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PREPARATION AND EVALUATION OF GLIPIZIDE MUCOADHESIVE MICROSPHERES

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ABSTRACT

Bioavailability is an important quality attribute of pharmaceutical dosage forms. Bioavailability is generally improved by gastro-retentive drug delivery systems. Mucoadhesive dosage forms occupy prominent part of these novel drug delivery systems. Glipizide mucoadhesive microspheres were prepared by orifice-ionic gelation technique employing sodium carboxymethyl cellulose and oats powder as mucoadhesive polymers. A total of seven formulae were designed and all the prepared microspheres were subjected to flowability, particle size, percent yield, encapsulation efficiency, *in-vitro* wash off test, and *in-vitro* dissolution study. Encapsulation efficiency was present in the range of 85.4% to 89.8%. Microspheres containing oats powder exhibited better mucoadhesive property compared to those containing sod CMC. However in microspheres containing oats powder the drug release was completed within 8-10 hours without sustaining the drug release up to 12 hours. The optimised formulation F₇ containing combination of sod CMC and oats powder showed the best results for mucoadhesion and sustained release up to 12 hours. Oats powder was found to be a promising mucoadhesive polymer in the present work. The drug release from all the prepared microspheres followed first order kinetics and diffusion mechanism.

Keywords: Sustained release, Glipizide, Mucoadhesive microspheres, ionic gelation technique, *in-vitro* wash-off test

INTRODUCTION

Mucoadhesive drug delivery systems offer several advantages over other oral controlled release systems by virtue of prolongation of residence time of drug in gastrointestinal tract. They can prevent first-pass metabolism. Mucoadhesive microspheres [1-5] are promising drug carrier systems used not only for sustained release but also for improved bioavailability. Mucoadhesive systems utilize the property of bioadhesion [6], which is a phenomenon in which two materials at least one of which is biological in nature are held together by means of interfacial forces. Microspheres are small spherical particles (typically 1 to 1000 μm), sometimes referred to as microparticles. The microspheres can be made up of either natural or synthetic polymers [7]. Bhabani S Nayaket *al.* prepared and characterized Famotidine microcapsules [8] employing carbopol 934 and HPMC, carbopol and methyl cellulose, carbopol and guar gum combinations. Koland Marina *et al.* formulated mucoadhesive microspheres of Famotidine for gastroretentive drug delivery. The microspheres of Famotidine were prepared by emulsification ionic-gelation technique using mucoadhesive polymers such as sodium alginate, carbopol 934 and HPMC in different ratios [9].

Glipizide is a second-generation sulfonylurea that lower the blood glucose level in humans by stimulating the release of insulin from the pancreas and is typically prescribed to treat type II diabetes (non-insulin dependent diabetes mellitus). It shows a short biological half-life of 3.4 ± 0.7 hours [10]. Thus, the development of controlled-release dosage forms would clearly be advantageous. Researchers have formulated oral controlled-release products of glipizide by various techniques. Moreover, the site of absorption of glipizide is in the stomach. Dosage forms that are retained in the stomach would increase the absorption, improve drug efficiency, and decrease dose requirements.

Mucoadhesive microspheres are controlled and targeted drug delivery systems and prepared as matrix encapsulated spheres which increase drug bioavailability and dose dumping does not occur. Mucoadhesive microspheres have many advantages as unit dosage form i.e, patient compliance and high bioavailability and rapid absorption as well as avoidance of first pass metabolism. The present work was envisaged to reduce the dosing frequency and improve oral bioavailability by designing and evaluating sustained release mucoadhesive microspheres of Glipizide for effective control of gastric

ulcers. In the present investigation a total of 7 formulae were designed and developed. The formulae contain sodium alginate as coating agent and oats powder and Sodium CMC as mucoadhesive agents. Oats powder was tried as a new mucoadhesive agent in the present study.

