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Formulation and *in vitro* evaluation of modified release Gliclazide tablet

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ABSTRACT

In the present work, modified release gliclazide once a daily tablet were designed for non-insulin dependent diabetes for better patient compliance by direct compression method, HPMC was used as polymer, Dibasic calcium phosphate and Maltodextrin as binder for direct compression. Estimation of MR Gliclazide in the prepared tablet formulations was carried out at 226 nm in phosphate buffer pH 7.4. The prepared formulations were further evaluated for hardness, friability, drug content uniformity, in vitro dissolution time. for in vitro drug release pattern in pH 7.4phosphate buffer and short-term stability (at 40ºC/ 75% RH for 3 months) and drug-excipient interaction (IR spectroscopy) were studied. Short-term stability studies on the promising formulations indicated that there are no significant changes in drug content and invitro dissolution time.

Keywords: MR Gliclazide, HPMC, Dibasic calcium phosphate and Maltodextrin.

INTRODUCTION

Modified release (MR) drug products are complex dosage forms designed to release drugs in a controlled manner to achieve desired efficacy and safety profiles. Usually this is to slow the release of the drug so that the medicine doesn't have to be taken too often and therefore improves compliance. The other benefit from modifying release is that the drug release is controlled and there are smaller peaks and troughs in blood levels therefore reducing the chance of peak effects and increasing the likelihood of therapeutic effectiveness for longer periods of time

GLICLAZIDE is used to control blood glucose (sugar) in patients with Type II diabetes mellitus. This type of diabetes is also known as non-insulin dependent diabetes (NIDDM), or maturity-onset diabetes). Why GLICLAZIDE is used for Type II diabetes mellitus. GLICLAZIDE is used when diet and exercise are not enough to control your blood glucose. GLICLAZIDE can be used alone or together with insulin or other medicines for treating diabetes.

Glucose is used by the body as fuel, and all people have glucose circulating in their blood. Diabetes, levels of blood glucose are higher than is needed, which is also known as hyperglycemia. If your blood glucose is not properly controlled, you may experience hypoglycemia (low blood glucose)or hyperglycemia (high blood glucose). High blood glucose can lead to serious problems with our heart, circulation and/or kidneys. It is very important to control high blood glucose whether or not you feel unwell. This really helps to avoid serious long-term health problems, which can involve the heart, eyes, circulation, and/or kidneys.

EXPERIMENTAL SECTION

Gliclazide was gifted sample from zydus-cadila pharmaceutical Ahmedabad, and DCP, Maltodextrin, were gifted sample from Lincoln pharmaceutical limited Ahmedabad.

Preparation of Modified release gliclazide tablet

All ingredients were accurately weighed. Gliclazide, polyvinylpyrrolidone and dibasic calcium hydrogen phosphate dihydrate were sifted through a suitable mesh to obtain a blend. The blend of step 2 was transferred into a granulator and mixed to obtain a homogenous powder mix. The powder mix of step 3 was granulated using purified water. The granules of step 4 were dried in a dryer for suitable time and then screened. Hydroxypropyl methylcellulose K4M CR sifted through a suitable sieve to obtain a blend. Granules of step 5 were mixed with the blend of step 6.Magnesium Stearate and colloidal silicon dioxide were sifted through a suitable sieve, separately, and mixed with the blend of step 7 to obtain a final blend. Tablets were compressed using the final blend of step 8.

Table **1** **Composition of Different Batches of Modified release gliclazide tablet**

Sr.No	Ingredients	G1	G2	G3	G4	G5	G6
1	Gliclazide	60.00	60.00	60.00	60.00	60.00	60.00
2	Dibasic calcium phosphate	53.90	63.90	53.90	53.90	53.90	53.90
3	Maltodextrin	08.00	08.00	12.00	10.00	14.00	13.00
4	HPMC K4M	10.00	05.00	10.00	08.00	13.00	10.00
5	HPMC K100M	15.00	15.00	11.00	15.00	10.00	15.00
6	Aerosil	01.50	01.50	01.50	01.50	01.50	01.50
7	Magnesium Stearate	01.50	01.50	01.50	01.50	01.50	01.50
8	Tartrazine lack color	00.10	00.10	00.10	00.10	00.10	00.10
9	Total	**150**	**150**	**150**	**150**	**150**	**155**

Evaluation of MR Gliclazide tablet

Physical Parameters (Shape, Size, Hardness & Friability)

The punches used to compress the tablets were 7.14mm, standard concave shaped. The shape and size of the tablets were found to be within the limit. The hardness of the tablets was found to be in the range of 6.9 $\pm$ 0.09 to 7.52 $\pm$ 0.29 Kg/ cm^2. It was within the range of monograph specification.

