



# Development of Glipizide-Loaded Floating Microspheres for Diabetes Treatment: Formulation, Characterization, and *in-vivo* Assessment

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Received: 26 Oct 2022 / Accepted: 24 Nov 2022 / Published online: 01 Jan 2023

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## Abstract

**Aim:** The goal of the current study was to create glipizide floating microspheres that would maintain their stability for a longer period of time in the upper gastrointestinal tract (GIT), perhaps improving absorption and bioavailability. By employing polymers such hydroxyl propyl methyl cellulose (HPMC), ethyl cellulose in various ratios, and glipizide in each formulation.

**Method:** The microspheres were made using the solvent evaporation process. The USP apparatus type I was used to carry out *in vitro* drug releases, and FTIR was used to determine the polymer compatibility of the microspheres. We investigated the yield, particle size, buoyancy percentage, drug entrapment efficiency, *in vivo* antidiabetic effectiveness of glipizide loaded microspheres, *in vivo* radiographic behavior, and *in vitro* drug release of the glipizide-laden microspheres. **Result:** The range of the yield of floating microspheres loaded with glipizide was determined to be 46.25±0.79% to 94.54±1.06%. The particle size ranged from 17.33 ±0.57 µm to 43.6±1.15 µm, with the maximum drug entrapment efficiency being 56.64 ±0.32 % and the buoyancy percentage being 90.33±0.91 %. With different formulations, the medication release characteristics changed.

## Keywords

Glipizide; Floating microspheres; *In vitro* release studies; *In vivo* study.

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## 1. INTRODUCTION:

The development of gastro-retentive floating microspheres as an effective tool for increasing the bioavailability and regulated distribution of numerous medications. As delivery technology becomes more sophisticated, more gastroretentive drug delivery methods will be created in order to maximize the delivery of compounds with low bioavailability and extensive first pass metabolism.

For medications that are absorbed largely in the duodenum and upper jejunum segments, a gastric floating drug delivery system can at least partially address these issues. It can also prolong the period that dose forms are retained in the GIT, improving the oral bioavailability of the medication (Gangadharappa *et al.*, 2007). The next ten years may be devoted to controlling gastrointestinal transit,

which could lead to novel therapeutic opportunities with significant patient advantages.

Diabetes is a metabolic illness in which the body cannot effectively create or use the hormone insulin, which is needed to turn sugar, carbohydrates, and other foods into energy. The hallmark of diabetes mellitus is persistently high blood glucose levels (sugar). The human body uses insulin and glucagon to keep the blood glucose level within a fairly small range. The purpose of glucagon is to trigger the liver's release of glucose from its cells into the blood, which is necessary for generating energy (Arunachalam and Gunasekaran, 2002). One of the most often given medications for the treatment of people with type II diabetes mellitus is glipizide, an oral hypoglycemic agent (Brogden *et al.*, 1979). Although it is nearly insoluble in water, the absolute bioavailability is close to 1. As a result, it is classified as a biopharmaceutical of class 2 in the BCS (BCS). Due to the relatively short (2-4 h) elimination half-life of glipizide, it must be administered often. Additionally, taking it orally frequently results in severe hypoglycemia symptoms as nausea, vomiting, heartburn, anorexia, and an increase in hunger (Mutalik and Udapa., 2006).

Therefore, there is a significant clinical need and market opportunity for a dosage form that will provide glipizide to a patient who needs this medicine in a regulated manner, leading to improved patient compliance. The goal of the current effort is to create a controlled drug delivery system that will provide the medication while minimizing side effects, improving absorption, increasing bioavailability, and increasing compliance with regard to distribution. Due to their versatility in achieving a desired drug release profile, affordability, and broad regulatory approval, HPMC & EC as hydrophilic polymers are being used in the proposed study to test floating microspheres of glipizide as a model drug for extension of the stomach retention time.

## 2. EXPERIMENTAL:

### 2.1. Materials

Glipizide was provided from M/s Aristo Pharmaceuticals Private Ltd, Mumbai, as a gift sample. (India). The following items were procured from Central Drug House (P) Ltd.: dichloromethane, hydroxyl propyl methyl cellulose (HPMC), ethyl

cellulose (EC), and Tween 80. (India). All additional substances/reagents were of analytical grade.

### 2.2. Preparation of floating microspheres

The solvent evaporation process used by Struebel *et al.* (2003) was used to fabricate microspheres. An ethanol and dichloromethane solution containing glipizide, HPMC, and EC was dissolved at room temperature. This was added to 250 mL of water that contained 0.01% Tween 80 and was kept at a temperature of 30 to 40 °C. After that, the mixture was agitated for 20 minutes at varying agitation speeds to allow the volatile solvent to evaporate. The resulting microspheres were filtered, cleaned with water, and vacuum-dried.

The preparation of floating microspheres involves a number of process variables, but the following ones were chosen for formulation optimization: the impact of polymer ratio, the impact of emulsifying agent concentration, the impact of temperature, and the impact of stirring rate. These variables were identified and their effects on the preparation and characteristics of microspheres were studied.

### 2.3. Characterization of microspheres

#### 2.3.1. Particle size

An optical microscopic technique was used to determine the size distribution of the microspheres in terms of average diameter. At least 200 particles were counted using a compound microscope outfitted with a calibrated ocular micrometer and stage micrometer slide.

#### 2.3.2. Morphology

Scanning electron microscopy was used to examine the microspheres' internal and exterior morphology (SEM). The powder was sparingly sprinkled on a piece of double-sided adhesive tape that was fastened to an aluminium stub to create the samples for SEM. Then, using a gold sputter module in a high-vacuum evaporator, the stubs were coated with gold to a thickness of around 300 while being exposed to an argon environment. After that, the coated samples were randomly scanned, and a SEM was used to take photomicrographs (Fig (JEOL JSM-6380 LA, Tokyo, Japan).