MATERIALS AND METHODS

MATERIALS

Glipizide and Sodium alginate were procured from Yarrow chemical products, Mumbai. Oats powder was procured from Local Market, Quaker brand. Sodium CMC and Hydrochloric acid were procured from Qualigens. Calcium chloride was procured from Fisher Scientific. All the materials used were of pharmacopoeial grade.

METHODS

A) Preparation of Glipizide mucoadhesive microspheres:

Microspheres were prepared by using sodium alginate as coat material and Sod. CMC and oats powder as mucoadhesive polymers. The technique used for this process is orifice-ionic gelation method. The detailed procedure for formulation-1 is given below. Materials for 25 doses were taken in this procedure. The drug: coat polymer: mucoadhesive polymer were present in the ratios of 1:1:0.5, 1:1:1, 1:1:1.5 in different formulations.

1 gm of sodium alginate and 0.5 gm of sodium CMC were taken in a clean and dry mortar. About 50 ml of water was added slowly in small quantities and triturated until a good pourable mucilage was obtained. To this polymer dispersion 1 gm of glipizide and 1.5 gm of lactose were added and triturated thoroughly to get smooth viscous dispersion. By using syringe with needle no.18 gauge the dispersion was added dropwise into 100 ml of 10% w/v calcium chloride solution. These liquid droplets were retained in the solution for 30 minutes to complete reaction and to get rigidity. These microspheres were separated by decantation and thoroughly washed with distilled water and petroleum ether and dried for 12 hours at 50°C in the oven. After completion of drying, the microspheres were collected, weighed and labelled properly. They were stored in the desiccator for further use. All the other formulations were prepared in similar procedure by taking the materials as given in **Table 1**. Lactose was included as a diluent to maintain constant weight of granules which contain equal amount of drug.

B) Evaluation of mucoadhesive microspheres:

1) Flow properties

a) Angle of repose

A funnel was fixed to a stand at certain height from the surface. 5 gm of

microspheres were passed from the funnel, so that they form a pile. The height and the radius of the heap was measured and angle of repose [11] was calculated by

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

Where, θ =angle of repose, h = height, r = radius

b) Bulk density and tapped density

Accurately weighed 5 gm microspheres were transferred to a graduated cylinder to measure bulk volume. The measuring cylinder was tapped for 200 times and tapped volume was measured. Then the bulk density and tapped density were calculated by:

$$\text{Bulk density } (\rho_b) = \frac{\text{Weight of microspheres (g)}}{\text{Bulk volume } (v_b) \text{ (ml)}}$$

$$\text{Tapped density } (\rho_t) = \frac{\text{Weight of microspheres (g)}}{\text{Tapped volume } (v_t) \text{ (ml)}}$$

c) Carr's index

Carr's index was calculated by

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

d) Hausner's ratio

Hausner's ratio was calculated by

$$\text{Hausner's Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

2) Particle size measurement

To determine the particle size of mucoadhesive microspheres, 100 microspheres from each formulation were

measured using an optical microscope at a magnification of 50x (Eye piece magnification=10x and objective magnification=5x) with an ocular micrometer which was calibrated using a stage micrometer (Erma, Tokyo). The average size of microspheres can be given by the following formula.

$$\text{Average size} = \frac{\sum nd}{\sum n}$$

Where, **n** is the number of microspheres and **d** is the size of microsphere.

3) Percentage yield

The microspheres were evaluated for percentage yield. The yield was calculated as per the equation given below.

$$\text{Percentage Yield} = \frac{\text{Weight of microspheres recovered}}{\text{Weight (drug + polymer)}} \times 100$$

