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Formulation, characterization and in-vivo floating study of Glipizide loaded floating microspheres.

Pritam Rajkumar Siraskar*, Dinesh Kumar Mishra, Sagar Naresh Firke

1. *School of Health Science and Pharmacy, Career Point University, Kota, Rajasthan*
2. *Indore Institute of Pharmacy, Indore, Madhya Pradesh*
3. *Nanded Pharmacy College, Nanded, Maharashtra*

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ABSTRACT

The goal of the current study was to produce floating microspheres of glipizide to obtain an extended retention in the upper GIT, which may lead to better bioavailability and enhanced absorption. By employing ethyl cellulose in various quantities, floating microspheres containing glipizide were created utilizing the emulsion solvent diffusion process. The USP apparatus type I was used to carry out in vitro drug releases, and FT-IR was used to assess the microspheres' polymer compatibility. Studies were done on glipizide-loaded microspheres to determine their yield, particle size, buoyancy percentage, drug entrapment efficiency, in vitro drug release, and in vivo anti-diabetic effectiveness.The yield of floating microspheres with glipizide added ranged from 53.49±±0.54% to 86.60 ±0.63%. The range of particle sizes was 281.00±5.56 m to 389.66±2.51 m, with the maximum drug entrapment effectiveness being 71.01±0.82% and the buoyancy percentage being 85.77±1.13%. The formulation affected the drug release characteristics.

Keywords: In vitro release studies, glipizide, floating microspheres, In vivo anti-diabetic efficacy

I. 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 gastro retentive drug delivery methods will be created in order to maximize the delivery of compounds with low bioavailability and extensive first pass metabolism. A gastric floating drug delivery system can help with at least some of these issues. It is especially helpful for medications that are absorbed primarily in the duodenum and upper jejunum segments. It can also extend the time that dosage forms are retained in the GIT, improving the oral bioavailability of the medication [1]. The next ten years may be devoted to controlling gastrointestinal transit, which could lead to novel therapeutic opportunities with significant advantages for patients.

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. In order to produce energy, glucagon instructs the liver to release glucose from its cells into the blood [2].

One of the most often given medications for the treatment of people with type II diabetes mellitus is glipizide, an oral hypoglycemic agent [3]. Although it is nearly insoluble in water, the absolute bioavailability is close to 1. So, according to the Biopharmaceutical Classification System (BCS) [4], it is classified as class 2. Due to the relatively short (2-4 h) elimination half-life of glipizide, it must be administered often. Additionally, taking it by mouth frequently results in severe hypoglycemia symptoms as nausea, vomiting, heartburn, anorexia, and an increase in hunger [5]. 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. Because of their versatility in achieving a desired drug release profile, cost-effectiveness, and broad regulatory approval, the proposed study is intended to test floating microspheres of glipizide as a model medication for prolonging the stomach retention duration by employing EC as hydrophilic polymer.

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II. EXPERIMENTAL

2.1. Materials

Glipizide was received from M/s Aristo Pharmaceuticals Pvt Ltd, Mumbai, as a gift sample (India). The following substances were procured from Central Drug House (P) Ltd.: dichloromethane, ethyl cellulose (EC), polyethylene glycol (PEG), polyvinyl alcohol, and Tween 80. (India). All additional substances/reagents were of analytical grade.

2.2. Preparation of floating microspheres

According to Sato et al.[6], floating microspheres containing Glipizide were created utilising the emulsion solvent diffusion process and ethyl cellulose in different concentrations. Different concentrations of polyethylene glycol (PEG) were used as a plasticizer. Plasticizer was also added after the medication and polymer mixture was dissolved in 15 ml of dichloromethane. The aforementioned combination was poured into a 200 ml 0.25% polyvinyl alcohol solution. The final mixture was agitated for an hour at 1000 rpm with a mechanical stirrer. The created floating microspheres underwent filtering, a water wash, room-temperature drying, and storage in a desiccator until needed.

Numerous process factors are involved in the creation of floating microspheres, but only the following were chosen. Different formulation factors that may have an impact on the creation and characteristics of microspheres, including as the amount of EC, the concentration of the emulsifying agent, the concentration of the plasticizer, and the stirring rate, were identified and analyzed.

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.

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

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.

$$\text{Buoyancy (\%)} = \frac{Wf}{(Wf + Ws)} \times 100$$

Wf and Ws are respectively the weights of the floating and settled microparticles.

2.3.6 .Fourier transform infra-red analysis

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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 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 aluminium 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-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 normally 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 either pure glipizide or EC floating microspheres of glipizide orally via 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

Microspheres loaded with barium sulphate were utilised as a diagnostic tool or as the main

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component in the explanation of the generated microspheres' in vivo floating behaviour. A wistar rat was given an oral suspension of EC floating microspheres following a small meal. The stomach of a wistar rat was X-rayed at an appropriate period and is depicted in Figure 10. Throughout the whole trial, all rats are allowed access to water and regular mobility. In Jabalpur, Madhya Pradesh, a government veterinary hospital conducted this study.