Thicknesses of the tablets were found to be in the range of 3.37 $\pm$ 0.02 to 3.41 $\pm$ 0.01 mm. The friability of the tablets was found to be less than 1% and it was within the range of standard specification.

Weight Variation and Drug Content

Weight variation test helps to check whether the tablet contain proper quantity of the drug. From each of the formulations ten tablets were randomly selected and weighed. The average weights of the tablets were found to be within the prescribed official limit. Drug content for each of the

formulations were estimated. The drug content for all the batches were found to be in the range of 98.12 ± 0.21 to 100.89 ± 0.51%

Table 2 *In vitro* dissolution study

Apparatus	USP XXII Dissolution apparatus
Dissolution medium	Phosphate buffer pH- 7.4
Temperature	37 ± 0.5 ^{0} C
RPM	100
Vol. withdrawn and replaced	5 ml
λ max	226 nm
Blank solution	Phosphate buffer pH- 7.4
Duration of study	24 hrs
Volume of dissolution media	900 ml

In-vitro drug release studies were carried out using USP XXII dissolution apparatus type II (Electro lab, Mumbai, India) at 100 rpm. The dissolution medium consisted of 900 ml of pH 7.8 phosphate buffer, maintained at 37 ± 0.5^{0}C. The drug release at different time intervals was measured using an ultraviolet visible spectrophotometer (Labindia, Mumbai, India) at 226 nm. The study was performed in triplicate.

FTIR study

FTIR spectra of the selected formulation were taken and compared with the spectrum of pure drug. The characteristic peaks of drug were checked in the formulation spectra.

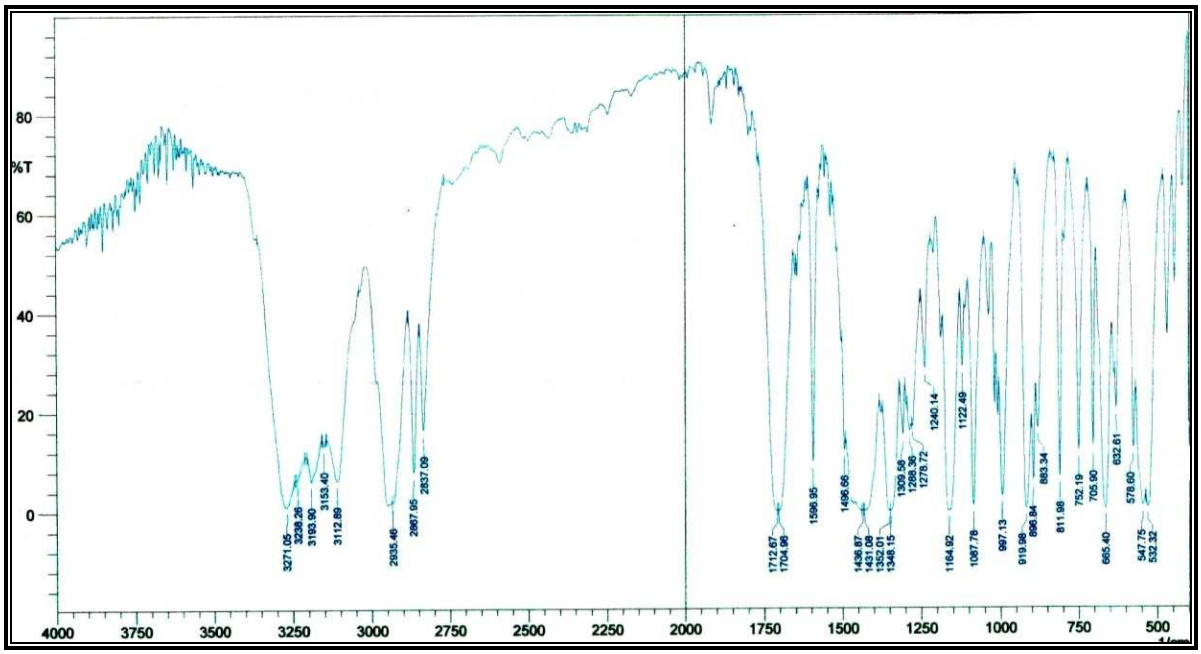

Figure 1.1 FTIR spectra of Gliclazide

Stability study

Stability studies of pharmaceutical products were done as per ICH guide lines. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions.

