CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1435088

Available online at: http://www.iajps.com Research Article

GASTRO RETENSIVE DRUG DELIVERY OF GLIMEPIRIDE BY FLOATATION-MUCOADHESION TECHNOLOGY

Vandana K*, Thushara B S, Rajitha K, Praseetha K

Department of Pharmaceutical Chemistry, National College of Pharmacy,
Kozhikode 673602, Kerala, India

Abstract:

Glimepiride is a FDA approved sulphonyl urea oral antidiabetic drug, which has rapid and complete absorption after oral administration. Diabetics affect the gastric emptying rate thus incomplete absorption of the drug is often accompanied by lesser bioavailability. Currently several studies were carrying out for increasing the bioavailability as well as for shortening the frequency of drug administration using mucoadhesive and floating technologies. In our studies an attempt is made to combine both mucoadhesive and floating technology to achieve targeted controlled drug delivery in the stomach. Floating and mucoadhesive tablets of Glimepiride were developed with an aim of improving the patient compliance by decreasing the frequency of administration and to enhance bioavailability. Floating-mucoadhesive Glimepiride tablets were prepared using polymers such as Carbopol, HPMC and Methyl cellulose by direct granulation method. The fabricated tablets showed acceptable weight variation, hardness and friability. The effect of floating lag time was studied for these formulations and found to be different for each samples. Formulation S2 having HPMC as polymer shows appreciable floating lag time of 2 min. Invitro Dissolution studies were performed for all the formulations for 48 hours and formulation containing combination of all three polymers S3 achieved the objective of targeted controlled release for 48 hours.

Keywords: *Glimepiride, Floating-mucoadhesive technique, Dissolution, HPMC, Carbopol.*

Corresponding author:

Vandana K,

Department of Pharmaceutical Chemistry
National College of Pharmacy
Manassery (po), Mukkom
Kozhikode 673602
Kerala
Email:- vandanaksuresh@gmail.com

QR code

Please cite this article in press Vandana K et al., ***Gastro Retensive Drug Delivery of Glimepiride by Floatation-Mucoadhesion Technology.,*** *Indo Am. J. P. Sci, 2018; 05(09).*

INTRODUCTION:

Floating-mucoadhesive drug delivery systems mainly focus on the principle mechanism of floatation – mucoadhesion to achieve gastric retention. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drug. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drug that is less soluble in a high pH environment. C. Rubina et al. 2011, developed floating matrix tablets of Glimepiride to prolong the gastric residence time and there by increased drug bioavailability.

Floating and mucoadhesive tablets of Glimepiride were developed with an aim of improving the patient compliance by decreasing the frequency of administration and to enhance bioavailability. In present work an attempt is made to find out whether the combination or single polymer is better to formulate mucoadhesive tablets of Glimepiride.

OBJECTIVES

To formulate floating mucoadhesive tablets of Glimepiride with an aim of

- Improving patient compliance by decreasing the frequency of administration.
- To achieve targeted controlled drug delivery in the stomach and thus improving the bioavailability of the drug.
- To sustain the delivery of drug up to 48 hrs

MATERIALS AND METHODS:

Glimepiride was supplied by Sangrose laboratories pvt (Alappuzha, kerala) ltd and polymers, carbopol obtained from Medilise chemicals (Kannur, Kerala), HPMC from Ozone international laboratory (Mumbai). All the chemicals and products used in this study comply with the pharmaceutical and analytical standards respectively.

Here the research works was carried out at Devaki amma Memorial College of pharmacy, Malappuram, Kerala during year 2013.

1) UV Spectrum: UV spectroscopy is concerned with the study of absorption of UV radiation which ranges from 200nm to 400nm. The drug Glimepiride was subjected to UV spectral analysis, to obtain its maximum absorbance wavelength.
2) Calibration of standard curve of Glimepiride
   a) Preparation of sodium acetate buffer solution (p^H 2.8)
   Place 2g sodium acetate in 50ml distilled water. Add 5ml dimethyl formamide into the solution. Then add glacial acetic acid into the solution till it reaches p^H 2.8. Finally it made up the volume with distilled water.
   b) Preparation of stock solution
   A stock solution was prepared by dissolving 100mg Glimepiride powder in 5ml dimethyl formamide and make up the solution into 100ml with sodium acetate buffer solution (A). From solution A prepared series of std solutions ranging from 10, 20, 30, 40, 50µg/ml. At 241nm the absorbance is measured and plot the graph, concentration vs absorbance.