III. RESULTS & DISCUSSION

3.1 Particle size

To evaluate the impact of polymer concentration on microsphere particle size, increasing EC concentration and a fixed drug concentration were both utilised. The mean particle size of microspheres considerably increased with increasing ethyl cellulose concentration as demonstrated in the investigation of the effect of polymer concentration, and was in the range of 334.66±3.21 m to 385.00±4.00 m. It was caused by the fact that when polymer content was raised, solution viscosity increased and stirring speed decreased, which resulted in larger particle sizes [7]. To determine how the concentration of the emulsifying agent affected the particle size of the microspheres, glipizide-loaded floating microspheres were created using an emulsifying agent whose concentration was gradually increased. With increasing emulsifying agent concentration, the mean microsphere particle size dramatically decreased, falling between 357.33±4.04 µm to 323.33±4.04 µm. It was due to the fact that more stable droplet formation occurs as emulsifying agent concentration rises, preventing the fusing of smaller droplets to bigger aggregates. To determine the impact of plasticizing agent concentration on the particle size of the microspheres, glipizide-loaded floating microspheres were created using a steadily increasing concentration of plasticizing agent.

Due to the creation of tiny droplets and the presence of an emulsifying agent, the mean particle size of microspheres dramatically increased with increasing concentrations of plasticizing agent, ranging from 303.33±4.04 µm to 366.33±3.05 µm. To determine the impact of stirring rate on the particle size of the microspheres, glipizide-loaded floating microspheres were created using a gradually rising stirring rate. Due to the high shear force that caused the creation of smaller droplets, the mean particle size of the microspheres considerably dropped with increasing stirring rate and was in the range of 389.66±2.51 µm to 281.00±5.56 µm.

3.2 Surface morphology

Scanning electron microscope images were used to observe the surface morphology, which revealed the population's size distribution as well as the external and internal morphologies of the microspheres. The manufactured microspheres had a hollow inside with a spherical surface and an exterior shell made of a medicine and a polymer. Microsphere's exterior is a smooth surface that also exhibited no aggregation. The internal morphology of a microsphere with pores. These pores may be the result of the volatile solvent quickly escaping from the polymer matrix. The microspheres' capacity to float was also a result of their hollow structure.

3.3 Percentage yield of microspheres formed

The yield of floating microspheres with glipizide loaded varied from 53.49±0.54 % to 86.60±0.63 %.

3.4 Drug entrapment efficiency

To evaluate the impact of polymer concentration on the percentage of drug entrapment of the microspheres, increasing EC concentration and fixed concentration of drug were utilised. When the concentration of the polymer was studied, it was found that the drug entrapment reduced from 71.01±0.82% to 57.36±0.56%, which may have been caused by an increase in viscosity. To determine how the concentration of the emulsifying agent affected the percentage of drug entrapment, glipizide-loaded floating microspheres were created using an emulsifying agent whose concentration was gradually increased.Due to the production of smaller particles, which in turn reduced drug entrapment, the drug entrapment of microspheres considerably dropped with increasing emulsifying agent concentration, and was in the range of 36.12±0.73% to 26.72±1.26%. To determine the impact of plasticizing agent concentration on the percentage of drug entrapment in the microspheres, glipizide-loaded floating microspheres were created using a steadily increasing concentration of plasticizing agent.

With increasing plasticizing agent concentration, the drug entrapment of microspheres considerably dropped and was in the range of 51.620.88% to 40.150.71% as a result of increased viscosity. 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

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stirring rate. With increased stirring rate, the drug entrapment of microspheres significantly increased and ranged from 39.340.58% to 54.910.75%. (Table 4). More medication is enclosed in polymer and aggregation is prevented by vigorous stirring.

3.5 Floating behavior

To evaluate the impact of polymer concentration on microsphere buoyancy, increasing EC concentration and a fixed drug concentration were utilized. The percentage buoyancy of microspheres increased dramatically with increasing EC concentration and ranged from 56.161.07% to 77.390.87%. This was caused by air, which swelled as a result of increased polymer concentration [8]. In order to determine how the concentration of the emulsifying agent affected the microspheres' buoyancy, glipizide-loaded floating microspheres were created using an emulsifying agent whose concentration was gradually increased. Due to limited air entrapment, which reduced buoyancy, the percentage of buoyancy of microspheres considerably fell with increasing emulsifying agent concentration and was in the range of 84.16±0.83% to 71.58±1.20%. To determine the impact of plasticizing agent concentration on the microspheres' buoyancy, glipizide-loaded floating microspheres were created using a steadily increasing concentration of the plasticizing agent. Due to air entrapment, the buoyancy of microspheres dramatically increased with increasing concentrations of plasticizing agent and ranged from 66.52±0.87% to 75.4±1.04%. To determine the impact of stirring rate on the microspheres' buoyancy, glipizide-loaded floating microspheres were created using a progressively rising stirring rate. Due to air entrapment, the buoyancy of the microspheres dramatically increased with increasing stirring rate and ranged from 77.57±0.78% to 85.77±1.13%.

3.6 Fourier transform infra-red analysis

To study the chemical attraction between drug and polymer, FTIR spectra of glipizide, EC, a physical mixture of drug and polymer, and glipizide-loaded floating microspheres were conducted. The aliphatic C-H stretching peak in the glipizide's FTIR spectrum was at 2860.53 cm-1; the C=O stretching peak was at 1691.63 cm-1; the C-C stretching peak was at 1446.66 cm-1; the C-C rocking peak was at 1330.93 cm-1; and the C-H bending peak was at 895.0 and 831.35 cm-1.

