Floating Hollow Microspheres as Gastroretentive Drug Delivery System for Rosiglitazone Maleate

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Abstract

The aim of the present study is to formulate floating hollow microspheres of Rosiglitazone maleate (RGM) for the prolongation of gastric residence time by using modified Quasi-emulsion diffusion technique using Ethyl cellulose, polyethylene oxide and Eudragit S100 as polymers. Preliminary studies revealed that the polymer: drug ratio, concentration of polymer, and stirring speed significantly affected the characteristics of microspheres. The optimum batch exhibited a prolonged drug release, remained buoyant for more than 12 h, high entrapment efficiency, and particle size in the order of 302µm. In vivo of floatation behaviour evidences by taking the X-ray at 4th hr, 8th hr & 12th hr it can be concluded the floatation behaviour of hollow microspheres. The in vitro release showed the F3 formulation was maintain up to the 12th hr and blood glucose was found to be 88.9 mg/dL. Results of the stability studies showed that there were no significant changes in the drug content and physical appearance.

Key Words: Hollow microspheres, Rosiglitazone Maleate, Ethyl cellulose, Eudragit S100, polyethylene oxide.

Introduction

Oral route is the most convenient and extensively used route for drug administration. This route has high patient acceptability, primarily due to easy of administration. Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for other routes. Most of the oral controlled drug delivery systems rely on diffusion, dissolution or combination of both mechanisms, to release the drug in a controlled manner to the Gastrointestinal Tract (GIT) and the drug profile data, such as dose, absorption properties and the quantity of drug needed, one can determine the desired release rate of the drug from controlled release dosage form. Several approaches have been developed to prolong the residence time of dosage forms in the stomach. Various

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approaches have been used to retain the dosage form in the stomach as a way of increasing the gastric residence time (GRT), including floatation systems; high-density systems; mucoadhesive systems; magnetic systems; and superporous hydrogel system. Floating drug delivery systems or hydrodynamically balance system (HBS) are among the several approaches that have been developed to increase the GRT of dosage forms. Both single & multiple unit system have been developed. The single-unit floating systems are more popular. Surprisingly, however, less attention has been focused on the development of floating microspheres. In contrast, multiple-unit particulate dosage form (e.g. microspheres) have the advantages that they pass uniformly through the gastrointestinal tract (GIT) to avoid the vagaries of gastric emptying and provide an adjustable release, thereby reducing the intersubject variability in absorption and risk of local irritation. Recently hollow microspheres with a lower density than that of the GI fluids was adopted. They decrease intersubject variability in absorption and minimize the possibility of dose dumping by uniform distribution within the gastric content and provide longer duration of action.

Rosiglitazone maleate is an antidiabetic drug for type II diabetes that improves insulin sensitivity in muscle and adipose tissues through activation of peroxisome proliferator-activated γ receptor (PPARγ) that are involved in transcription of insulin-responsive genes responsible for glucose production, transport, and utilization. The drug shows linear pharmacokinetics over a dose of 0.2–20 mg with biological half-life of 3–4 h with oral bioavailability of 99.8%. The drug is highly soluble in simulated gastrointestinal fluid (SGF). But the solubility gradually decreases with increment of pH. Above pH 7, the solubility of the drug is very low. Therefore, the rate and extent of absorption viz. bioavailability of the drug is mainly controlled by its dissolution rate. Following rosiglitazone monotherapy for 8 to 12 weeks, the dose should be increased to 8 mg/day in case of insufficient glycemic control, which results in higher incidents of dose-dependent side effects such as gastrointestinal disturbances, headache, altered blood lipids, edema, and hypoglycaemia. Further, clinically significant adverse effects such as edema, anemia, and weight gain are frequently reported with conventional dosage forms of the drug. Clinical studies showed that 4-mg twice-per-day regimen compared to 8 mg once a day provides statistically greater improvement in glycemic control. RGM is highly soluble in simulated gastrointestinal fluid (SGF). But the solubility gradually decreases with increment of pH. Above pH 7, the solubility of the drug is very low. Therefore, the rate and extent of absorption viz bioavailability of the drug is mainly controlled by its dissolution rate. Hence, hollow microspheres are prepared to improve the bioavailability and achieve steady-state plasma concentration of the drug.
MATERIALS:
Rosiglitazone maleate was gift sample from “Matrix Lab Hyderabad” as a model drug, Eudragit L100, Polyethylene oxide, Aldrich; Mumbai; Ethyl cellulose were obtained from Aldrich Germany. Tween 80 was procured from Loba chemie, India. All other reagents were analytical grade.

