RESEARCH ARTICLE

Design, Devlopment and Evaluation of Gastroretentive Floating Microspheres of Glibenclamide: *In-vitro In-vivo* Studies

Radheshyam Samanta[1*], Gaurav Tiwari[1], Naveen Gupta[1], Dharmendra Singh Rajput[1]
Prasenjit Maity[2]

[1]*Department of Pharmacy, Patel College of Pharmacy, Madhyanchal Professional University, Bhopal, Madhya Pradesh, India.*
[2]*Department of Pharmaceutical Science and Technology, BIT MESRA, Ranchi, Jharkhand, India.*

Received: 15th March, 2024; Revised: 23rd May, 2024; Accepted: 13th August, 2024; Available Online: 25th September, 2024

ABSTRACT

The current research study was designed to characterize the ethyl cellulose act as a carrier mediator used to prepare a floating microsphere of glibenclamide for developed gastroretentive sustain release floating drug delivery. Different microspheres of glibenclamide were formulated by the emulsion solvent evaporation technique of glibenclamide with EC in different ratios by using two solvent systems (ethanol and chloroform). After evaluating the micropolitics properties, %of yield value, drug loading efficiency, entrapment efficiency, diameter and surface morphology of the microsphere by using DLS and SEM, in-vitro drug release in gastric content, in-vitro buoyancy, and *in-vivo* floatation using animal model, compatibility study by FTIR, DSC and any other analytical study to demonstrate all formulation (especially GM2) was showing excellent results. So this work shows great gastro etentive floating drug delivery system for prolonged periods of time which is very useful in future for further study.

Keywords: Gastroretentive, Solvent evaporation, Floatation, Microspheres.

International Journal of Drug Delivery Technology (2024); DOI: 10.25258/ijddt.14.3.48

How to cite this article: Samanta R, Tiwari G, Gupta N, Rajput DS, Maity P. Design, Devlopment and Evaluation of Gastroretentive Floating Microspheres of Glibenclamide: *In-vitro In-vivo* Studies. International Journal of Drug Delivery Technology. 2024;14(3):1591-1598.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

There are different route for the delivery of drugs, mainly oral, parenteral and topical. Among these, oral routes have a common way for delivery of drugs because of their several benefits like easy administration by the patient, low cost, and patient comfortability.[1,2] Many conventional dosage forms are available and used to improve the oral control release drug delivery in past few decades for their better action due to the whole of the drug reaching the site (gastric and intestinal fluid) and retaining long time, circulating sustainable whole site of the action and absorbed maximum to produced bioavailability and decrease the wastage of drugs.[3-5] Many more oral control release drug delivery system available but in few decades later, gastroretentive drug delivery systems show their impact in this field due to their better improvement in sustained delivery because these gastroretentive dosage form retain much time in gastrointestinal fluid and slow drug release for a predetermined period at a constant rate.[6,7] Floating drug delivery system,[8-10] high-density drug delivery,[11] super porous hydrogel system,[12,13], magnetic system,[14] swellable system,[15,16] mucoadhesive or bioadhesive drug delivery system,[17-19] expendable and unfoldable drug delivery system[20,21] is the different way for stomach specific/gastroretentive drug delivery system. Here, my current research works to design, develop and evaluate gastroretentive microsphere of glibenclamide by applying ethyl cellulose.

Glibenclamide is one of the crucial drugs for altering diabetic mellitus and it has a short elimination half-life and requires more than one dosing frequently in a day.[22] Ethyl cellulose is one of the important water-insoluble release retardants, economical, fabricated biocompatible polymers.[23-25] So here we have to design to formulate gastroretentive microsphere by using glibenclamide as a model drug and ethyl cellulose drug-releasing polymer applying proper solvent system ethanol and chloroform by emulsifying solvent evaporation method. Previously it was reported many works in this area with different proportions[26-29] but here, we have changed the proportion to simply enhance the release the

**Author for Correspondence: radheshyamsamanta93@gmail.com*

drug for prolonged periods of time by evaporating the solvent of the drug-polymer mixture and producing small floating microsphere to sustain the release of the drug and to check the characteristic of floating microsphere like their shape and size by SEM and DLS to promote better designing and also check interaction study by the help of FTIR and DSC. Finally, it also evaluated *in-vitro* and *in-vivo* buoyancy/gastroretention through a beaker containing simulated gastric content and an animal model for better floating and sustained release the drug.

MATERIALS AND METHODS

Materials

All the materials needed for this research work were collected from different sources with good analytical quality. Glibenclamide was collected from Ajanta Pharmaceutical Pvt. Ltd. Ethyl cellulose was collected from Sigma Aldrich. Ethanol, chloroform, tween 80 were collected through Loba Chemical Private Limited. Distilled water and any other materials were collected from the market commercially with high standards.