The distinctive peaks for glipizide-loaded floating microspheres were 2833.52 cm-1 for C-H stretching, 1712.85 cm-1 for C=O stretching, 1624.12 cm-1 for C=C stretching, 1437.02 cm-1 for C-C stretching, 1346.36 cm-1 for C-H rocking bending, and 906.57 cm-1 for C-H opposing bending. 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 of glipizide, EC, a physical drug and polymer combination, and floating microspheres with glipizide inside. Glipizide showed an endothermic peak at 214.66°C, which is the same temperature as its melting point. At 165°C, an EC endothermic peak was seen. Due to the high polymer drug ratio, this peak was also visible in the thermogram of the physical mixture, though it was less pronounced. 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. Therefore, it was possible to draw the conclusion that the medication had broken down or had been contained in a polymer matrix because its own melting endothermic peak had vanished.

3.8 X-ray diffraction analysis (XRD)

XRD study was performed to investigate the physical state of the drug whether amorphous or crystalline before and after floating microspheres formulation. XRD examinations were conducted for the glipizide, EC, physical mixture of drug and polymer and glipizide loaded floating microspheres. From XRD patterns of glipizide has shown characteristic intense peaks between 2θ values of 3, 12, 15, 18, 23, 26 due to its crystalline nature, while EC exhibited amorphous form.

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 results are supported by the XRD pattern of the glipizide-loaded floating microspheres, which displayed an amorphous pattern with no drug peak in the formulations.

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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 EC increased during the manufacture of the microspheres, the drug release rate dropped from 79.6±1.5 to 77.6±1.5. The concentration of the emulsifying agent was increased from 79.0±2.0 to 81.0±2.0, which also resulted in an increase in the medication release rate. Along with the rise in plasticizing agent from 77.6±0.5 to 72.0±1.0, the medication release rate also reduced. As the stirring rate climbed from 72.6±2.0 to 76.0±1.0, the rate at which drugs were released also increased. The particle size distribution may have changed as the stirring rate changed. Microsphere mean size often decreases as the stirring rate is increased.

3.10.1 Antidiabetic activity of floating microspheres of glipizide

Glipizide-loaded floating microspheres were studied for in vitro drug release in SGF (pH 1.2). When assessing the hypoglycemia impact brought on by oral administration of the optimized floating microspheres in healthy normal wistar rats, the medication release rate reduced. In the form of a suspension, 800 g/kg of both pure glipizide and EM floating microspheres of glipizide were delivered. When pure glipizide suspension was provided, blood glucose 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.

Blood glucose levels dropped gradually (238.33 mg/dl to 138 mg/dl) in the case of EM floating microspheres of glipizide, reaching their lowest point 15 hours after oral treatment, as shown in Fig. 9. These lower blood sugar levels persisted for extended periods of time (15 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

For the in vivo radiographic examination, the optimized floating microspheres were chosen because they demonstrated good in vitro buoyancy and controlled release behavior. The optimized formulation remained buoyant and evenly distributed in the gastric contents for the duration of the investigation, which lasted for eight hours, according to an examination of the consecutive x-ray images collected during the experiment (Fig.10). It was possible to obtain prolonged gastric retention time (GRT) of more than 8 hours, which stayed buoyant in the stomach for the whole test duration.

IV. CONCLUSION

Due to its biodegradability, biocompatibility, and appropriateness for oral applications, floating microspheres made of EC polymer have the potential to be an effective, practical, safe, and economical method of glipizide administration. By using the emulsion solvent diffusion method, floating microspheres with glipizide loaded into them were created. The current glipizide formulation study was carried out in an effort to create a floating medication delivery system. The microspheres' incorporation of 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 recipe 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.