4) Encapsulation efficiency

100 mg of drug equivalent microspheres were taken in a mortar and crushed into a fine powder. 2 to 3 drops of glacial acetic acid was added and transferred into 100 ml volumetric flask and the volume was made up to 100 ml with pH 7.4 phosphate buffer to get 1000 µg/ml. From this solution, 10 ml was taken in 100 ml volumetric flask and the volume was made up to 100 ml with pH 7.4 phosphate buffer to get 100 µg/ml and the solution was filtered and from the filtrate 1ml was taken in 10 ml volumetric flask and

the volume was made up to 10ml with pH 7.4 phosphate buffer to get 10 µg/ml and absorbance was measured at λ_{\max} of 276nm. Encapsulation efficiency was calculated by the following formula

$$\text{Encapsulation efficiency} = \frac{\text{Estimated drug content}}{\text{Theoretical drug content}} \times 100$$

5) *In vitro* wash-off test

The mucoadhesive property of the microspheres was evaluated by an *in vitro* adhesion testing method known as wash-off method [12]. A piece of goat intestinal mucus (2x2cm) was mounted onto glass slide with elastic bands. Glass slide was connected with a suitable support. About 50 microspheres were spread onto each wet tissue specimen, and there after the support was hung onto the arm of a USP tablet disintegration test machine (Veego). The disintegration machine containing tissue specimen was started to move up and down in 0.1 N HCl at 37°C taken in a beaker. At the end of 8 hours the machine was stopped and the number of microspheres still adhering onto the tissue was counted.

$$\% \text{ Mucoadhesion} = \frac{\text{No. of microspheres remains}}{\text{No. of applied microspheres}} \times 100$$

6) *In vitro* dissolution test

The release of glipizide from the prepared microspheres was studied using USP-Type II basket apparatus [13]. Drug release test was carried out in 900ml of pH 7.4

phosphate buffer maintained at $37 \pm 0.5^\circ \text{C}$ temperature at 50 rpm. 40 mg of microspheres equivalent to 10 mg (one dose) of glipizide were taken for the test. Three trials were carried out for each formulation. 5ml of samples were withdrawn at regular time intervals and the test was carried upto 12 hours. The samples were analysed at λ_{\max} of 276 nm by UV spectrophotometer (ELICO-SL 159). Different graphs were constructed from the obtained data.

RESULTS AND DISCUSSION:

The present work was ultimately aimed at reducing the dosing frequency and improving oral bioavailability by designing and evaluating sustained release mucoadhesive microspheres of glipizide for effective control of diabetes.

Sodium alginate was used in combination with the mucoadhesive polymers in the ratios of 1:0.5, 1:1 and 1:1.5. All the formulations produced discrete microspheres of uniform size and almost spherical shape. The relevant evaluation tests were performed for the microspheres and all the obtained data was given in the form of mean \pm standard deviation.

The microspheres prepared were evaluated for flow properties, the results were shown in **Table 2**. The results indicated that the microspheres prepared exhibited

excellent flow properties. The results of particle size, percent yield and encapsulation efficiency data were shown in **Table 3**. The size of the microspheres was present in the range of 1067-1124 μm . The encapsulation efficiency was present in the range of 85.4% to 89.3%. The percent yield values were present in the range of 89.2 ± 3.46 to 95.6 ± 4.35 .

Mucoadhesion strength was determined by *in vitro* wash off test. Formulations F₄-F₆ containing the oats powder (**Table 4**) showed superior mucoadhesion strength compared to F₁-F₃ formulations containing sodium CMC. As the viscosity of the polymer increases, swelling increases and mucoadhesion depends on the swelling of the gum. This improves the consolidation step that increases the mobility of the molecules and facilitates the interpretation with mucus layer, thus mucoadhesion increases. The polymer dissolves in presence of water. As the hydrophilicity of the polymer increases, the interaction between water and hydrogel will increase too, this facilitates water diffusion and leads to greater swelling [14].