Formulation of Glibenclamide Floating Microsphere

The floating microsphere of glibenclamide was prepared by an emulsifying solvent evaporation method, generally, drug glibenclamide mixed with polymer ethyl cellulose in different proportions (ratio) and dissolved in a mixture of a solvent system (ethanol: chloroform). The mixture will be stirred continually with the help of a glass rod manually until complete dissolution of the drug-polymer mixture in the solvent system. Then, this mixture is loaded in a syringe and poured slowly into the 0.2% tween 80 as an emulsifying agent containing 100 mL of distilled water. The result will form o/w type of emulsion and it will be rotated continually with the help of a magnetic stirrer until solvent evaporation and polymer precipitate to engulf the drug and form small spherical, rigid microspheres. After removing the complete organic solvent, these microspheres were received and washed with the help of distilled water many times and finally dried at room temperature within 24 hours. The formula of different ratio drug: polymer containing floating microspheres of glibenclamide is shown in Table 1.

Analysis of Micromeritics Properties

It is important to analyze the micromeritics properties of powder samples required for the formulation of floating microspheres of glibenclamide. For that we have to check these parameters.[22]

Table 1: Formula of different floating microsphere of glibenclamide

Ingredients	*Formulation code*				
	GM1	*GM2*	*GM3*	*GM4*	*GM5*
Drug:Polymer	1:1	1:2	1:3	1:4	1:5
Ethanol	5	5	5	5	5
Chloroform	5	5	5	5	5
Tween 80 %	0.2	0.2	0.2	0.2	0.2
Water	100	100	100	100	100

Bulk Density

For the analysis of bulk density, we can take a known quantity of powder sample from each formulation and measure the weight in a digital weighing machine than it was transferred to a 50 mL measuring cylinder then measured the volume of this powder in the measuring cylinder without tapping. Finally, the bulk density will be calculated using this data in the given formula.

B.D. = weight of the powder/untapped powder volume

Tapped Density (T.D.)

Similarly, the tapped density was analyzed by taking a known quantity of powder sample from each formulation and measuring the weight in digital weighing machine. Than it was transferred to a 50 mL measuring cylinder then, measure the volume of this powder in the measuring cylinder after tapping. Finally, the tapped density will be calculated using this data in the given formula.

T.D = weight of the powder/volume of powder after tapping

Compressibility Index

The compressibility index was analyzed to check the compress ability of the powder samples calculated by using the given formula.

C. I. = [(T.D.-B.D.) x 100]/T.D.]

Hausner's Ratio

H.R. used for analysis of flow ability as well as stability of this powder sample calculated by using this formula

H. R. = T.D. / B. D.

Angle of Repose

A.O.R are help for the analysis of flow characterized of powder samples to improve the stability of the formulation, it may be defined as the angle produced in between height of the powder and the plan base or tile on hold the powder samples. It will be measured by taking a required quantity of powder samples and introducing in a glass funnel that is already set with the help of a stand near about 10 cm above the plan base or tile then a powder hip will be produced then the angle will be measured by height of powder hip (h) and radius (r) of circle occur due to introduction of powder samples. Finally, this value will used to determine A.O.R by given formula.

$$\text{Tan } \theta = h/r$$
$$\text{A.O.R } (\theta) = \tan^{-1} h/r$$

Analysis of Average Particle Diameter of Microsphere

Average particle diameter of floating microspheres was analyzed by using DLS method. In this method first taken required quantity of microspheres from each formulation then prepared the slurry mixture by dispersion with ethanol. This dispersion slurry was analyzed by differential light scattering to measure the mean particle size.[24,26]

Evaluate Surface Morphology of Microspheres

SEM was used for the analysis of surface morphology and characteristic properties of the internal surface of prepared floating microspheres. It was conducted by taking microspheres in aluminum stubs containing double adhesive tape by thin coating gold layer under vacuum conditions and than analyzing with a scanning electron microscope (JSM T-SEM, Japan).

Analysis of % yield of floating microspheres

To analyze the production yield of prepared floating microspheres first weigh the required quantity of microspheres then this weight was divided by total amount of drug-polymer mixture. The formula for calculating the %yield was given below.[24]

Yield value% = (actual weight of prepared microspheres / drug-polymer total weight) x 100

Analysis for Efficiency of entrapment and loading of drug

In this study first 100 mg of microspheres was dissolved in a sufficient quantity of ethanol. The final mixture was transferred to a beaker containing 100 mL of gastric content as a dissolution medium (pH 1.2) then it was stirred with the help of a rotating stirrer within 1-hour. Then, these solutions were filtered by using I grade Whatmann^R filter paper and diluted to measure the entrapment efficiency and loading efficiency by using a double-beam spectrophotometer (UV-VIS spectrophotometer) at a wavelength of 307 nm against a blank sample. Finally, the %efficiency of drug entrapment and %efficiency of drug loading was calculated by using this formula.[23,24,27,29]

%efficiency of drug entrapment = (drug content on practically / drug content on theoretically)

%efficiency of drug loading = (original drug content / actual weight of the microspheres) x 100

Analysis of *In-vitro* Drug Release

This study was analyzed by using USP dissolution apparatus (Type-II, paddle) in gastric medium by maintaining 37 ± 0.5°C temperatures at a speed of 50 rpm at for not less than 12 hours. At first, the 100 mg of the formulation was transferred into 900 mL of simulated gastric fluid containing paddle type of dissolution apparatus then, after a certain period's gap 5 mL of the sample was withdrawn from this apparatus and a new sample of simulated gastric fluid was added in same quantity by maintaining the sink condition. This withdrawn sample of different time intervals was filtered by using Whatmann filter paper and diluted with suitable dilution, then the *in-vitro* release of glibenclamide by using a double-beam spectrophotometer (UV-VIS spectrophotometer) at a wavelength of 307 nm against a blank sample.[27]