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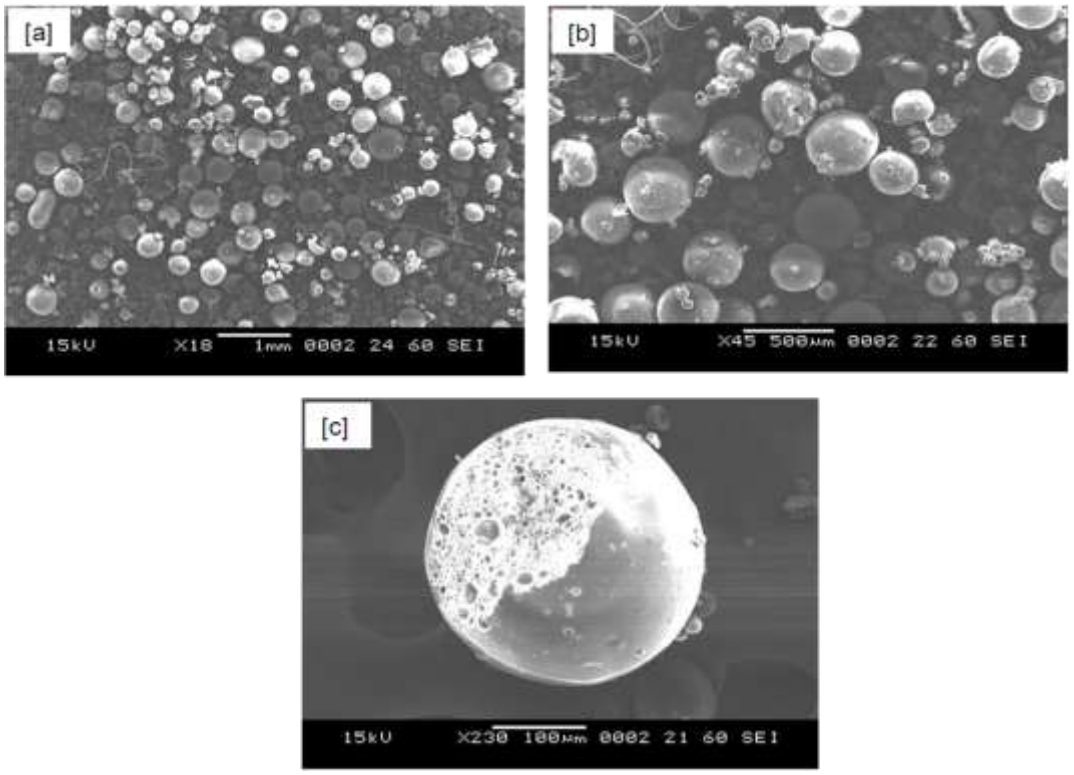

Fig. 1. Scanning electron photomicrographs; [a] population of floating microspheres, [b] external smooth surface of microspheres, [c] internal surface of microsphere

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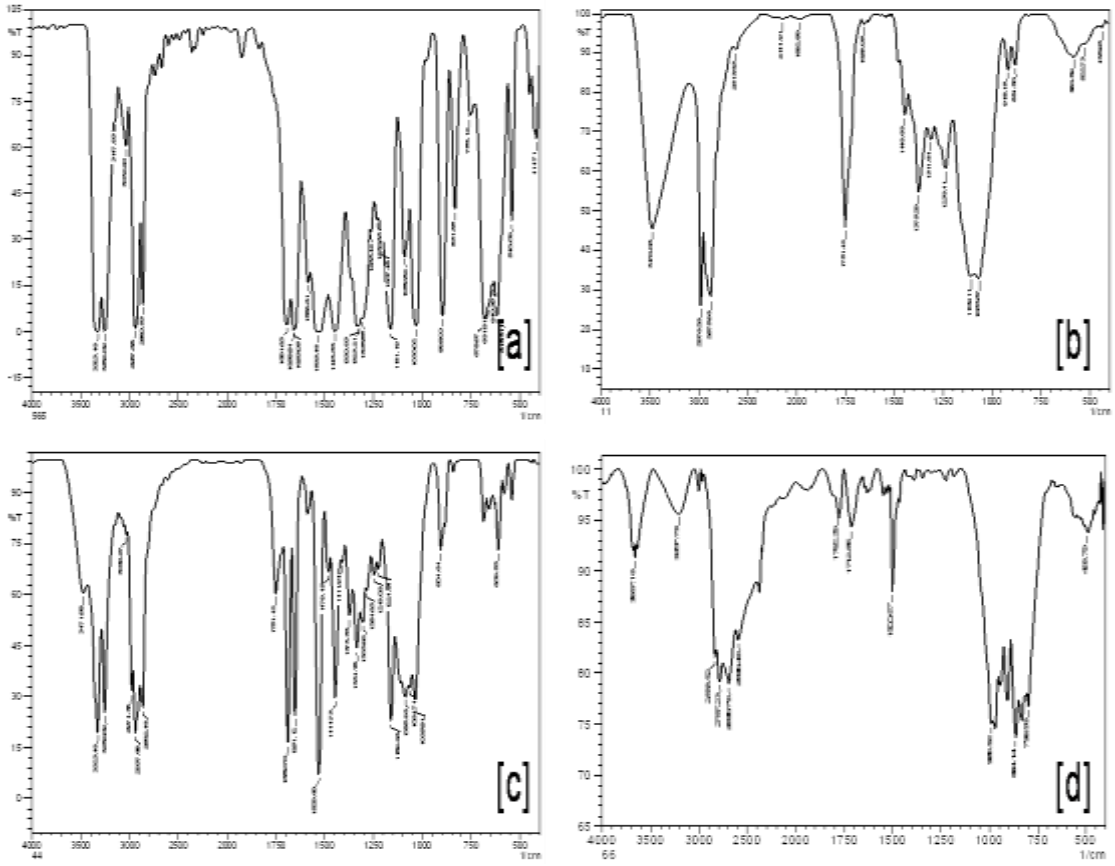

Fig. 2: FTIR spectrum of glipizide [a], ethyl cellulose [b], physical mixture [c] and glipizide loaded floating microspheres [d]