Glimepiride drug sample was standardized and validated by using UV spectroscopy at 241nm. 4 different tablet compositions was prepared by direct granulation method.

3) Formulation of tablets

Sample	Carbopol	Methyl cellulose	HPMC	Tartaric acid	Glimepiride	Magnesium stearate	$NaHCO_3$	Talc
SAMPLE1	46mg	20mg	-	80mg	4mg	5mg	45mg	50mg
SAMPLE2	-	20mg	46mg	80mg	4mg	5mg	45mg	50mg
SAMPLE3	23mg	20mg	23mg	80mg	4mg	5mg	45mg	50mg
SAMPLE4	-	66mg	-	80mg	4mg	5mg	45mg	50mg
SAMPLE5	66mg	-	-	80mg	4mg	5mg	45mg	50mg
SAMPLE6	-	-	66mg	80mg	4mg	5mg	45mg	50mg

4) Evaluation of Glimepiride formulation
Glimepiride tablets was evaluated for following physical properties
Physical analysis is done by Hardness test, Weight variation test, Floating lag time, Friability and Dissolution test.

a) Hardness test – Tablets required a certain amount of strength of hardness and resistant to friability to withstand mechanical stock of handling in manufacture, packing and shipping. The monitoring of tablets is defined, as force required breaking a tablet in diametric compression test. Tablet hardness tester (Monsanto tester) is used to measure the degree that required breaking the tablet in diametric compression. The force is measured in kilogram.

Procedure – Monsanto hardness tester has a spring and graduated scale with coding in kg/cm^2. The tablet to be placed in between the hardness tester. The scale is moved by the pressure is then applied till it break. The reading is noted which indicate the pressure or force required to break.

b) Weight variation – when a tablet is designed, it will contain a specific amount of drug in specific amount of tablet formula. The weight of the tablet being made in routinely measured to ensure that a tablet contain a proper amount of drug. The weight variation test should be a satisfactory method of determining the drug content uniformity problem in tablet.

Percentage deviation

$$= \frac{Average\ weight\ of\ tablets - Individual\ weight\ of\ tablet}{Average\ weight\ of\ tablets} \times 100$$

Procedure – Select 20 tablets and determine its average weight. Weigh each individual tablet separately. Calculate the weight variation and percentage deviation. From the interpret the test by criteria given in IP, not more than two of the individual weight divides from average weight by more than percentage.

c) Floating lag time – The floating lag time is the time required for the tablets to rise to the surface and float. Floating lag time is also called as Buoyancy. Lag time is the time period between placing the tablet in medium and time of tablet floating in media. The medium used is 0.1N HCl of p^H 2.

Procedure – The prepared floating mucoadhesive tablets of Glimepiride were subjected to the buoyancy test. The tablets were placed in 100ml glass beaker containing 0.1 N HCl and the time required for the tablet to rise to the surface and float was determined as floating lag time.

d) Friability test – Roche Friabilator apparatus determines the tablet friabilities or tendency to crumble by allowing it or roll with in the drum. Resistance to loss of weight indicates the tablets ability to withstand abrasion during handling, packing and shipment. A minimum weight loss of volume more than 1% generally is considered acceptable for most products. Drum rotates at 25±1rpm.

Percentage friability = $\frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$

Procedure – 10 tablets were selected from each batch and weighted. Then tablets were rotated at 25rpm for 4 min. The tablets were then will dust and re-weighed to determine the loss in weight.