Estimation of *In-vitro* Release Kinetics Data

For analyzed in-vitro kinetics mechanism of floating microspheres of glibenclamide, all data (*in-vitro* release) of glibenclamide was set to mathematically curve fitted different models like zero order kinetics model, first-order kinetics model, Higuchi kinetics model, Korsmeyer peppes kinetics model and Hickson-crowell kinetics model [24]. The release exponent n value expresses the release mechanism of the drug. If n value ≤ 0.5 is called a Fickian diffusion mechanism. When n ranges within 0.5-1 expressed as a non-Fickian diffusion mechanism. Also, if n ≥ 1.0 was expressed as case-II transport release mechanism that is controlled relaxation.[29]

Analysis of FTIR characterization

Different samples of floating microspheres of glibenclamide were analyzed by using a Fourier transform infrared spectroscopy instrument (Alpha II compact FTIR Spectroscope, Germany). Drug glibenclamide, polymer ethyl cellulose and the drug-polymer mixture will placed IR grade potassium bromide pellets containing sample holders in these instruments separately then spectroscopy scanning was determined within a range of 4000 to 500 cm^{-1}.

Analysis of DSC characterization

All the samples of floating glibenclamide microspheres were analyzed by using a differential scanning calorimeter (DCS-3, Mettler Toledo, Switzerland). The sample was introduced in an AI pan of this calorimeter as taking of reference pan of indium at a starting temperature 50°C/min while creating the atmosphere of nitrogen in the sample holding chamber and then heating conducts up to 400°C to produce different readings.

Analysis of *in-vitro* Buoyancy

For determination of *in-vitro* floating characterization of glibenclamide microspheres, immersed 100 mg of formulation in 500 mL of 0.1 N HCL (pH 1.2) in a galas beaker at maintaining 37 ± 0.5°C temperatures at 100 rpm for not less than 12 hours. After a certain time period the magnetic stirrer is off and visually, the floating behavior of glibenclamide floating microspheres indicates the *in-vitro* floating periods. After the 12 hours of floating the microspheres were collected, then dried and weighed. Finally, the buoyancy %of these floating microspheres was determined by this formula.[27]

% of Buoyancy = (microspheres weight after floating/actual weight of the microspheres before floating) x 100

***In-vivo* analysis of gastroretention study through X-ray photography**

For *in-vivo* gastroretention studies were conducted by using New Zealand white rabbits through X-ray radio photography of these microspheres.[30] This experiment was conducted with the help of IAEC (Registration no - PCP/IAEC/2023/JAN/20) by the scrutiny of the CPCSEA (Registration no - 1698/Re/S/13/CPCSEA). For this experiment, I use 2.85 ± 0.35 Kg weight male rabbits. The rabbits were conventional to the new environment and were fed the diet of the standard laboratory. The conventional rabbits were fasted overnight before the experiment and the rabbits were engaged with maintaining temperature individually. Then, this rabbit was held overnight (encaged) without food before the experiments. Then conduct the experiment from early morning 6 pm to evening 6 pm for completion and minimize the suffering of animals only by supplying sufficient water. Here, the formulation GM2 will replace the drug to $BaSo_4$ and be introduced in rabbit mouth with the help of tube flushing water carefully. Then X-ray photography of gastric region in rabbits was captured at 3, 6 and 12 hours time intervals.[26,30]

Statistical Analysis

All data obtained from this research should be analyzed by Microsoft Excel and release data (*in-vitro*) of glibenclamide conducted using Kinet Ds software by imputing the *in-vitro* curve fitting kinetics data.

RESULTS AND DISCUSSION

Formulations of Non-effervescent Floating Microspheres of Glibenclamide

In recent days, the gastroretentive floating microspheres have expressed an impactful effect on the delivery of sustainable drugs for prolonged periods of time, especially those that are absorbed in the stomach as well as the small intestine. Floating microspheres have low density to easily float and release drug over long periods. Previously, many works reported preparing this type of floating microspheres by using this ingredient, but here, we have to design the floating microspheres of glibenclamide by using the spheres-specific polymer ethyl cellulose with a different ratio. In this research work non, effervescent floating microspheres will be prepared by mixing the drug with a suitable ratio of ethyl cellulose by a suitable solvent system of chloroform and ethanol. Than this completely dissolved dispersion system is slowly introduced in tween 80 as an emulsifying agent containing distill water to evaporation of the organic solvent (emulsifying solvent evaporation method) and to form small spherical floating microspheres. The fixed stirring speed, changing the proportion of polymer and the time to stirrer of this system to engulf the drug in polymer and low density producing the small size of floating microspheres to float and improved the release of drug over a prolonged period of time.