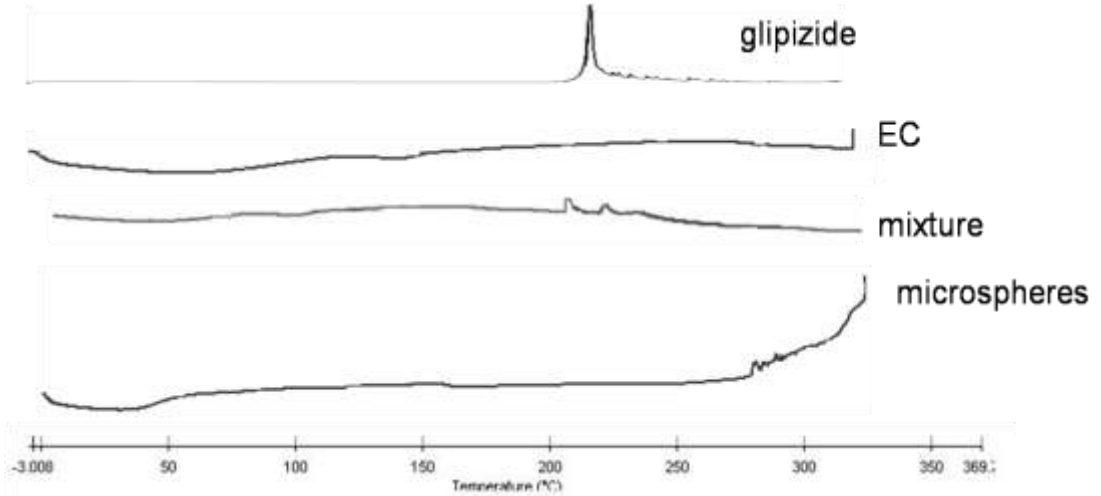

Fig. 3: DSC thermogram of glipizide, ethyl cellulose, physical mixture and glipizide loaded floating microspheres

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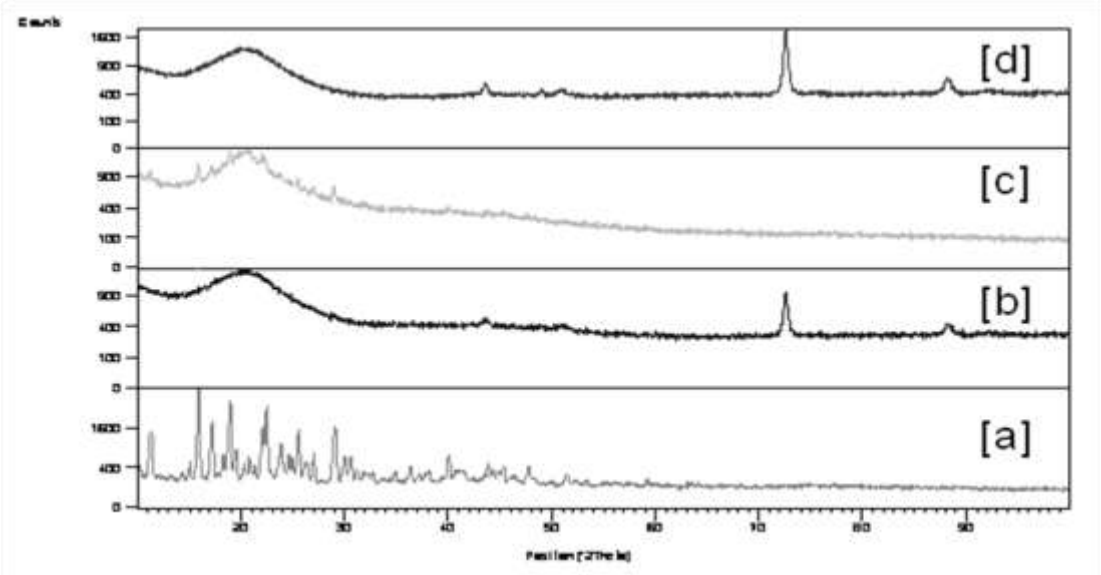

Fig. 4: XRD patterns of glipizide [a], ethyl cellulose [b], physical mixture [c] and glipizide loaded floating microspheres [d]