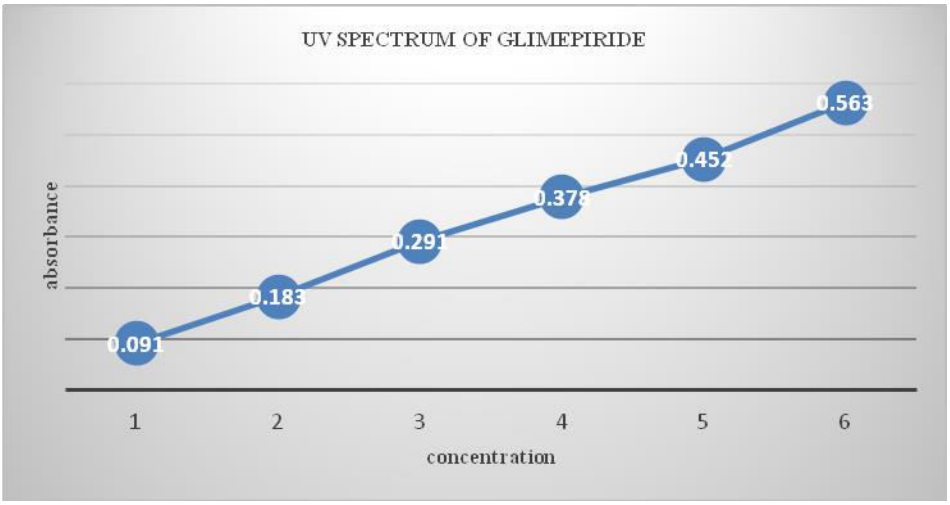
e) Dissolution test – The rate of drug absorption for acidic drug moieties that are absorbed high in the GI tract is often determined by the rate of drug dissolution from the tablet. The rate of dissolution may thus be directly related to the tablet product as well as to bioavailability difference between formulations. Dissolution carried out in dissolution apparatus.

Procedure – The tablet is placed in a wire mesh basket fastened to the bottom of the shaft connected to a variable speed motor. The basket is immersed in the sodium acetate buffer solution contained in a 100ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at 37°c±0.5 by a constant temperature bath. The motor is adjusted to turn at the specified speed, and samples of the fluid are withdrawn at intervals of 30 min, 1hr, 2hr, and 3hr to 48hrs to determine the amount of drug in solution.

RESULTS:

Spectral analysis: UV Spectroscopy
Method:
prepare 100µg conc stock solution in pH 2.8 using sod.acetate buffer adding 5 drops of dimethylformamide.
Glimipride max abs (λmax) = 0.659 at 241.5nm.

SL.No	Concentration (µg)	Absorbance
1	1	0.091
2	2	0.183
3	3	0.291
4	4	0.452
5	5	0.563



PHYSICAL ANALYSIS

AVERAGE HARDNESS & WEIGHT VARIATION

SAMPLE NO	AVERAGE HARDNESS	WEIGHT VARIATION
S1	4.5 kg/cm^2	220mg to 232mg
S2	3 kg/cm^2	232mg to 240mg
S3	3.83 kg/cm^2	227mg to 235mg
S4	3.16 kg/cm^2	240mg to 245mg

FRIABILITY TEST

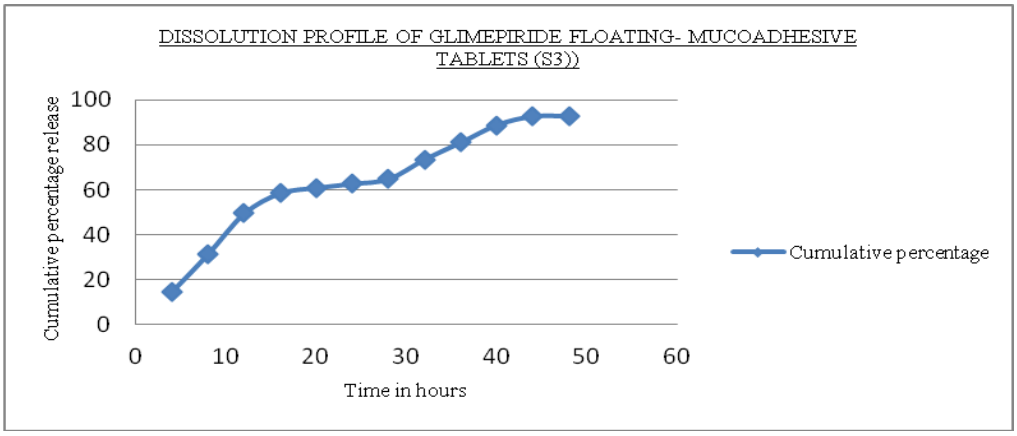
SAMPLE NO	Rpm	No of rotation	Time taken	Initial weight	Final weight	Weight loss	Percentage friability
S1	25	100	4 min	2.21g	2.20g	0.01g	0.45%
S2				2.64g	2.62g	0.02g	0.75%
S3				2.40g	2.39g	0.01g	0.41%
S4				2.53g	2.50g	0.03g	1.18%