Micromeritic Properties

All formulations containing powder samples showed good micromeritics properties that will be mentioned in Table 2. The data of compressibility index refer in-between 10.15 to 14.09, Hausner's ratio 1.11 to 1.16 and angle of repose 23.33 to 28.32 as compared to the reference value that developed the dosage form by improving the compressibility, flow ability and stability of this system.

Average particle diameter

The average particle diameter of glibenclamide floating microspheres will be represented in Table 3. Differential light scattering (DLS) of floating microspheres also expresses the size distribution of particles from each formulation. The overall size of these microspheres was good after evaluating the DLS and the diameter of the particles raised by the elevated proportion of polymer due to the increasing interfacial tension that will be a little beat controlled by maintaining the stirring speed with suitable duration of periods. However, it clearly stated that the average diameter of microspheres will be increased by increasing the proportion of the polymer.

Scanning electron microscope (SEM) for surface morphology

The surface morphology of glibenclamide floating microspheres (formulation GM2) by SEM is shown in Figure 1. It is clearly seen that the exterior of this microsphere was smooth, white, and spherical. However the interior of these microspheres was showing some spores. These spores occur gradually through solvent evaporation entrapped to microparticulate dense core form and it will help to release the drug sustainably over a prolonged period of time.

Percentage of Yield Value

The production %of glibenclamide floating microspheres is shown in Table 3. It is clearly noticed that the % yield increases due to the increasing polymeric concentration.

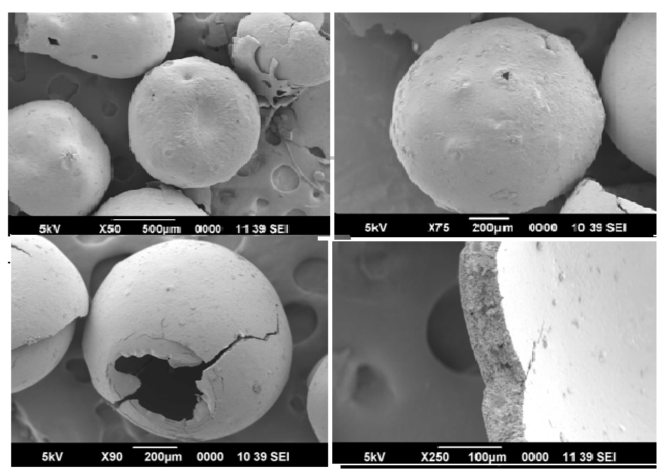

Figure 1: SEM images of glibenclamide floating microspheres (Formulation GM2) in different magnification

Table 2: Micromeritics properties of different floating of glibenclamide

Formulation Code	*(BD in gm/cm³)*	*(TD in gm/cm³)*	*(CI in %)*	*(HR in degree)*	*(AOR in degree)*
GM1	0.519	0.592	12.33	1.14	26.75
GM2	0.573	0.667	14.09	1.16	28.32
GM3	0.668	0.753	11.28	1.12	24.48
GM4	0.717	0.798	10.15	1.11	23.33
GM5	0.735	0.824	10.80	1.12	24.76

Table 3: Average particle diameter, %of yield, drug entrapment and loading efficiency of glibenclamide floating microspheres

Formulation code	*Mean particle diameter* in mm*	*%of yield value**	*Drug entrapment efficiency* in%*	*Drug loading efficiency* in%*
GM1	1.03 ± 0.06	68 ± 2.34	78 ± 1.59	16.37 ± 0.93
GM2	1.07 ± 0.07	71 ± 2.09	81 ± 2.01	17.45 ± 1.65
GM3	1.19 ± 0.09	73 ± 2.37	79 ± 2.34	18.67 ± 2.32
GM4	1.24 ± 0.11	75 ± 2.56	81 ± 2.89	17.18 ± 2.05
GM5	1.32 ± 0.07	77 ± 2.85	83 ± 2.98	18.97 ± 2.77

*Mean ± standard deviation, n = 3

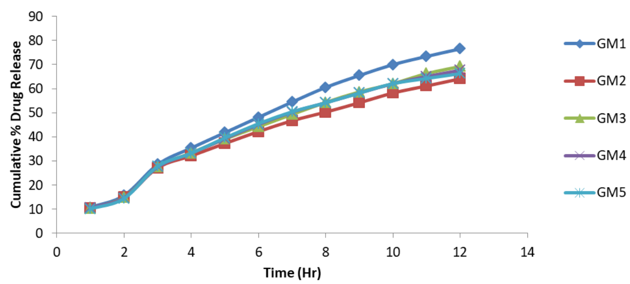

Figure 2: Drug release (*in-vitro*) graph of glibenclamide floating microspheres in gastric content (pH: - 1.2)

Efficiency of Drug Entrapment and Loading

Drug incorporation or entrapment efficiency and drug loading of this glibenclamide floating microspheres are shown in Table 3. The maximum amount of drug was encapsulated within these floating microspheres by using this emulsifying solvent evaporation method. According to U.S.P specification, 60 to 70% of drug entrapment passes as acceptance. Here, drug entrapment occurs within the range of 78 ± 1.59 to 83 ± 2.98, which proves the stability.