#### 2.3.3. Percentage yield of microspheres formed

The overall percentage yield of floating microspheres was calculated by dividing the measured weight of the prepared microspheres by the sum of all the non-volatile ingredients employed in their creation.

$$\% \text{ Yield} = \frac{\text{Measured weight of floating microspheres}}{\text{Sum of drug, polymer and nonvolatile components}}$$

#### 2.3.4. Drug entrapment efficiency

The 50 mg of floating microspheres were precisely measured and crushed. The microsphere powder was dissolved in a little amount of methanol, and then 10 ml of PBS with a pH of 7.4 was added to a volumetric flask (100 ml) and thoroughly mixed. After that, the solution was set aside for 12 hours. Then, Whatmann filter paper No. 1 is used to filter this solution. The absorbance at 276 nm was measured using a UV spectrophotometer following the appropriate dilution, and the percentage of medication entrapped was determined.

#### 2.3.5. Floating behavior

In 100 ml of the simulated stomach fluid (SGF, pH 1.2) containing 0.02% w/v tween 20, 50 mg of the floating microspheres were added. A magnetic stirrer was used to stir the fluid at 100 rpm. The layer of buoyant microspheres was pipetted and filtered after 8 hours. Filtration divided the particles in the sinking particulate layer. Both kinds of particles were dried in a desiccator until they reached a constant weight. Both microsphere fractions were weighed, and the weight ratio of the floating particles to the total of the floating and sinking particles was used to calculate buoyancy.

$$\text{Buoyancy (\%)} = \frac{W_f}{(W_f + W_s)} \times 100$$

$W_f$  and  $W_s$  are respectively the weights of the floating and settled microparticles.

#### 2.3.6. Fourier transform infra-red analysis.

On the FTIR-8400S Spectrometer, FTIR measurements of drugs, polymers, physical mixtures of drugs and polymers, and tailored microspheres were obtained (Shimadzu, Japan). In order to prepare samples, they were mixed with KBr and then put in the sample container. The spectra that were scanned over the 4000-400  $\text{cm}^{-1}$  wavenumber range at room temperature are shown in Fig.2.

#### 2.3.7. Differential scanning calorimetry (DSC)

On a Modulated DSC PERKIN ELMER apparatus with a thermal analysis data system, differential scanning calorimetric (DSC) measurements were performed. Internal standards of indium (156.600 °C) and zinc (419.470 °C) were used to calibrate the instrument. Al-Crucibles, 40 Al aluminum pans containing samples weighing 10 mg were sealed. Under a nitrogen environment, the probes were heated from 30 to 360 °C at a rate of 10 °C/min. In Fig.3, the DSC thermograms are provided.

#### 2.3.8. X-ray diffraction analysis (XRD)

The XPERT-PRO x-ray diffractometer device performed X-ray diffraction analyses for pure drugs, polymers, physical mixtures of drugs and polymers,

and improved formulations of floating microspheres of glipizide. The patterns of x-ray diffraction were automatically captured. Using an x-ray diffractometer with a goniometer radius of 240 mm, diffraction patterns were obtained. Ni filtered the Cu Ka radiation ( $K=1.54060$ ). A system with 1° and 0.1 mm wide diverging and receiving slots was employed. 45 kV of tube voltage and 40 mA of tube current were used to gather the pattern, which was then scanned across a 2-range of 5-600. In Figure 4, the XRD patterns are displayed.

#### 2.3.9. In vitro drug release studies

With the help of a veego basket type Six Station dissolution equipment, the in vitro release of Glipizide from the various formulations was investigated. The basket was filled with floating microspheres equal to 10 mg of medication. The dissolution media, which was 900ml of simulated stomach fluid with a pH of 1.2 and no enzymes, was kept at a constant temperature of 37°C while rotating at a speed of 100 rpm. At regular intervals, an aliquot of 5 ml of the solution was removed and replaced with 5 ml of new dissolving medium. After being filtered via a 0.45- $\mu\text{m}$  membrane filter (Millipore), samples were spectrophotometric ally analyzed at 276 nm and are seen in Figs. 5, 6, 7 and 8.

#### 2.3.10 In vivo studies

##### 2.3.10.1 Antidiabetic activity of floating microspheres of glipizide

Wistar rats that were generally healthy and weighed 250 to 300g each were used in in vivo evaluation experiments for floating microspheres of glipizide. The in vivo study was conducted in accordance with the institutional animal ethical committee protocol approved by Kalaniketan Polytechnic, Jabalpur, and in accordance with the regulations approved by the Committee for the Purpose of Control and Supervision of Animal Experiments (CPCSEA), Ministry of Social Justice and Empowerment, Government of India. The study employed the four groups of five wistar rats each, which were fasted (with water) for at least 12 hours before to the procedures. Saline water (3ml/kg) was given to group I, the healthy control (non-diabetic, untreated), while group II, the diabetic control, received no treatment (diabetic, untreated) group II (diabetic, treated) and received saline solution, group III (diabetic, treated) and received pure glipizide medication, and group IV (diabetic, treated) and received floating microspheres with 800 g/kg of glipizide loaded in them. Wistar rats were given 100 mg/kg of alloxan monohydrate to develop diabetes. 72 hours later, the glucose level was used to evaluate and stabilize the diabetic status. Diabetes was

defined as having a blood glucose level between 150 and 250 mg/dl, and these animals were employed in experiments. Each rat had a tail vein blood sample obtained prior to the administration of the medication. Using the glucose-measuring device accucheck, the blood glucose level was determined. To prevent lens contamination, the equipment was self-calibrated, and samples were allowed to dry before the results were read. Each group received oral administration of either pure glipizide or a mixture of glipizide-containing HPMC & EC floating microspheres through stomach intubations. Each rat received an administration of glipizide in suspension form at a dose of 800 g/kg. The blood glucose level was assessed using the previously published method, and blood samples were taken at specified times at 1-hour intervals up to 24 hours. The decrease in blood sugar level was quantified and shown in Fig. 9.