The results of *in vitro* drug release studies were shown in figures 1, 2 and 3. Microspheres prepared using different ratios

of sodium alginate and mucoadhesive polymer showed drug release for a period of 8 -12 hours respectively. In formulations F₄-F₆ the total amount of the drug was dissolved within 8-10 hours. In F₃ only 88.60% of the drug was dissolved within 12 hours. Although formulation F₁ showed 98.42% drug dissolved in 12 hours, its mucoadhesive strength was low and present around 82%. The drug release retardation was higher in case of formulations containing sodium CMC compared to those containing oats powder. However the mucoadhesion strength was lower for sodium CMC polymer. Hence formulation F₇ was developed containing sodium CMC and oats powder in combination. Formulation F₇ showed drug release upto 12 hours and superior mucoadhesive property also. Hence Formulation F₇ was considered as the best formulation in this study.

To ascertain the kinetics and mechanism of drug release, the dissolution data was analysed by first order and Higuchi equations and corresponding (**Figures 2 and 3**) graphs were plotted. The drug release kinetics followed first order as the correlation coefficient values obtained were higher as shown in table 5. Drug release followed Higuchi diffusion mechanism [15, 16].

Table 1: Composition of Glipizide mucoadhesive microspheres

Ingredients (gm)	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆	F ₇
Glipizide	1	1	1	1	1	1	1
Sodium Alginate	1	1	1	1	1	1	1
Sodium CMC	0.5	1	1.5				0.5
Oats Powder				0.5	1	1.5	0.5
Lactose	1.5	1	0.5	1.5	1	0.5	1
Purified Water (ml)	50	50	50	50	50	50	50

Table 2: Flow properties of Glipizide microspheres

Formulation	Evaluation parameters (Mean \pm SD)				
	Angle of repose (θ)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's Index (%)	Hausner's ratio
F ₁	11.12 \pm 0.12	0.62 \pm 0.018	0.64 \pm 0.018	4.46 \pm 0.16	1.04 \pm 0.012
F ₂	11.34 \pm 0.12	0.69 \pm 0.016	0.73 \pm 0.020	5.56 \pm 0.14	1.05 \pm 0.019
F ₃	11.85 \pm 0.18	0.62 \pm 0.018	0.69 \pm 0.016	8.98 \pm 0.18	1.09 \pm 0.013
F ₄	13.49 \pm 0.19	0.66 \pm 0.017	0.71 \pm 0.018	6.75 \pm 0.15	1.07 \pm 0.013
F ₅	14.03 \pm 0.20	0.55 \pm 0.015	0.62 \pm 0.018	10.61 \pm 0.20	1.11 \pm 0.019
F ₆	15.64 \pm 0.15	0.56 \pm 0.015	0.64 \pm 0.018	12.75 \pm 0.36	1.14 \pm 0.018
F ₇	16.17 \pm 0.16	0.55 \pm 0.015	0.63 \pm 0.017	11.42 \pm 0.40	1.12 \pm 0.017

Table 3: Particle size of Glipizide microspheres

Formulation	Particle size (μ m)	Percentage yield (%)	Encapsulation efficiency (%)
F ₁	1124 \pm 22	89.2 \pm 3.46	85.6 \pm 2.56
F ₂	1117 \pm 19	94.2 \pm 2.57	87.4 \pm 3.42
F ₃	1096 \pm 18	94.2 \pm 4.44	89.3 \pm 2.42
F ₄	1101 \pm 21	91.2 \pm 2.49	88.2 \pm 2.46
F ₅	1088 \pm 20	93.2 \pm 2.08	89.8 \pm 1.26
F ₆	1067 \pm 24	92.7 \pm 1.89	86.2 \pm 2.24
F ₇	1094 \pm 19	95.6 \pm 4.35	85.4 \pm 2.32

Table 4: *In - vitro* wash off test (Mean \pm SD)

Formulation	Zero order	First order	Higuchi
F ₁	0.930	0.991	0.978
F ₂	0.940	0.993	0.983
F ₃	0.910	0.981	0.967
F ₄	0.761	0.814	0.858
F ₅	0.831	0.892	0.909
F ₆	0.862	0.960	0.983
F ₇	0.900	0.989	0.989

Table 5: Correlation coefficient values of drug release kinetic data fitted to various models