Also, the loading value ranges from 16.37 ± 0.93 to 18.97 ± 2.77 to prove acceptance according to specification.

Drug Release Activity through *In-vitro*

The release of glibenclamide through *in-vitro* from all formulations in gastric content (pH: - 1.2) was shown in Figure 2. All the formulations express great drug release through *in-vitro* formulated by taking of drug glibenclamide with different proportions of polymer ethyl cellulose. It was noticed that *in-vitro* drug release was a little bit frictuated (decrease) by increasing the polymer concentration except formulation 1. Also, the mean particle size and pores present above the interior surface of microspheres will affect the *In-vitro* release. Here formulation 2 show better *in-vitro* sustain drug release for a prolonged periods of times (more than 12 hours) however all the formulation express similarly sustain release the drug over a prolong periods of time.

The mathematically *in-vitro* release kinetics data of different formulation was express in Table 4. All formulation of glibenclamide floating microspheres fit in Korsmeyer-Peppas model (R^2 = 0.976 to 0.987) and the release exponent (n) value represent within this range of 0.75 to 0.82 to all the formulated floating microspheres express as non-fickian anomalous control release mechanism.

FTIR Characterization

FTIR spectra of ethyl cellulose (polymer), glibenclamide (drug) and the formulation GM2 (drug-polymer mixture) for characterization of chemical interaction were shown in Figure 3. The FTIR spectrum of polymer and drug-polymer mixture (Formulation GM2) will show different characteristic peaks due to the presence of differential function group according to the stretching and bending. This type of peak campare to the standard specification and proved to no interact in between drug and polymer and maintaining stability.

DSC Characterization

DSC thermogram of ethyl cellulose, glibenclamide and formulation GM2 (drug-polymer mixture) for maintaining the stability will be shown in Figure 4. The endothermic peak of the drug, polymer and drug-polymer mixture (formulation GM3) shows no significant changes occurring stability of the formulation.

Buoyancy by *in-vitro*

The floatation (*in-vitro*) characteristic of glibenclamide microspheres (GM2) in gastric content (pH: 1.2) is shown in Figure 5. All formulations are prepared by emulsifying

Table 4: Drug release kinetics (*in-vitro*) data of different glibenclamide floating microspheres

Formulation code	*R² Value*					*n value*
	Zero order	*First order*	*Higuchi*	*Korsmeyer-peppes*	*Hickson-crowell*	
GM1	0.977	0.851	0.830	0.987	0.907	0.82
GM2	0.968	0.835	0.886	0.982	0.891	0.75
GM3	0.974	0.849	0.859	0.984	0.899	0.79
GM4	0.965	0.835	0.866	0.981	0.890	0.78
GM5	0.956	0.819	0.863	0.976	0.876	0.79

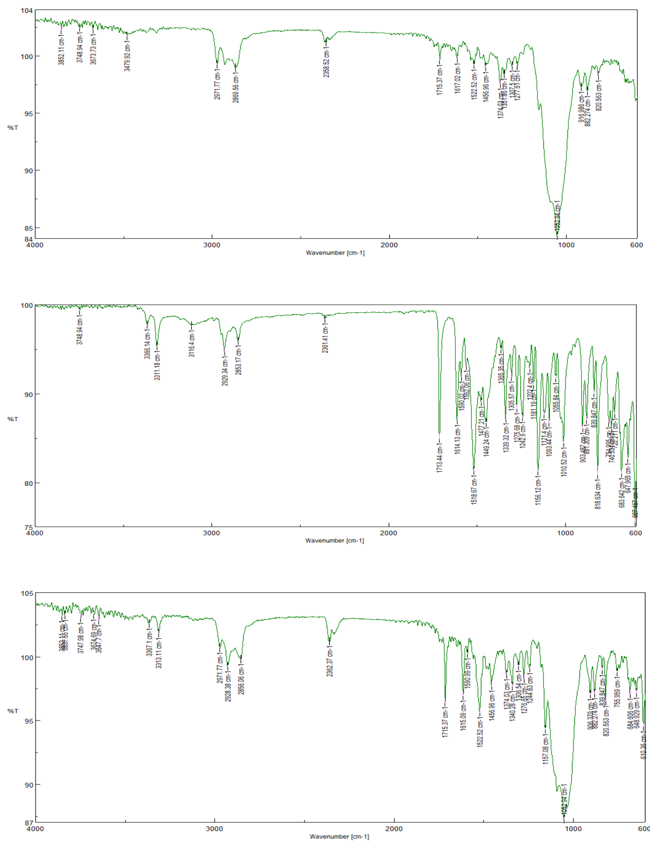

Figure 3: FTIR spectra of EC (Polymer), Glibenclamide (Drug) and Formulation of GM2 glibenclamide floating microspheres

Table 5: %Buoyancy of glibenclamide floating microspheres.

Formulation code	*% of buoyancy**
GM1	78 ± 1.34
GM2	83 ± 1.98
GM3	77 ± 1.56
GM4	87 ± 2.88
GM5	81 ± 1.99

*Mean ± standard deviation, n = 5

solvent evaporation method to evaporate organic solvent by stirring and drug entrap to form a spherical small microsphere having low density to easily float surface of gastric content (pH:- 1.2) containing container for more than 12 hours. Here, also check the % of floating ability to all the formulations shown in Table 5.