#### 2.3.10.2 *In vivo* radio graphical study

A diagnostic tool or the primary factor in the explanation of the created microspheres' *in vivo* floating behaviour was barium sulphate-loaded microspheres. After a short meal, a wistar rat was administered an oral suspension of a combination of HPMC and EC floating microspheres. Figure 10 shows an X-ray of a wistar rat's stomach taken at the proper time. All rats participating in the experiment are given access to water and are given regular movement. This research was carried out in a government veterinary hospital in Jabalpur, Madhya Pradesh.

### 3. RESULTS & DISCUSSION:

#### 3.1 Particle size

To determine the impact of polymer concentration on microsphere particle size, increasing EC concentration was combined with a fixed concentration of HPMC and a fixed concentration of medication. The mean particle size of microspheres was found to dramatically rise from  $17.33 \pm 0.57 \mu\text{m}$  to  $43.6 \pm 1.15 \mu\text{m}$  as the EC concentration was raised. This was caused by the fact that increasing the EC concentration increased the solution's viscosity, while decreasing the stirring speed caused an increase in particle size. Nepal *et al.* (2007) observed the same outcome. Glipizide-loaded floating microspheres were made using an emulsifying agent concentration that was gradually increased to see how it affected the particle size of the microspheres. The mean particle size of microspheres ranged from  $29.33 \pm 1.52 \mu\text{m}$  to  $16.3 \pm 1.15 \mu\text{m}$ , and it significantly shrank as the concentration of the emulsifying agent rose. As the concentration of the emulsifying agent rose, more stable droplets were formed, preventing the fusing of smaller droplets into larger aggregates.

Glipizide-loaded floating microspheres were made using a constantly increasing temperature to examine the effects of temperature on particle size, drug entrapment, and buoyancy of the microspheres. Microspheres' mean particle sizes ranged from  $19.6 \pm 0.54 \mu\text{m}$  to  $35.66 \pm 1.52 \mu\text{m}$ , and as the temperature rose, they grew much larger. This happened as a result of the solvent evaporating more quickly as the temperature rose. Since less time is available to break up the droplets as a result, polymer solidification eventually occurs.

A continuously increasing stirring rate was used to make glipizide-loaded floating microspheres in order to examine the effect of stirring speed on the size of the microspheres' particles. The mean particle size of the microspheres, which ranged from  $43.67 \pm 1.15 \mu\text{m}$  to  $18.3 \pm 1.53 \mu\text{m}$  with increasing stirring rate, significantly decreased with increasing stirring rate due to the high shear force that resulted in the production of smaller droplets.

#### 3.2 Surface morphology

The surface morphology was investigated by scanning electron microscopy, revealing the size distribution of the population as well as the exterior and internal morphologies of the microspheres. The synthetic microspheres featured an external shell comprised of a medication and a polymer and an interior hollow with a spherical surface. The surface of the microsphere is smooth and did not aggregate. The morphology of a microsphere's interior, which has pores. The volatile solvent may have swiftly escaped from the polymer matrix, leading to the formation of these pores. The hollow nature of the microspheres contributed to their ability to float.

#### 3.3 Percentage yield of microspheres formed

The yield of floating microspheres with glipizide was discovered to be between  $46.25 \pm 0.79 \%$  to  $94.54 \pm 1.06 \%$ .

#### 3.4 Drug entrapment efficiency

To evaluate the impact of polymer concentration on the percentage of drug entrapment of the microspheres, increasing EC concentration was combined with a fixed concentration of HPMC and a fixed concentration of drug. The drug entrapment reduced with rising EC concentration from  $56.64 \pm 0.32\%$  to  $29.87 \pm 0.40\%$  because more aggregates formed as EC concentration rose. To determine the impact of emulsifying agent concentration on the amount of drug entrapped in the microspheres, glipizide-loaded floating microspheres were created using a steadily increasing concentration of the emulsifying agent.

Due to smaller particle production, which in turn reduced drug entrapment, the drug entrapment of microspheres dropped with increasing emulsifying

agent concentration, and was in the range of  $46.26 \pm 0.82\%$  to  $40.22 \pm 0.90\%$ . In order to evaluate the impact of temperature on the percentage of drug entrapment in the microspheres, glipizide-loaded floating microspheres were manufactured at a temperature that was gradually increased. With rising temperature, the drug entrapment in microspheres significantly decreased, falling between  $46.25 \pm 0.33\%$  and  $20.11 \pm 0.35\%$ . To determine the impact of stirring speed on the percentage of drug entrapment in the floating microspheres, glipizide was added to floating microspheres using a progressively rising stirring rate.

The drug entrapment of microspheres was in the range of  $28.56 \pm 0.70\%$  to  $50.81 \pm 0.38\%$  and dramatically increased with increasing stirring rate. More medication is enclosed in polymer and aggregation is prevented by vigorous stirring.

### 3.5 Floating behavior

To determine the impact of polymer concentration on the microspheres' buoyancy, increasing the EC concentration was combined with a fixed concentration of HPMC and a fixed concentration of medication. The buoyancy of the microspheres considerably increased as the EC concentration increased, ranging from  $64.28 \pm 1.08\%$  to  $90.33 \pm 0.91\%$ . This was produced by air expansion as a result of the higher EC concentration (Chudiwal *et al.*, 2009). To determine the impact of emulsifying agent concentration on the microspheres' buoyancy, glipizide-loaded floating microspheres were created using a steadily rising concentration of the emulsifying agent.

Due to low air entrapment in the formulation, the buoyancy of microspheres dramatically decreased with increasing emulsifying agent concentration and was in the range of  $86.34 \pm 1.05\%$  to  $65.66 \pm 1.25\%$ . To determine the impact of temperature on the microspheres' buoyancy, glipizide-loaded floating microspheres were created using a progressively increasing temperature. Because air was trapped in the formulation, the buoyancy of the microspheres dramatically increased with temperature, ranging from  $65.37 \pm 0.70\%$  to  $76.52 \pm 1.01\%$ .

To determine the impact of stirring rate on the microspheres' buoyancy, glipizide-loaded floating microspheres were created using a progressively rising stirring rate. Microsphere buoyancy ranged from  $69.42 \pm 0.97\%$  to  $86.52 \pm 1.26\%$ , and it considerably increased with increasing stirring rate.