1. Preparation of hollow microspheres:
Floating microspheres with a central hollow cavity were prepared by using a modified Quasi-emulsion diffusion technique. Weighed quantities of RSM, Ethyl cellulose, Eudragit L100, and polyethylene oxide were dissolved in a mixture of ethanol and dichloromethane (1:1 solvent ratio) at room temperature in a magnetic stirrer at 50 rpm for 50 min. This solvent was poured drop wise into 100 ml distilled water containing 2 ml of Tween 80 maintained at a temperature of 50 ± 2 °C. The resultant solution was stirred with a pitched-blade-type impeller type agitator at 1100 rpm for 3 h to allow the volatile solvent to evaporate. This resulted in the formation of microspheres.

% Drug entrapment efficiency and % yield of floating microspheres:
Floating microspheres equivalent to 4 mg of drug was dissolved in 10 ml ethanol. The samples were assayed for drug content using UV spectrophotometer at 228 nm after suitable dilution. No interference was found due to the other floating microspheres components at 228nm. The percentage drug entrapment efficiency and yield were calculated as follows $^{10, 11}$. The results are given in table 2.

\[
\% \text{ Drug entrapment efficiency} = \frac{C_{\text{cal.}}}{C_{\text{theo.}}} \times 100 \quad (1)
\]

\[
\% \text{ Yield} = \frac{W_{\text{m.s}}}{W_{D+P}} \times 100 \quad (2)
\]

\[W_{\text{m.s}} = \text{Total weight of floating microspheres} \]
\[W_{D+P} = \text{Total weight of drug and polymer}\]

2. Drug-Excipient Compatibility Studies:
A. Fourier Transform Infrared Spectroscopy
The Fourier transform infrared (FT-IR) spectra of samples were obtained using FT-IR spectrophotometer (Shimadzu, 8400 S, Japan). About 2–3 mg of samples was mixed with dried potassium bromide of equal weight and compressed to form a KBr disc. The samples were scanned from 400 to 4,000 cm$^{-1}$ wave number. The spectra for pure drug and formulation are represented in Figures 1 and 2.

B. Differential Scanning Calorimetry
Differential scanning calorimetry (DSC) experiments were carried out to characterize the physical state of RZM in microspheres as well as to find out the presence of any interaction among drug and the excipients. Rosiglitazone, Ethyl cellulose, eudragit S100 and polyethylene oxide were put in
aluminium pan and hermetically sealed. The heating rate was 10°C/min; nitrogen served as purged gas and the system was cooled down by liquid nitrogen. The differential thermal analyzer (Pyris Diamond TG/DTA PerkinElmer; Singapore) was used for this purpose. In the present investigation, DSC thermograms of pure drug, drug loaded hollow microspheres (formulation F3 & F8) were taken as shown in Figure 3 and 4.

C. Surface morphology
The surface morphology of the microspheres was examined by scanning electron microscopy (SEM; JSM-5200, Jeol, Japan) operated at 15 kV on samples gold-sputtered for 120 s at 10 mA, under argon low pressure. The photograph of SEM analysis is represented in Figure 5.