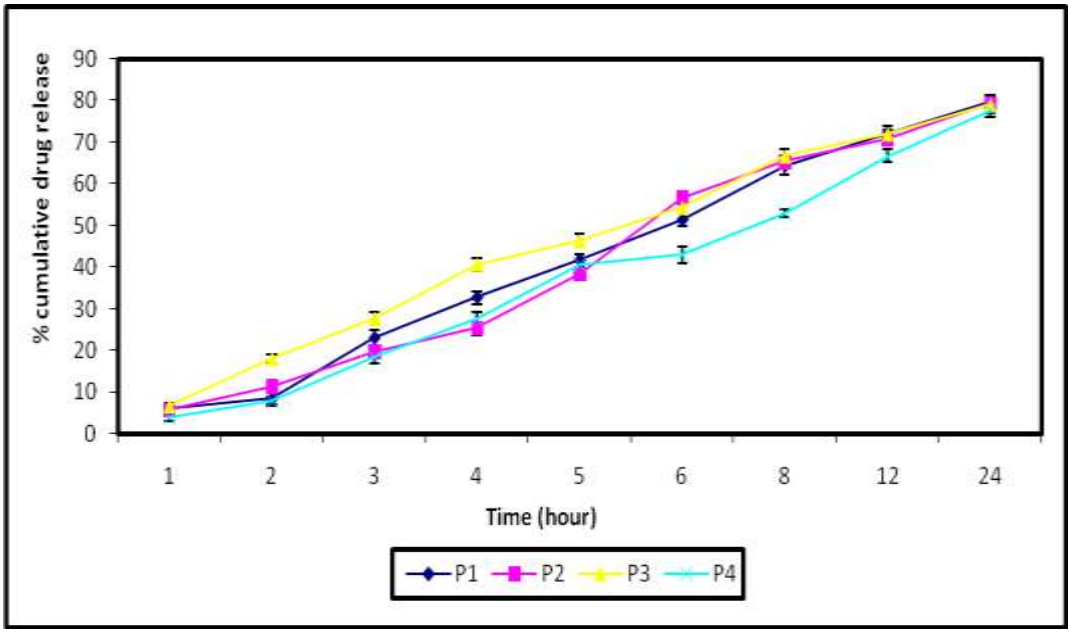

Fig. 5: Effect of amount of EC on in vitro drug release of glipizide loaded floating microspheres

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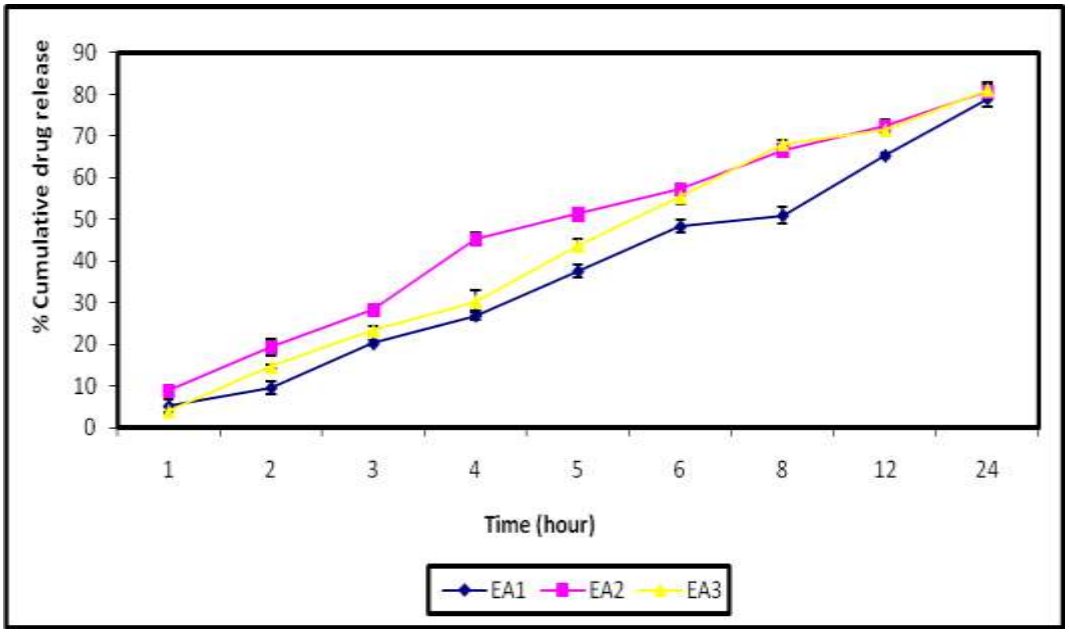

Fig. 6: Effect of amount of emulsifying agent on in vitro drug release of glipizide loaded floating microsphere

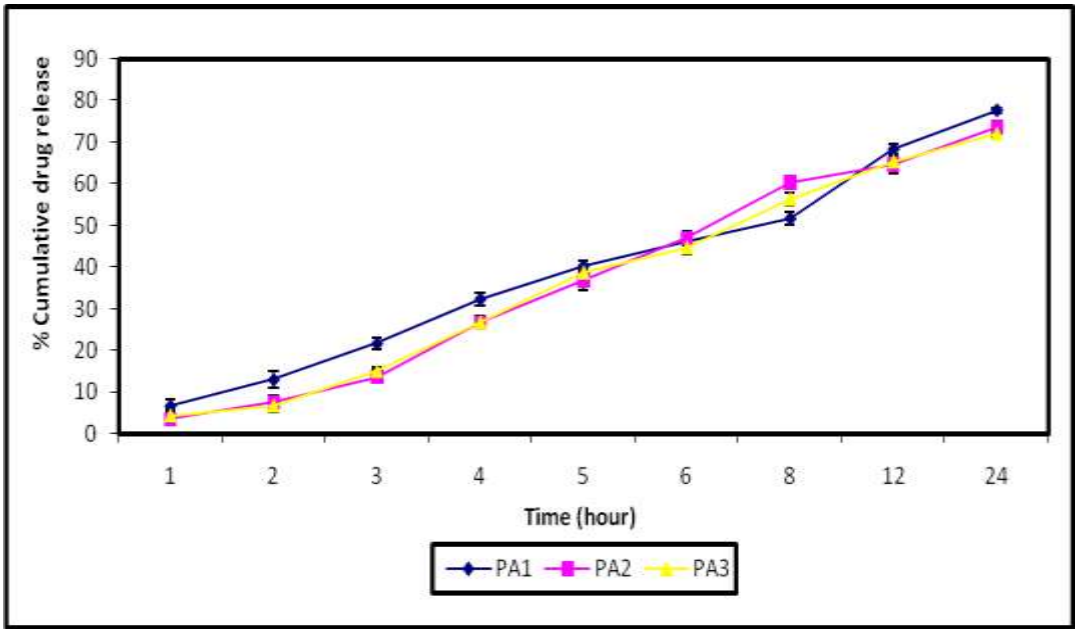

Fig.7: Effect of amount of plasticizer agent on in vitro drug release of glipizide loaded floating microspheres