### 3.6 Fourier transform infra-red analysis

To examine the chemical attraction between the drug and the polymers, FTIR spectra of glipizide, polymers, a physical mixing of the drug and polymer

(1:6), and glipizide-loaded floating microspheres were conducted.

The characteristic peaks in the FTIR spectrum of glipizide were observed at  $2937.68$  and  $2860.53$   $\text{cm}^{-1}$  due to C-H stretching (aliphatic), at  $1691.63$   $\text{cm}^{-1}$  due to C=O stretching, at  $1533.46$   $\text{cm}^{-1}$  due to C=C stretching, at  $1446.66$   $\text{cm}^{-1}$  due to C-C stretching, and at  $1305.85$ ,  $1263.42$ ,  $1207.48$ , and  $1089.82$   $\text{cm}^{-1}$  due to C-N stretching. The distinctive peaks of glipizide-loaded floating microspheres were seen at  $2929.97$  and  $2874.03$   $\text{cm}^{-1}$  due to C-H (aliphatic) stretching,  $1523.82$   $\text{cm}^{-1}$  due to C=C stretching,  $1444.73$   $\text{cm}^{-1}$  due to C-C stretching, and  $1309.71$ ,  $1274.99$ ,  $1201.69$ , and  $1089.82$   $\text{cm}^{-1}$  due to C-N stretching.

According to the findings, the optimized microspheres' FTIR spectra displayed all of the typical medication and polymer peaks. These findings demonstrated that there is no drug-polymer interaction.

### 3.7 Differential scanning calorimetry (DSC)

The physical state of the drug within the microspheres was investigated using DSC since it might affect how the drug is released from the systems in vitro and in vivo. DSC spectra for glipizide, HPMC, EC, a physical drug-polymer combination (1:6), and floating microspheres with glipizide inside. Glipizide showed an endothermic peak at  $214.66^\circ\text{C}$ , which is the same temperature as its melting point. The endothermic peak for HPMC was recorded at  $215.14^\circ\text{C}$ , while the endothermic peak for EC was recorded at  $165^\circ\text{C}$ . Due to the high polymer drug ratio, the drug peak is also visible in the thermogram of the physical mixture, though it is less obvious. In the thermogram of the glipizide-loaded floating microspheres, the glipizide endothermic peak completely vanished, demonstrating the absence of crystalline drug in the microsphere samples, at least at the particle surface level. As a result, it was possible to draw the conclusion that the medication had dissolved in the polymer matrix and that its own melting endothermic peak had vanished.

### 3.8 X-ray diffraction analysis (XRD)

In the instance of glipizide, an endothermic peak at  $214.66^\circ\text{C}$ , which corresponds to its melting point, was seen. Endothermic peaks for HPMC and EC were both recorded at  $215.14$  and  $165$  degrees Celsius, respectively. The thermogram of the physical mixture likewise displays the drug peak, however it is less obvious because to the high polymer drug ratio. The lack of the crystalline drug, at least at the particle surface level, is demonstrated by the fact that the glipizide endothermic peak completely vanished from the thermogram of glipizide-loaded floating microspheres. The medication had apparently

dissolved in the polymer matrix because its own melting endothermic peak had vanished.

The physical drug and polymer mixture's XRD pattern revealed peaks that corresponded to the mixtures crystalline drug molecules. Despite the fact that their intensity was relatively low due to the large polymer drug ratio used, their presence showed that the drug was disseminated in the polymer. The DSC result is supported by the improved formulation's XRD pattern, which displayed an amorphous pattern with no drug peak. As a result, it was possible to draw the conclusion that the medication had dissolved in the polymer matrix and that its own melting endothermic peak had vanished.

### 3.9 *In vitro* drug release studies

Glipizide-loaded floating microspheres were studied for *in vitro* drug release in SGF (pH 1.2). As the amount of polymer ratio increased during the manufacture of the microspheres, the medication release rate dropped from  $79.0 \pm 2.0$  to  $70.3 \pm 2.0$ . Additionally, smaller microspheres with a larger surface area exposed to the dissolution media were created at a lower quantity of polymer ratio and a higher stirring rate, leading to a quicker release of the medication.

The concentration of the emulsifying agent was increased from  $68.3 \pm 1.5$  to  $74.0 \pm 1.0$ , which also resulted in an increase in the rate of drug release. The rate of drug release similarly increased when the temperature rose from  $62.0 \pm 2.0$  to  $65.3 \pm 1.5$ . The rate of drug release increased when the stirring rate increased from  $72.6 \pm 1.1$  to  $79.3 \pm 1.5$  rpm. The particle size distribution may have changed as the stirring rate changed. Microsphere mean size often decreases as the stirring rate is increased.

### 3.10 *In vivo* studies

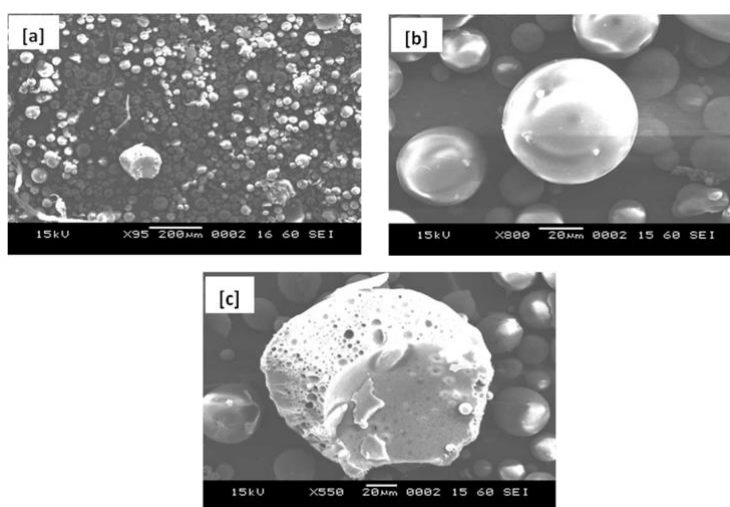
#### 3.10.1 *Antidiabetic activity of floating microspheres of glipizide*

Using healthy, normal Wistar rats, the *in vivo* effectiveness of the optimised floating microspheres was evaluated by assessing the hypoglycemic response to oral treatment. In the form of a suspension, 800 g/kg of both pure glipizide and HEM floating microspheres of glipizide were given. When pure glipizide suspension was provided, blood sugar levels dropped quickly, reaching their lowest point up to four hours later ( $252$  mg/dl to  $138$  mg/dl), following which they quickly returned to normal (Fig.9).