Formulation	Mucoadhesion (%)
F ₁	82 \pm 2.46
F ₂	86 \pm 1.15
F ₃	87 \pm 1.28
F ₄	92 \pm 3.46
F ₅	94 \pm 1.18
F ₆	94 \pm 1.26
F ₇	94 \pm 1.48

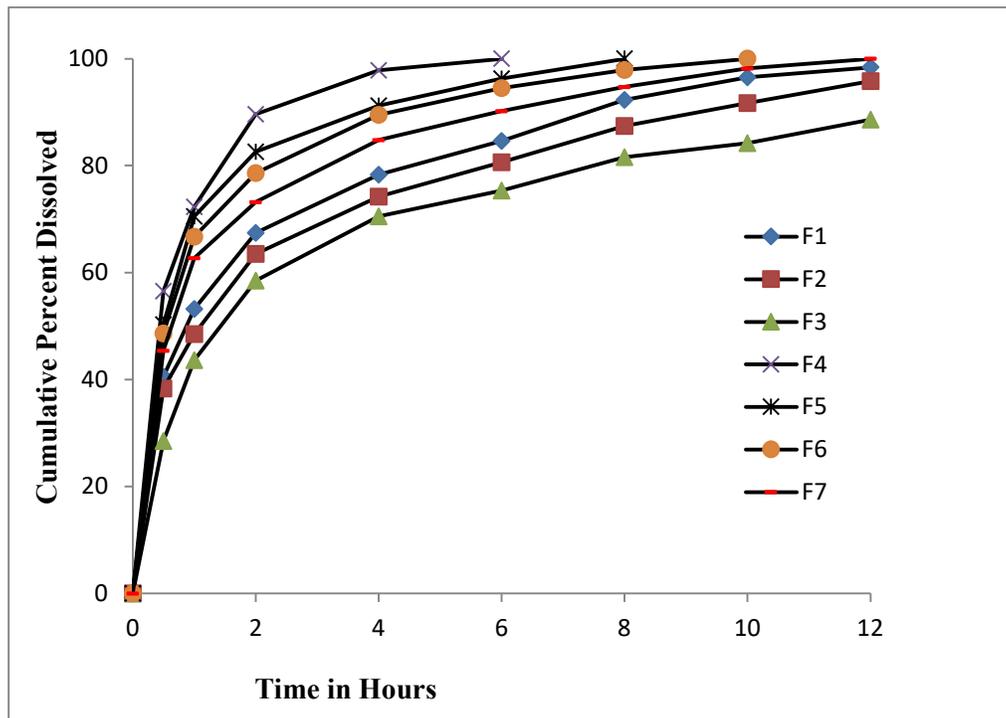


Figure 1: Drug release profiles of Glipizide mucoadhesive microspheres

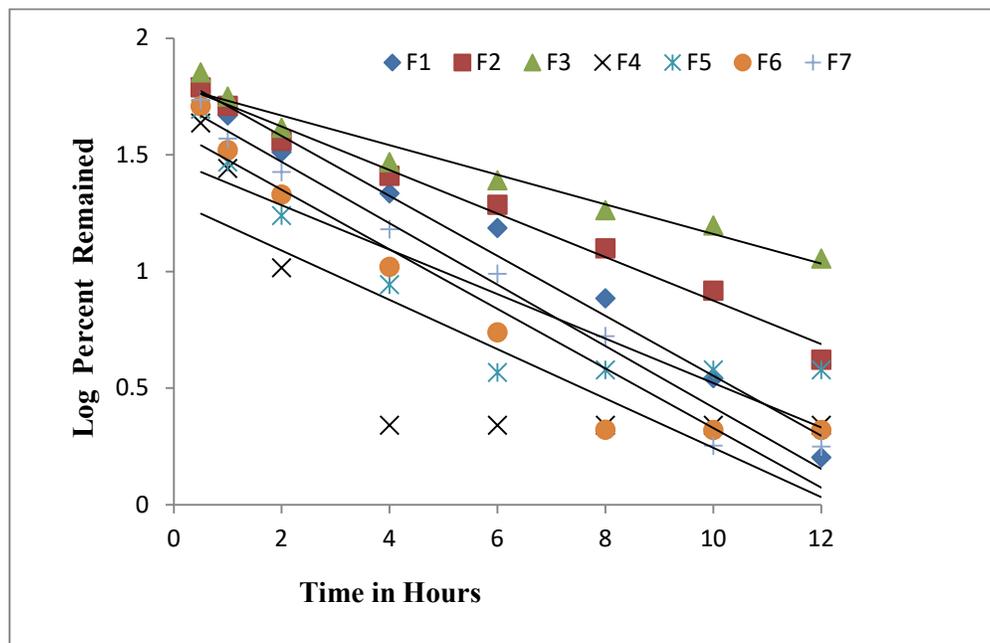


Figure 2: First order plots of Glipizide mucoadhesive microspheres

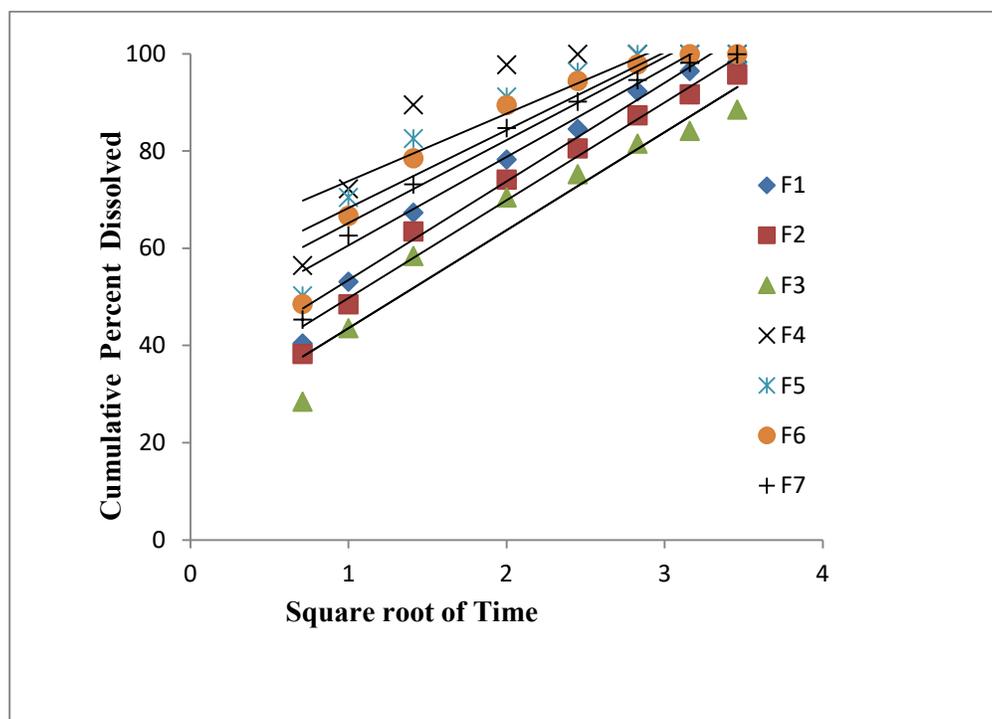


Figure 3: Higuchi plots of Glipizide mucoadhesive microspheres

CONCLUSIONS

Ionic-gelation method was found to be a suitable method for the preparation of glipizide mucoadhesive microspheres in the laboratory. The glipizide microspheres prepared with mucoadhesive polymers such as sodium CMC and oats powder were distinct, free flowing and almost spherical in shape. Sodium CMC showed more release retardation and oats powder showed better mucoadhesive property. Formulation F7 containing both sodium CMC and oats powder was found to be the best formulation. It was found that an increase in concentration of mucoadhesive polymer increases the mucoadhesion strength. Drug release

mechanism of all the formulations followed Higuchi diffusion and the drug release kinetics followed first order. Oats powder was found to be a promising mucoadhesive polymer.