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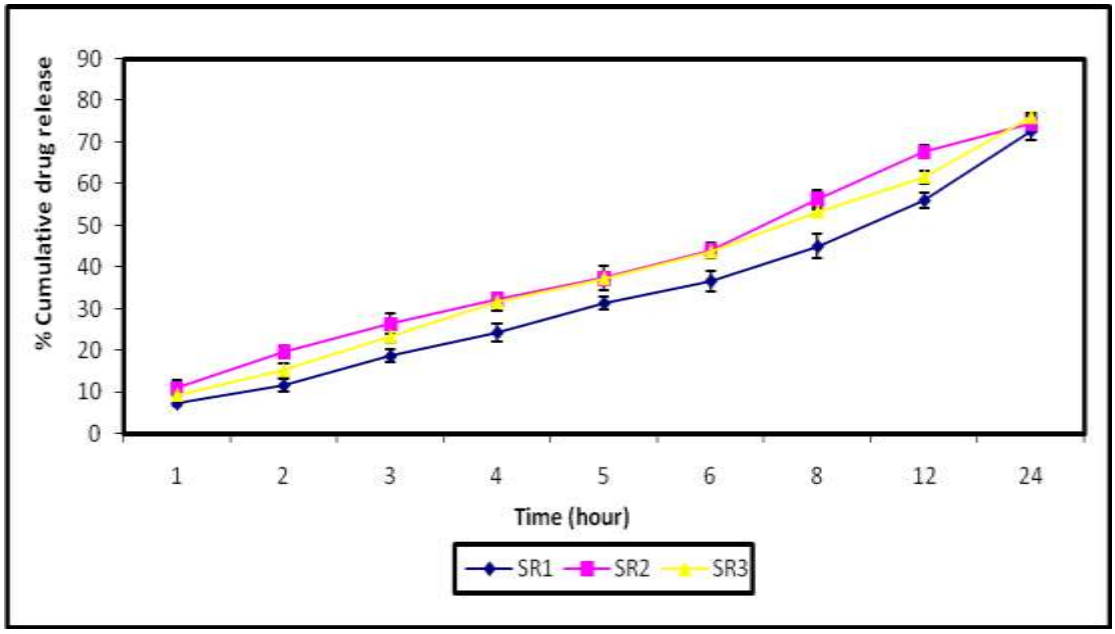

Fig. 8 : Effect of stirring rate on in vitro drug release of glipizide loaded floating microspheres