FLOATING LAG TIME (Buoyancy test)

SAMPLE NO	FLOATING LAG TIME (min)
S1	8
S2	2
S3	10
S4	No floating

DISSOLUTION STUDY (*In vitro* release for S3)

Time in hours	Absorbance	Concentration (µg/ml)	Amount of drug (mg/ml)	Percentage release	Cumulative percentage release (%)
1	0.009	0.1	0.0001	0.09	4.05
10	0.102	1.1	0.0011	0.99	49.5
20	0.122	1.35	0.00135	1.2186	60.93
40	0.146	1.97	0.00197	1.7762	88.81
48	0.153	2.059	0.002059	1.8536	92.68



DISCUSSION:

Floating mucoadhesive Glimepiride tablets were prepared by direct granulation method and carried out various physical analyses. The tablets of different batches were found uniform with respect to hardness within the range of 3-4.5 kg/cm^2 indicating that tablets has sufficient strength to withstand during packaging and transportation. The weight variation was found to be within the range of ±5 which indicating prepared tablets has uniformity in drug content and weight. It was observed that formulation S1 contains carbopol as polymer and S3 containing the combination of polymers, showing floating lag time of 6hr and 8hr. This may be due to the little amount of polymeric material; therefore unable to hold the carbon dioxide within the tablet matrix as a result they are taking more time to float. Whereas the S2 formulations having HPMC as polymer shows appreciable floating lag time of 2 min. The percentage friability was found to be within the limit of not more than 1% which indicating that the prepared tablets have sufficient friability. In vitro test serve as a guide in estimating the amount of drug released with respect to time. Formulation S3 showed a release of 92% at 48 hr, which may be due to the strong combined binding effect of three polymers, methyl cellulose, HPMC and Carbopol.

CONCLUSION:

Glimepiride is a FDA approved sulphonyl urea oral antidiabetic drug, which has rapid and complete absorption after oral administration. Diabetics affect the gastric emptying rate thus incomplete absorption of the drug is often accompanied by lesser bioavailability. Currently several studies were carrying out for increasing the bioavailability as well as for shortening the frequency of drug administration using mucoadhesive and floating technologies. In our studies an attempt is made to combine both mucoadhesive and floating technology to achieve targeted controlled drug delivery in the stomach. Floating and mucoadhesive tablets of Glimepiride were developed with an aim of improving the patient compliance by decreasing the frequency of administration and to enhance bioavailability. Floating-mucoadhesive Glimepiride tablets were prepared using polymers such as Carbopol, HPMC and Methyl cellulose by direct granulation method. The fabricated tablets showed acceptable weight variation, hardness and friability. The effect of floating lag time was studied for these formulations and found to be different for each samples. Formulation S2 having HPMC as polymer shows appreciable floating lag time of 2 min. Invitro Dissolution studies were performed for all the

formulations for 48 hours and formulation containing combination of all three polymers S3 achieved the objective of targeted controlled release for 48 hours.

ACKNOWLEDGEMENTS:

This work was entirely dedicated to Devaki amma Memorial College of pharmacy, Malappuram, Kerala for their guidance and valuable cooperation in my research work

REFERENCES:

1. Ghada E Yassin, Afaf A Ramadan. Box-Behnken experimental design in development of Glimepiride floating matrix tablets. Journal of applied science research, 2012.
2. Palamakula A, Mohamad T H N, Khan M A. Response surface methodology for optimization and characterization of limonene based coenzyme Q 10 self nanoemulsified capsule dosage form. AAPS Pharm Sci Tech, 2004; 5(4): 66.
3. Panchagnula R, Singh R, Ashok raj Y. In vitro evaluation of modified release formulations od nifedipine from indian market. Ind J Pharm Sci, 2007.
4. Rosa M, Zia H, Rhodes T. Design and testing in vitro of bioadhesive and floating drug delivery system for oral application. Int J Pharm, 1994; 105: 65-70
5. Rubina R C, Bhagya L J, Ravi T K. Studies on formulation and in vitro evalution of Glimepiride floating tablets. J Chem Pharm Res, 2011; 3(3): 159-164.
6. Shweta A, Javerd A, Alka A, Roop K K, Sanjulam B. Floating drug delivery system: A review. AAPS Pharm SciTech, 2005; 2(6): 65-69.