Gastroretention through *in-vivo* by X ray photography

In-vivo X-ray photography of floating microspheres in the stomachs of New Zealand white rabbits of different time intervals is shown in Figure 6. Here drug will be replaced by the radio-opaque agent barium sulfate and is similarly prepared for the microspheres by the addition of the same proportional polymer and other compatible solvents and excipients, then insert these microspheres to a suitable male rabbit. It is clearly

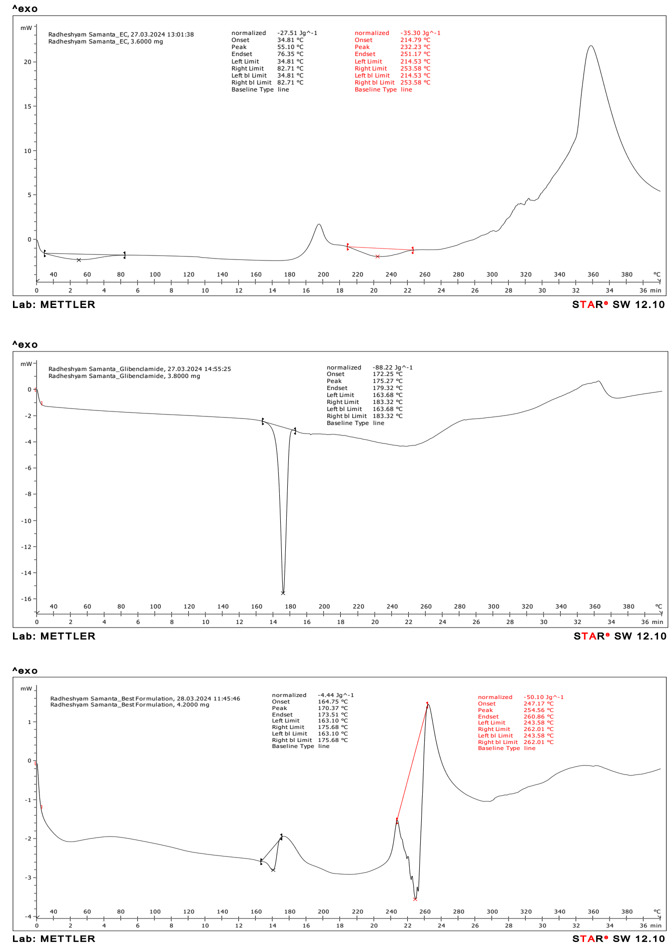

Figure 4: DSC graph of EC (Polymer), Glibenclamide (Drug) and Formulation of GM2 glibenclamide floating microsphere

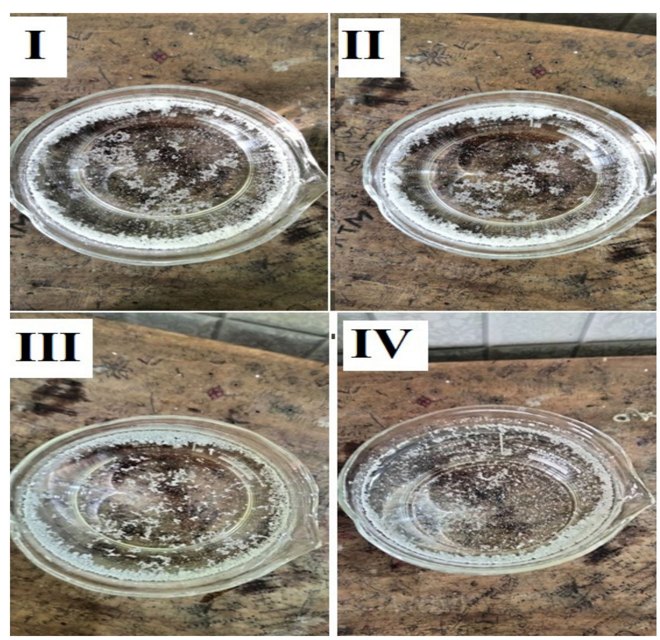

Figure 5: Floating behavior (*in-vitro*) of glibenclamide microspheres (GM2) in gastric content (pH: – 1.2): After (I) 1 hour, (II) 3 hours, (III) 6 hours, and (IV) 12 hours