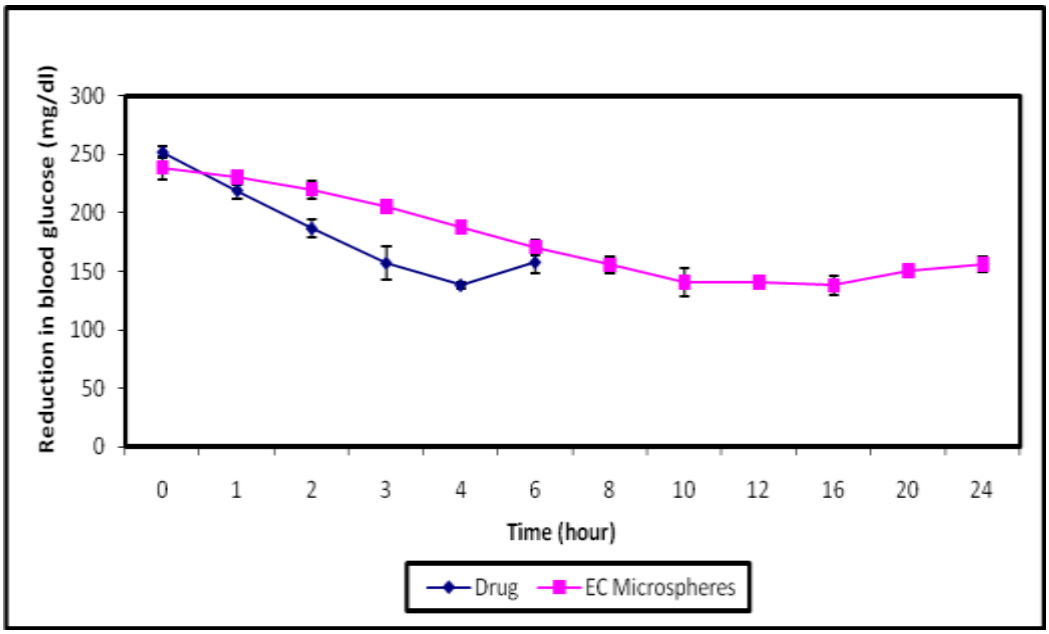

Fig. 9: Antidiabetic activity of EC floating microspheres of glipizide

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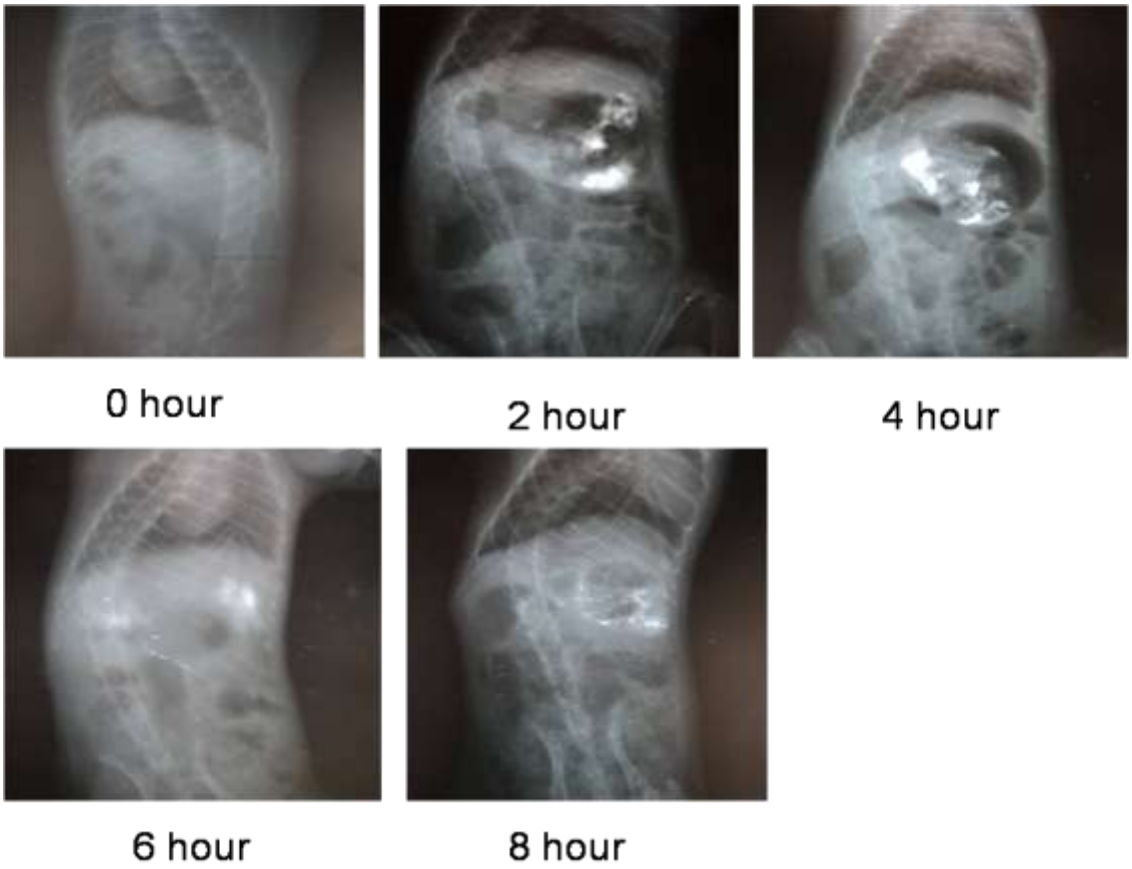

Fig. 10: X-ray photograph of wistar rat's stomach showing in vivo floating behavior of EC floating microspheres

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

Formulation Code	Amount of EC (mg)	% Yield	Size(µm)	% DEE	% Buoyancy
P1	500	53.49±0.54	334.66±3.21	71.01±0.82	56.16±1.07
P2	1000	74.54±0.96	356.66±2.51	70.05±0.72	65.24±0.14
P3	1500	85.3±1.02	368.33±3.51	58.46±0.50	76.17±1.95
P4	2000	86.60±0.63	385.00±4.00	57.36±0.56	77.39±0.87

Mean±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(µm)	% DEE	% Buoyancy
EA1	0.15	85.28±0.95	357.33±4.04	36.12±0.73	84.16±0.83
EA2	0.25	84.59±1.28	345.00±3.00	34.79±0.55	82.74±0.72
EA3	0.35	71.36±1.09	323.33±4.04	26.72±1.26	71.58±1.20

Mean±standard deviation (n=3)

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

Formulation Code	Concentration of plasticizer %	% Yield	Size(µm)	% DEE	% Buoyancy
PA1	10	60.21±0.81	303.33±4.04	51.62±0.88	66.52±0.87
PA2*	20	83.15±1.79	351.33±4.04	47.24±0.42	73.56±0.56
PA3	30	86.25±1.09	366.33±3.05	40.15±0.71	75.4±1.04

Mean±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(µm)	% DEE	% Buoyancy
SR1	800	61.63±1.20	389.66±2.51	39.34±0.58	77.57±0.78
SR2	1000	79.38±0.65	299.00±4.00	48.10±0.29	84.64±0.39
SR3	1200	82.27±1.07	281.00±5.56	54.91±0.75	85.77±1.13

Mean±standard deviation (n=3)