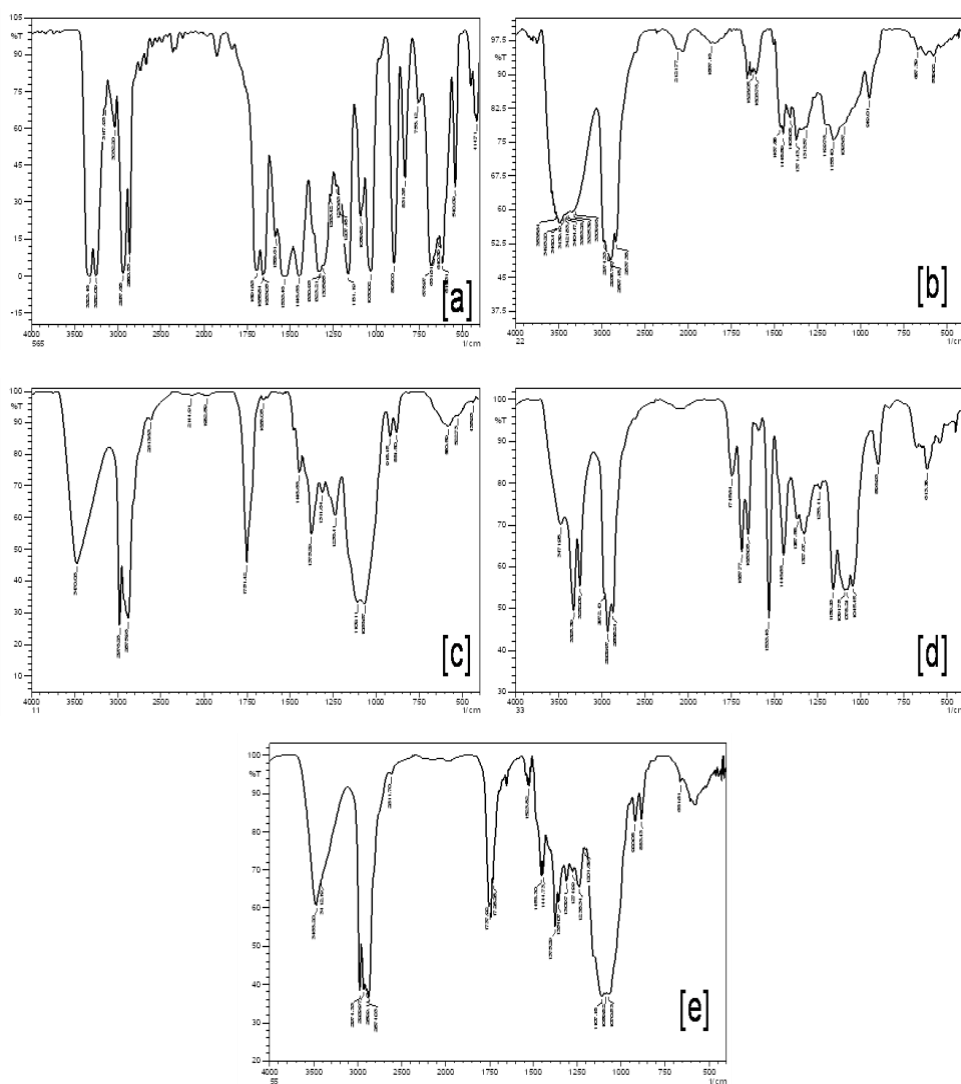
The blood glucose level dropped gradually (from  $256.667$  mg/dl to  $136.6$  mg/dl) in the case of HEM floating microspheres of glipizide, reaching its greatest drop 12 hours after oral delivery, as shown in Fig. 9. These lower blood sugar levels persisted for extended periods of time (12 hour). When it came to lowering blood sugar levels, glipizide sustained release floating microspheres were noticeably superior than the pure glipizide suspension. The negative effects of glipizide may be reduced if it is formulated as a floating sustained release dose form.

#### 3.10.2 *In vivo* radio graphical study

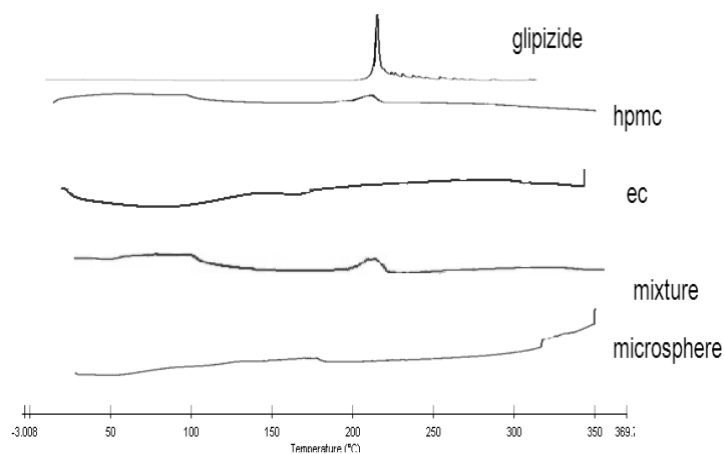
It took HEM floating microspheres of glipizide 12 hours after oral treatment to reach their optimum blood glucose decrease (from  $256.667$  mg/dl to  $136.6$  mg/dl), as illustrated in Fig. 9. This drop in blood sugar was maintained over extended periods of time (12 hour). Glipizide sustained release floating microspheres effectively reduced blood glucose levels compared to pure glipizide solution. A reduction in adverse effects may also be seen if glipizide is formulated in a floating sustained release dose form.