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REFERENCES

- [1] Yadav S, Jain S, Prajapati S, Motwani M and Kumar S., Formulation and *in vitro* and *in vivo* characterization of Acyclovir loaded mucoadhesive

- microspheres., J of Pharm. Science and Technology., 2011; 3(1): 441-447.
- [2] Jain D, Panda AK and Majumdar DK, Eudragit S100 entrapped Insulin microspheres for oral delivery, AAPS Pharm Sci Tech., 2005;6(1):E100-E6.
- [3] Dandagi PM, Mastiholmith VS, Gadad AP and Iliger SR., Mucoadhesive microspheres of Propranolol hydrochloride for nasal delivery., Int J Pharm Science., 2007; 69(3): 402-7.
- [4] Sahoo SK, Mallick AA, Barik BB and Senapati PC., Formulation and *in-vitro* evaluation of Eudragit microspheres of Stavudine., Trop J Pharm Res., 2005;4(1): 369-75.
- [5] Halder A, Biswanath S., Preparation and *in-vitro* evaluation of polystyrene coated Diltiazem-Resin complex by o/w emulsion solvent evaporation method., AAPS Pharm Sci Tech., 2006; 7(2):E1-E8.
- [6] Bhawna Sharma, Anand Chaurasia, Dharmendra Singh Rajput, Naveen Gupta. Mucoadhesive Microspheres: A Promising Delivery System for Helicobacter Pylori (H. pylori) Treatment. Chinese Journal of Applied Physiology, 2024; 27(6):e20240006
- [7] Dey NS, Mukherjee B. Development and optimization of mucoadhesive microspheres of ciprofloxacin for Helicobacter pylori eradication. J Drug Deliv Sci Technol. 2022; 73: 103204
- [8] Bhabani S Nayak, Sunil K Ghosh and K. Tripathi B Patro., Preparation and characterization of Famotidine microcapsules employing mucoadhesive polymers in combination to enhance gastroretention for oral delivery, International Journal of Pharmacy and Pharmaceutical Sciences, 2009; 1(2): 112-120.
- [9] Koland Marina, Jacob Ansu, PrabhuPrabhakara and shettyNishaGirish., Mucoadhesive microspheres of Famotidine for gastroretentive drug delivery., International Journal of Drug Development and Research, 2012; 4(1): 59-64.
- [10] Foster RH, Plosker GL. Glipizide: A review of the pharmacoeconomic implications of the extended-release formulation in type 2 diabetes mellitus. Pharmacoeconomics. 2000;18:289-306.

- [11] Michael E Aulton , *Pharmaceutics: The science of dosage form design* , 2nd edition Churchillivingstone, 2006; 205-206.
- [12] Nayak A K, Hasnain M S, Beg S and Alam M I, *Mucoadhesive beads of Gliclazide: Design, Development and evaluation*, *Science Asia.*, 2010; 36: 319-325.
- [13] The United States Pharmacopeial Convention. *The United States Pharmacopeia. XXVI.* Rockville, MD: The United States Pharmacopeial Convention, Inc; 2003:859
- [14] Jayvadan K. Patel, Rakesh P. Patel, Avani F Amin and Madhabhai M. Patel. *Formulation and Evaluation of Mucoadhesive Glipizide Microspheres*, *AAPS PharmSciTech* 2005; 6 (1): E49-55.
- [15] Thombre AG, Denoto AR, Gibbes DC. *Delivery of glipizide from asymmetric membrane capsules using encapsulated excipients.* *J Control Release.* 1999;60:333-341
- [16] Chowdary KPR, Balatripura G. *Design and in vitro evaluation of mucoadhesive controlled release oral tablets of glipizide.* *Ind J Pharm Sci.* 2003;65:591-594.