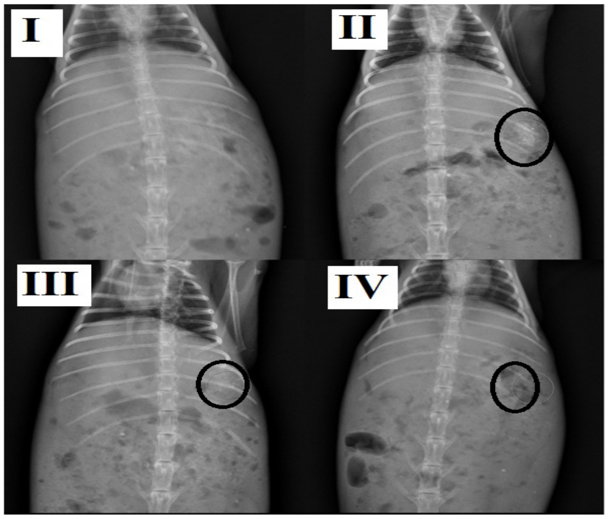

Figure 6: X ray photography (*in-vivo*) of floating microspheres in stomach of rabbits: (I) before administration, (II) after 3 hours, (III) after 6 hours and (IV) after 12 hours of administration

visible by using X-ray photography that these microspheres will remain float in the gastric region of the rabbit (stomach) over a prolonged period of time (i.e. after 3, 6 and 12 hours), which is compared to the before administration. So, it will be demonstrated that this type of floating microsphere of the preferable drug will remain float in our stomach or gastric region for a long periods of time and improve the sustained release with the help of this animal model.

However, in this current research work, it was clearly concluded that the formulation of non-effervescent glienclamide floating microspheres prepared by the suitable ratio of ethyl cellulose by emulsifying solvent evaporation methods express excellent release of a drug. *In-vitro* sustain release of drug to all formulations (especially GM2) in gastric content (pH: -1.2) is greater 12 hours. Similarly *in-vitro* floating behaviors of all glibenclamide microspheres (especially GM2) were excellent performance. X-ray images of microspheres in the gastric region of rabbits proved that *in-vivo* gastroretention of this type of microspheres prepared by different ratio ethyl cellulose containing emulsifying solvent evaporation method over a prolonged period of time by replacing the drug with barium sulfate. So, in the future, this type of floating microspheres of another drug with this composition very useful for gastroretentive delivery. The drug is sustainable over a prolonged period of time due to their high yield, entrapment, loading efficiency as well as reliable, economical and minute interaction ability.

CONCLUSION

In this current research work, it was clearly concluded that the formulation of non-effervescent glibenclamide floating microspheres prepared by suitable ratio of ethyl cellulose by emulsifying solvent evaporation methods express excellent release of drug in-vitro and *in-vivo* circumstances. The release (in-vitro) of all formulations (especially GM2) in gastric content (ph-1.20) was not less than 12 hours. Similarly, *in-vitro* floating behaviors of all glibenclamide microspheres (especially GM2) were excellent performance, not less than 12 hours. X-ray images of microspheres in the gastric region of rabbits prove that *in-vivo* gastroretention of this type of microspheres prepared by different ratio ethyl cellulose containing emulsifying solvent evaporation method over a prolong periods of time by replacing the drug with barium sulfate. So, in the future this type of floating microspheres of another drug with this composition will be very useful for gastroretentive delivery. The drug is sustainable over a prolonged period of time due to its high yield, entrapment, loading efficiency as well as reliable, economical and minute interaction ability.

STATEMENT OF ETHICS

This experiment was carried out according to the Institutional Animal Ethics Committee (Registration no- PCP/IAEC/2023/JAN/20) by the scrutiny of CPCSEA (Registration no- 1698/Re/S/13/CPCSEA).

AUTHOR CONTRIBUTION

Investigation: Radheshyam Samanta, Gaurav Tiwari, Naveen Gupta, Dharmendra Singh Rajput. Methodology: Radheshyam Samanta, Gaurav Tiwari, Naveen Gupta, Dharmendra Singh Rajput, Biswarup das. Prasenjit Maity. Supervision: Gaurav Tiwari, Naveen Gupta, Dharmendra Singh Rajput. Writing-original draft: Radheshyam Samanta. Writing-review and editing: Gaurav Tiwari, Naveen Gupta, Dharmendra Singh Rajput.

ACKNOWLEDGMENT

The author would like to thank all respect for guidance and help throughout this research work.

REFERENCES

1. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oral drug delivery. Front. Pharmacol. 2021; 12: 618411. doi.org/10.3389/ fphar.2021.618411.
2. He S, Liu Z, Xu D. Advance in oral delivery systems for therapeutic protein. J. Drug Target. 2019; 27: 283–291, doi: 10.1080/1061186X.2018.1486406.
3. Singh BN, Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release. 2000; 63: 235. doi.org/10.1016/S0168-3659 (99)00204-7.
4. Brahma NS, Kwon HK. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Controlled Release 2000; 63:35–259.
5. Renukuntla J, Vadlapudi AD, Patel A, Boddu SH, Mitra AK. Approaches for enhancing oral bioavailability of peptides and proteins. Int. J. Pharm. 2013; 447(1-2):75-93. doi: 10.1016/j.ijpharm.2013.02.030.
6. Prasad D, Parashar T, Khaudiyal S, Semwal A, Jakhmola V. Gastro retentive drug delivery system: Latest approaches towards novel drug delivery, IJPQA, 2023; 14 (4): 1256-1263.
7. Brijesh SD, Avani FA, Madhabhai MP. Gastro retentive drug delivery system of ranitidine hydrochloride: formulation and in-vitro evaluation. AAPS Pharm. Sci. Tech.; 2004; 5(2), 1-6.
8. Pallam NC, Maruvajala V, Mounika SS T, Design and Charecterization of Hallow Porous Floating Microspheres of