**Fig. 1.** Scanning electron photomicrographs; [a] population of floating microspheres, [b] external smooth surface of microspheres, [c] internal surface of microsphere



**Fig. 2: FTIR spectrum of glipizide [a], hydroxyl propyl methyl cellulose [b], ethyl cellulose [c], physical mixture [d] and glipizide loaded floating microspheres [e]**



**Fig. 3: DSC thermogram of glipizide, hydroxyl propyl methyl cellulose, ethyl cellulose, physical mixture and glipizide loaded floating microspheres**

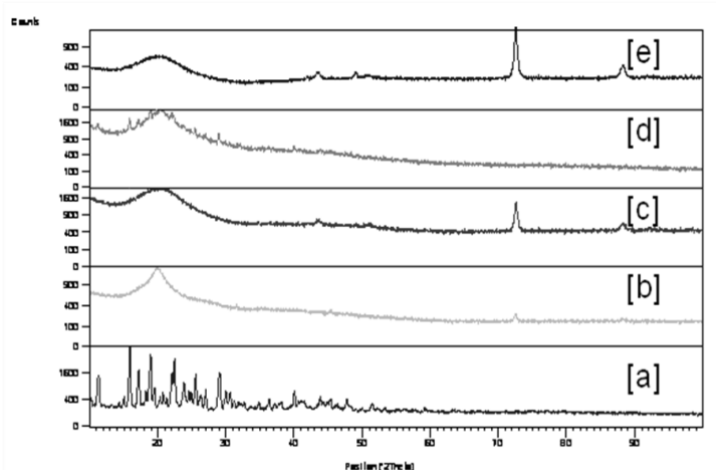


Fig. 4: XRD patterns of glipizide [a], hydroxyl propyl methyl cellulose [b], ethyl cellulose [c], physical mixture [d] and glipizide loaded floating microspheres [e]

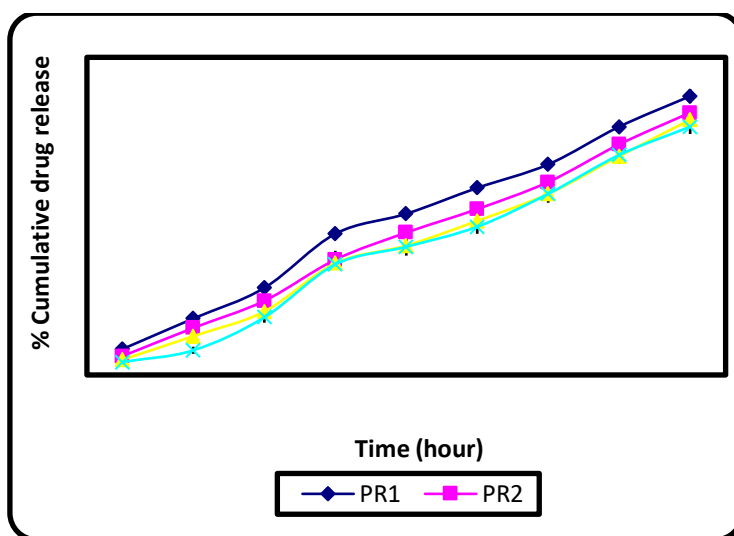


Fig. 5: Effect of amount of polymer ratio on *in vitro* drug release of glipizide loaded floating microspheres

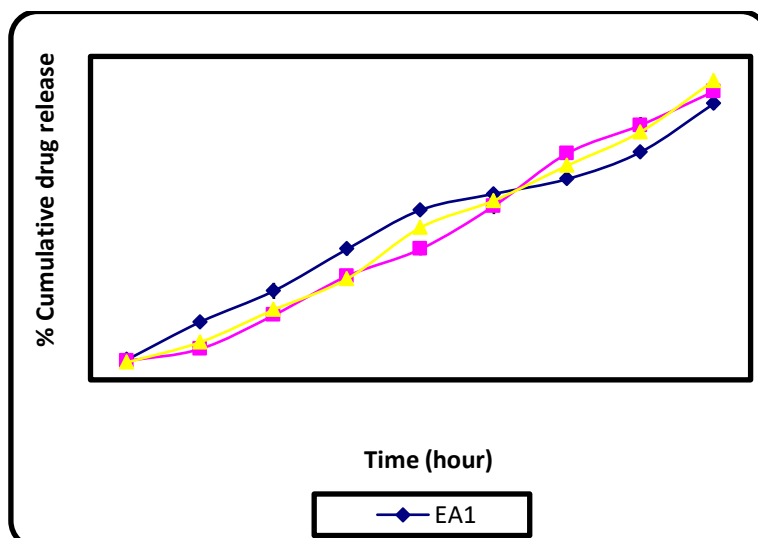


Fig. 6: Effect of concentration of emulsifying agent on *in vitro* drug release of glipizide loaded floating microsphere



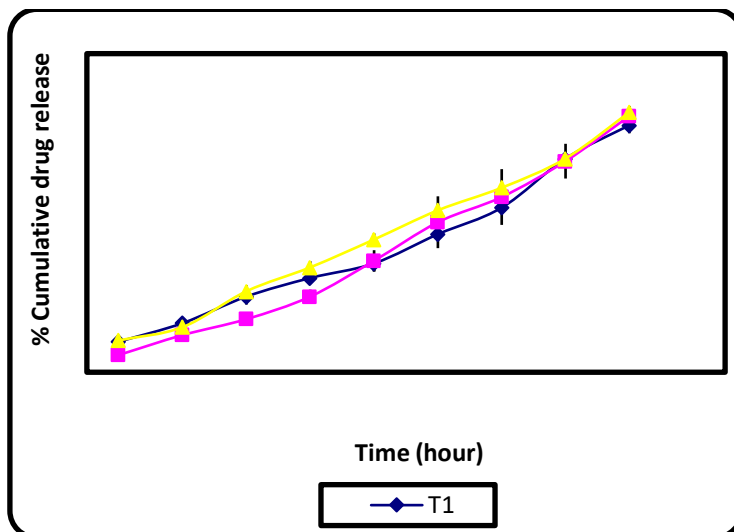


Fig. 7: Effect of temperature on *in vitro* drug release of glipizide loaded floating microspheres