D. Sphericity of the microspheres
To determine the sphericity, the tracings of prepared microspheres (magnification 45x) were taken on a black paper using camera lucida, (Model -Prism type, Rolex, India). Circulatory factor (S) was calculated as

\[ S = \frac{p^2}{12.56 X A} \quad \text{----- (3)} \]

Where A is area (cm²) and, \( P \) is the perimeter of the circular tracing.

3. Micromeritic properties of microspheres:
The microspheres are characterized by their micromeritic properties, such as particle size, tapped bulk density, and compressibility index, and angle of repose (values useful in prediction of flowability).

A. Particle size
The particle size of the microspheres was measured using an optical microscopic method and the mean particle size was calculated by measuring 25 particles with the help of a calibrated ocular micrometer with stage micrometer.

B. Angle of repose
Angle of repose (\( \theta \)) of different formulations, which measures the resistance to particle flow, was determined by using a fixed funnel method and calculated as follows

\[ \tan \theta = \frac{2H}{D} \quad \text{----- (4)} \]

Where H is height and D is the diameter microspheres heap of the pile, which is formed on a graph paper after making the microspheres flow from the glass funnel.

C. Tapped bulk density
The tapping method was used to determine the tapped density and percent compressibility index as follows:

\[ D_{\text{Tap.}} = \frac{M}{V} \quad \text{----- (5)} \]

\[ \text{M} = \text{Mass of microspheres} \\
\text{V} = \text{Vol. of microspheres after tapping} \]

\[ \text{Ic} = \left(1 - \frac{V}{V_0}\right) \times 100 \quad \text{----- (6)} \]

\[ \text{Ic} = \text{Compressibility index} \]
Where $V_0$ and $V$ are the volumes of the sample before and after the standard.

4. Floating Characteristics:

A. In vitro buoyancy of microspheres

The floatation study was carried out to ascertain the floating behaviour of the microspheres with various polymer combinations. Floating behaviour of hollow microspheres was studied using a USP dissolution test apparatus II by spreading the microspheres (100 mg) on 900 ml of 0.1 N HCl containing 0.02 % v/v Tween 80 as surfactant. The medium was agitated with a paddle rotating at 100 rpm and maintained at $37\pm 0.5$ °C for 12 h. Both the floating and the settled portions of microspheres were collected separately. The microspheres were dried and weighed. The percentage of floating microspheres was calculated using the following equation:

\[
\text{W} \% \text{ FC} = \left( \frac{W}{W_{\text{int.}}} \right) \times 100 \quad ---- (7)
\]

FC = floating capability

W = Weight of floating microspheres

$W_{\text{int.}}$ = Initial weight of floating microspheres

B. In vivo floating behaviour

Healthy rabbit weighing approximately 2.3 Kg was used to assess in vivo floating behaviour. Ethical clearance for the handling of experimental animals was obtained from the institutional animal ethical committee (IAEC) of JSS College of pharmacy, Mysore constituted for the purpose. The animal was fasted for 12 h and the first X-ray photographed to ensure absence of radio opaque material in the stomach. The rabbit were made to swallow barium sulphate loaded microspheres with 30 ml of water. During the experiment rabbit were not allowed to eat but water was provided. At predetermined time intervals the radiograph of abdomen was taken using an X-ray machine. The confirmation of in vivo buoyancy by X-ray studies is represented in Figure 6.

5. Evaluation of floating hollow microspheres of RGM:

A. In vitro drug release study

The release rate of RSM from microspheres was determined using USP dissolution testing apparatus II (basket type). The dissolution test was performed using 900 ml of 0.1 N HCl, at $37\pm 0.5$°C and 50 rpm. Microspheres equivalent to 4 mg RSM were used for the test. Aliquots (5mL) were withdrawn at hourly interval for 12 h, sample was replaced by its equivalent volume of fresh dissolution medium to maintain the sink condition. The samples were analyzed at 228 nm using shimadzu UV-1700 UV spectrophotometer. The release kinetics was fitted into various models using PCP dissolution v2.08 software. The in vitro release data for the Rosiglitazone Maleate formulations are given in the corresponding graphs are represented in Figure 7.
B. In vivo evaluation