Favipiravir. IJDDT. 2024; 14(1): 236-245.
9. Mujbaile S, Khobragade D, Mundhada D. Formulation and optimisation of microspheres of leaves extract of lantana camara 3^2 design approaches, IJPQA, 2023; 14: 268-273
10. Iyan S, Sriwidodo, Retno W, Norisca AP. A Review, Floating drug delivery system as a tool to improve dissolution rate in gastric, International jornal of applied pharmaceutic. 2020; 12(4): 51-54.
11. Bhange A M, Gunde C M, Ukey B S, Suruse B P. Formulation and Evaluation of Gastro Retentive Floating Tablet of Cetrizine Hydrochloride using Linseed Musilage Polymer. IJDDT. 2023; 13(4): 1544-1547.
12. Bajpai SK, Bajpai M, Sharma L. Investigation of water uptake behavior and mechanical properties of superporous hydrogels. J Macromol Sci. 2006; 43: 507-24.
13. Juthi AZ, Li F, Wang B, Alam MM, Talukder ME, Qiu B. pH-responsive super-porous hybrid hydrogels for gastroretentive controlled-release drug delivery. Pharmaceutics. 2023; 15: 816. doi.org/10.3390/pharmaceutics15030816.
14. Groning R, Berntgen M, Georgarakis M. Acyclovir serum concentrations following peroral administration of magnetic depot tablets and the influence of extracorporal magnets to control gastrointestinal transit. Eur J Pharm Biopharm. 1998; 46: 285-91.
15. Arza RAK, Gonugunta CSR, Veerareddy PR. Formulation and evaluation of swellable and floating gastroretentive ciprofloxacin hydrochloride tablets. AAPS PharmSciTech 2009; 10(1):220-6. doi: 10.1208/s12249-009-9200.
16. Siepmann, J, Kranz H, Bodmeier R, Peppas NA. HPMC matrices for controlled drug delivery: A new model combining diffusion, swelling and dissolution mechanisms and predicting the release kinetics. *Pharm. Res*. 1999; *16*: 1748-1756.
17. Pund S, Joshi A, Vasu K, Gastroretentive delivery of rifampicin: *In vitro* mucoadhesion and *in vivo* gamma scintigraphy. Int J Pharm. 2011; 4(11):106-12.
18. Varshosaz J, Tavakoli N, Roozbahani F. Formulation and in vitro characterization of ciprofloxacin floating and bioadhesive extended-release tablets. Drug Delivery. 2006; 13(4):277-85. doi: 10.1080/10717540500395106.
19. Janugada BU, Singla N. Formulation, In-vitro and In-vivo Evaluation of Chronology-based Mucoadhesive Drug Delivery System of an Antihypertensive Drug. IJDDT. 2024; 14(1): 94-101.
20. Kavimandan NJ, Lakshman JP, Matharu AS. Extended Release Gastro retentive Oral Drug Delivery System for Valsartan, JSTOR. 2009; 2061438.
21. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. J Control Release. 2003; 90: 143-62.
22. Riefflin A, Ayyagari U, Rury R, Jonathan C. The effect of glibenclamide on insulin secretion at normal glucose concentrations. 2015; 58: 43–49.
23. Parida P, Mishra SC, Sahoo S, Behera A, Nayak BP. Development and characterization of ethylcellulose based microsphere for sustained release of nifedipine**.** Journal of Pharmaceutical Analysis. 2016; 6(5): 341-344
24. Bipul N, Lilakanth N, Bhaskar M, Pradeep K, Niraj S, Bhanupratap S. Preparation and characterization of Salbutamol sulphate loaded Ethyl cellulose microspheres using water-inoil-in-oil emulsion technique. Iranian J. Pharm. Res. 2010; 9(2): 97-105.
25. Geng y, Williams GR. Developing and scaling up captopril-loaded electrospun ethyl cellulose fibers for sustained-release floating drug delivery. International Journal of Pharmaceutics. 2023; 648: 123557.
26. Dash SK, Khan AS, Das SR, Padhan A, Rout D. Formulation and In-Vitro Evaluation of Sustained Released Glibenclamide Microspheres. International Journal of Pharmaceutical Sciences and Research. 2012; 3: 1433-1443.
27. Rao AA, Rao N, Raju B. Mohammed J. Formulation and Evaluation of Floating Microspheres of Sitagliptin. 2023; 16(5): 343.
28. Rajpali D, Gupta V. Floating Microspheres Based Nizatidine Gastro Retentive Formulation to Control the Release of Drug. Letter in applied nanobioscience. 2020; 9(3): 1409 – 1419.
29. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. *In vitro* evaluation of floating and drug releasing behaviour of hollow microsphers (microballoons) prepared by emulsion solvent diffusion method. European journal of pharmaceutics and biopharmaceutics 2004; 57: 564.
30. Kokardekar RR, Chaudhari YS, Kumavat SD, Pawar HA. Development and Evaluation of Sustained Release Microspheres of Glibenclamide by Emulsion Solvent Evaporation Method. Clin Pharmacol Biopharm. 2014; 4(1): 234. doi: 10.4172/2167-065X.1000127.