallabh Prakashan: Delhi, 181-234.
9. Salsa, T., Veiga F., Pina, M.E. (1997). Oral controlled-release dosage forms. cellulose ether polymers in hydrophilic matrices. Drug Dev Ind Pharm, 23:929-938.
10. Khan, A., Pandey, G.K., Joshi, A., Dubey B.K., Jain A.K., Jain P. (2019). Formulation development and evaluation of fast dissolving oral film of a lipid-lowering drug. Asian Journal of Pharmaceutical Education and Research, 8 (1): 12-22
11. Gautam, S.P., Rai, J.P., Bshaiya, U., Jain, N., Vikram, P., Jain, D.K. (2013) Formulation and evaluation of mouth dissolving tablet of loperamide. International Journal of Pharmaceutical Sciences and Research. 4(5): 1782-1788.