Method: Selected formulations were stored at different storage conditions at elevated temperatures such as $25^{o}C\pm 2^{0}C$ / 60% ± 5% RH, $30^{0}C \pm 2^{0}C$ / 65% ±5% RH and $40^{0}C \pm 2^{0}$ / 75% ± 5% RH for 90 days. The samples were withdrawn at intervals of fifteen days and checked for physical changes, hardness, friability, drug content and percentage drug release

RESULTS AND DISCUSSION

Oral route of administration is the most widely accepted route of delivery due to the ease of administration, avoidance of pain and other risks of parenteral administration and has good patient compliance. The main advantage of the oral sustained release dosage form is that it maintains the therapeutic concentration over an extended period of time. Several new technologies have been developed to overcome the physicochemical and pharmacokinetic characteristic of drugs, while improving the patient compliance. One of these technologies is the matrix type of dosage forms.

Evaluation parameters for MR Gliclazide tablet

Table 3 Physical appearance of optimized formulations after stability studies

Temp. and relative humidity	F-5 and F-10							Parameters
	Days							
	0	15	30	45	60	75	90	
25°C± 2°C / 60% ± 5% RH	No change							Physical appearance
35°C± 2°C / 65% ± 5% RH								
40°C± 2°C / 60% ± 5% RH								

Table 4 **Results For the optimized formulation**

Parameter	Formulation code		
	G2	G4	G6
Hardness	7.23 ± 0.72	7.46 ± 0.76	7.5 ± 0.10
Thickness	3.2	3.1	3.2
Friability	0.174	0.169	0.185
Percent drug content	93.55	96.75	97.75

CONCLUSION

The present study conclusively indicates that formulation G6 is very much promising very much drug release than formulation G2 and G54in invitro dissolution study.

REFERENCES

[1] Aulton ME. Pharmaceutics- The science of dosage form design. 2nd ed. London: ELBS/ Churchill Livingstone; **2002**. p. 4.
[2] Remington. The science and practice of pharmacy. 20th ed. Vol. 1. New York: Lippincott Williams and Wilkins; **2000**. p. 903.
[3] N,K.Jain Controlled and novel drug delivery. 1st Ed. New Delhi: CBS Publications; **2004**. p. 1-2.
[4] A.R. Gennaro Extended Release Dosage Forms. In: Remington: The Science and Practice of Pharmacy. 20th ed. vol 1. U.S.A: Lippincott Williams and Wilkins; **2000**. p. 660-63.
[5] Sansom Lloyd N. Oral extended-release products. In: Therapeutic Guidelines Ltd, **1999**; 22: 88-90.

[6] Gilbert S, Banker, Christopher T, Rhodes. Modern Pharmaceutical. 3rd ed. p. 576-8 .
[7] JR, Robinson Lee VHL. Controlled drug delivery and fundamentals applications. 2nd ed. New York: Marcel Dekker; **1987**. p. 7.
[8] Lachman Leon, Lieberman Herbert A. Pharmaceutical Dosage Forms: Tablets. In: The Theory and Practice of Industrial Pharmacy. 2nd ed. Vol 1. U.S.A: Lea and Fibiger; **2002**. p. 247-84.
[9] Robinson JR, Eriksen, *J.Pharm.Sci*. **1966**; 55: 1254.
[10] Gennaro AR. Remington. The Science and Practice of Pharmacy. 19th ed. Vol. II, **1995**. p. 1662.
[11] Vyas SP, Khar RK. Controlled drug delivery: concepts and advances. 1st ed. Delhi; Vallabh Prakashan: **2002**.
[12] Prithiviraj A, Bhaskar K, Ramachandran S, Saravanan M, Vinod R. Eudragit, *Chem. Parma Bull.* **2002**; 50(11):1495-8.
[13] Ballagi-Pordány G, Köszeghy A, Koltai MZ, Aranyi Z, Pogátsa G (January **1990**). *Diabetes Res. Clinical. Pract.* **8** (2): 109–14.
[14] Shimoyama T, Yamaguchi S, Takahashi K, et al (**2006**). *Metabolism - Clinical and Experimental* **55** (6): 722–30.
[15] Rieutord A, Stupans I, Sheffield GM, Gross AS. *Xenobiotica* **1995**; 25: 1345–54.
[16] Identification of the human cytochromes P450 catalyzing the rate-limiting pathways of gliclazide elimination. Elliot DJ, Suharjono, Lewis BC, Gilliam EM, Birkett DJ, Gross AS, Miners JO. *Br J Clinical Pharmacology*. **2007** Park JY, Kim KA, Park PW, Park CW, Shin JG. Effect of rifampin on the pharmacokinetics and pharmacodynamics of gliclazide. *Clinical Pharmacology There* **2003**; 74: 334–40.