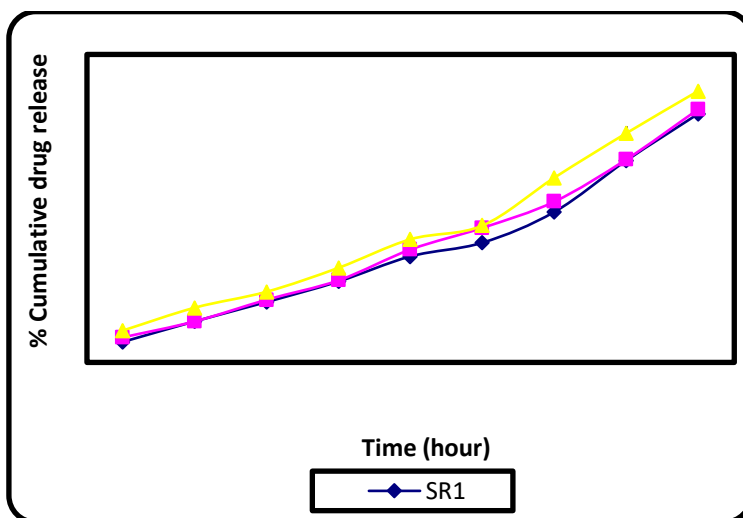


Fig. 8: Effect of stirring rate on *in vitro* drug release of glipizide loaded floating microspheres

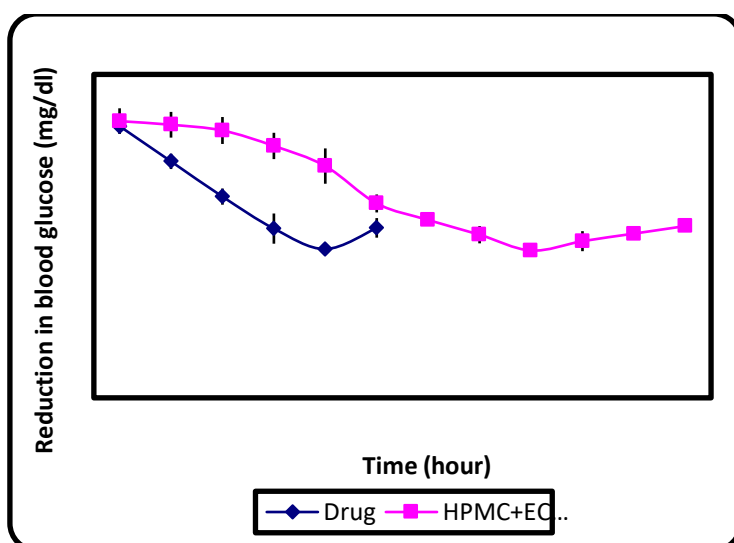
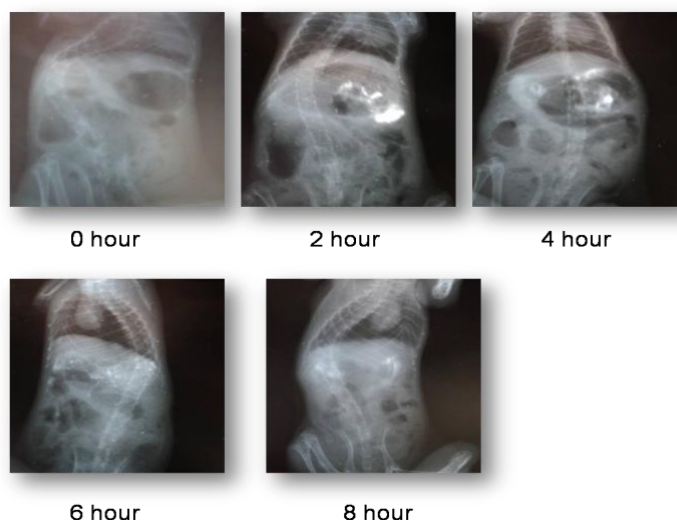


Fig. 9: Antidiabetic activity of combination of HPMC & EC floating microspheres of glipizide



**Fig. 10: X-ray photograph of wistar rat's stomach showing *in vivo* floating behavior of combination of HPMC & EC floating microspheres**

**Table 1: Effect of amount of polymer ratio on % yield, particle size, % drug entrapment efficiency and % buoyancy of glipizide loaded floating microspheres**

Formulation Code	Polymer ratio	% yield	Size ( $\mu\text{m}$ )	% DEE	% buoyancy
PR1	1:2	53.58 $\pm$ 1.08	17.33 $\pm$ 0.57	56.64 $\pm$ 0.32	64.28 $\pm$ 1.08
PR2	1:4	86.36 $\pm$ 0.85	23.33 $\pm$ 1.15	47.33 $\pm$ 0.89	80.51 $\pm$ 0.75
PR3	1:6	94.36 $\pm$ 0.85	29.6 $\pm$ 1.52	42.72 $\pm$ 0.35	89.26 $\pm$ 0.86
PR4	1:8	94.54 $\pm$ 1.06	43.6 $\pm$ 1.15	29.87 $\pm$ 0.40	90.33 $\pm$ 0.91

mean $\pm$ standard deviation (n=3)

**Table 2: Effect of concentration of emulsifying agent on % yield, particle size, % drug entrapment efficiency and % buoyancy of glipizide loaded floating microspheres**

Formulation Code	Concentration of emulsifying agent %	% yield	Size ( $\mu\text{m}$ )	% DEE	% buoyancy
EA1	0.01	86.88 $\pm$ 0.69	29.33 $\pm$ 1.52	46.26 $\pm$ 0.82	86.34 $\pm$ 1.05
EA2	0.02	74.5 $\pm$ 0.61	21.33 $\pm$ 1.1	45.36 $\pm$ 0.73	77.36 $\pm$ 1.10
EA3	0.03	67.38 $\pm$ 0.60	16.3 $\pm$ 1.15	40.22 $\pm$ 0.90	65.66 $\pm$ 1.25

mean $\pm$ standard deviation (n=3)

**Table 3: Effect of temperature on % yield, particle size, % drug entrapment efficiency and % buoyancy of glipizide loaded floating microspheres**

Formulation Code	Temperature ( $^{\circ}\text{C}$ )	% yield	Size( $\mu\text{m}$ )	% DEE	% buoyancy
T1	30	66.59 $\pm$ 1.02	19.6 $\pm$ 0.54	46.25 $\pm$ 0.33	65.37 $\pm$ 0.70
T2	40	58.19 $\pm$ 0.89	27.33 $\pm$ 0.57	44.70 $\pm$ 0.69	76.25 $\pm$ 1.07
T3	50	46.25 $\pm$ 0.79	35.66 $\pm$ 1.52	20.11 $\pm$ 0.35	76.52 $\pm$ 1.01

mean $\pm$ standard deviation (n=3)

**Table 4: Effect of stirring rate on % yield, particle size, % drug entrapment efficiency and % buoyancy of glipizide loaded floating microspheres**

Formulation Code	Stirring rate (rpm)	% yield	Size ( $\mu\text{m}$ )	% DEE	% buoyancy
SR1	900	92.17 $\pm$ 0.91	43.67 $\pm$ 1.15	28.56 $\pm$ 0.70	69.42 $\pm$ 0.97
SR2	1200	84.48 $\pm$ 1.18	21.6 $\pm$ 0.58	36.03 $\pm$ 0.86	81.58 $\pm$ 1.11
SR3	1500	47.69 $\pm$ 0.33	18.3 $\pm$ 1.53	50.81 $\pm$ 0.38	86.52 $\pm$ 1.26

mean $\pm$ standard deviation (n=3)

#### 4. CONCLUSION:

Due to their biodegradability, biocompatibility, and suitability for oral applications, floating microspheres made of a combination of HPMC and EC polymer have the potential to be an effective, practical, safe, and cost-effective method of glipizide administration. The solvent evaporation technique was used to create floating microspheres that were loaded with glipizide. The current glipizide formulation study was carried out in an effort to create a floating medication delivery system. The microspheres' incorporation of HPMC and EC as a hydrophilic polymer worked well to produce the desired release behavior and buoyancy.

These formulations' effectiveness was assessed, and the impact of several formulation variables was investigated. The developed system, which combines outstanding buoyant ability and a proper drug release pattern, may be helpful in terms of enhancing glipizide bioavailability. Easy preparation, good buoyancy, high drug entrapment efficiency, and prolonged drug release over several hours are some of the system's key benefits. The optimized floating microspheres were ultimately chosen for the in vivo radiographic research because they had demonstrated good in vitro buoyancy and controlled release behavior.

Examining the series of x-ray images obtained throughout the trial made it abundantly evident that the improved formulation stayed buoyant and evenly distributed throughout the gastric contents throughout the entire eight-hour study. During the test period, a prolonged gastric retention time (GRT) of more than 8 hours was attained and stayed buoyant in the stomach.

The created formulation eliminates and reduces the shortcomings and restrictions of sustained release preparations. The created formulations supplied the medication in a controlled way, reducing the frequency of administration while minimizing side effects. They also provided greater absorption, increased bioavailability, and delivery compliance. The microspheres might be formed into oral

solutions, crushed into tablets, or filled into capsules for reconstitution.

#### REFERENCES:

- [1] Firke Sagar N., Ghiware Nitin B., In vitro and in vivo Evaluation of Ivabradine Loaded Microspheres Prepared by Multiple Emulsion Solvent Evaporation Method. *International Journal of Pharmacy and Biological Sciences-IJPBS* (2019) 9 (4): 315-322
- [2] Sagar N Firke., Formulation and Optimization of Floating Microspheres of Ivabradine Hydrochloride by 3<sup>2</sup> Factorial Design Approach *International Journal of Pharmacy and Biological Sciences-IJPBS* (2019) 9 (3): 1025-1034
- [3] Arunachalam, S., Gunasekaran, S., 2002. Diabetic research in India and Chinatoday: from literature-based mapping to health-care policy. *Current Science*. 9–10, 1086–1097.
- [4] Brogden, R.N., Heel, R.C., Pakes, G.E., Speight, T.M., Avery, G.S., 1979. Glipizide: a review of its pharmacological properties and therapeutic use. *Drugs* 18, 329–353.
- [5] Chudiwal, P.D., Pawar, P.L., Nagras, M.A., Mandlik, S.K., Pandya, S.V., Watke, P., 2009. Statistical evaluation and optimization of influence of viscosity and content of polymer on floating microspheres of clarithromycin. *International Journal of PharmTech Research*. 1: 1366-1372.
- [6] Gangadharappa, H.V., Pramod Kumar, T.M., Shiva Kumar, H.G., 2007. Gastric floating drug delivery system: A review. *Indian J Pharm Educ Res*. 41, 329-336.
- [7] Mutalik, S., Udapa, N., 2006. Pharmacological evaluation of membrane moderated transdermal system of glipizide. *Clin. Exp. Pharmacol. Physiol*. 33, 17–26.
- [8] Nepal, P.R., Chun, M.K., Choi, H.K., 2007. Preparation of floating microspheres for fish farming. *Int J Pharm*. 341, 85-90.
- [9] Struebel, A., Siepmann, J., Bodmeier, R., 2003. Multiple units gastroretentive drug delivery systems: a new preparation method for low density microspheres. *J. Microencaps*. 20, 329–347.
- [10] Roge *et al*: Development, validation of RP-HPLC method and GC MS analysis of desloratadine HCL and its degradation products., *IJCRR* - 13(21), November 2021, 129-13.