*In vivo* evaluation studies of the optimized formulation and pure drug were carried out on normal healthy male albino rats selected with average body weight of about 300-350 gm. They were housed individually in polypropylene cages, maintained under standard conditions (12 h light and 12-h dark cycle; 27±2°C; 50±10% relative humidity); the animals were fed with standard rat pellet diet and water with glucose. Ethical clearance for the handling of experimental animals was obtained from the institutional animal ethical committee (IAEC) constituted for the purpose. Non-insulin dependent diabetes mellitus (NIDDM) was induced in overnight fasted animals by a single intraperitoneal injection of Alloxan. It was administered intraperitoneally at the dose of 120 mg/kg for all group animals except the group I animals, which were served as control. The blood glucose level was determined after 72 h of Alloxan administration. The blood glucose level was determined using Glucometer. The animals having blood glucose level more than 187 mg/dl were chosen for the experiment. All the animals showed hyperglycemia after 72 h of Alloxan administration. Only the rats found with permanent NIDDM were used for *in vivo* evaluation studies. For the control (group I & II), the fasting was done overnight and water with glucose was allowed. For group 3 and group 4, pure drug and hollow microspheres were administered orally with oral gauss in the morning following overnight fasting. No food and liquid except water with glucose were given to the animals during the experiment. After collection of zero-hour blood sample, optimized formulation of hollow microspheres was administered orally through oral gauss. Blood sample was taken by pricking from the tail vein of the rat at every 1 h interval. Plasma glucose levels were determined using one touch ACCU-Chek Active®. The anti-hyperglycemic effect of formulation and pure drug in diabetic rat’s at various time intervals is depicted in Figure 8.

C. Accelerated stability studies:

Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, leading to lower concentration of the drug in the dosage form, hence the stability of pharmaceutical preparation need to be evaluated. The objective of stability studies is to predict the shelf life of a product by accelerating the rate of decomposition, preferably by increasing the temperature and relative humidity (RH) conditions. Stability studies were carried out at 40±2 °C and 75± 5% relative humidity for 90 days.

D. Mathematical model fitting of obtained drug release data

The *in vitro* release studies data was fitted into various mathematical models to determine the best-fit model. The results indicated that, the best-fit model was found to data is given in table18.as from the literature reviews we can now
that low water soluble drug the self-erosion of the matrix will be the principal. Zero order kinetics was followed by the following formulation f1& f2 as in the case of hollow microspheres with low soluble drug following the profile release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a pharmacological action. Peppas was followed by the following formulation f3; f4 & f7 as in the case of hollow microspheres shows diffusion from a controlled release polymeric system that release occurs in one-dimensional way and that the system width-thickness or length-thickness relation in release. This model is generally used to analyze the release polymeric dosage forms or more than one type of release phenomena could be involved. The formulation f3 & f4 shows the fickian diffusion and only the f7 shows anomalous transport. Matrix (higuchi) was followed by the following formulation f6 & f8 as in the case hollow microspheres drug release from spherical homogeneous matrix system & planar or spherical system having granular matrix. The drug concentration in the matrix is lower than its solubility & the release occurs through pores in the matrix. Hixon crowell was followed by the following formulation f5 as in the case hollow microspheres shape factors for cubic or spherical particles should be kept constant if the particles dissolve in an equal manner by all side.

Results and discussion:
In the preformulation studies, compatibility studies were performed using FT-IR spectrophotometer. These results indicate the method used to prepare hollow microspheres does not affect the physicochemical properties of the systems. F3 formulations have comparatively more compatibility as compared two other to formulation F9. The encapsulation efficiency ranged between 53±2.2 and 89±1.9, and was found the encapsulation efficiency was increased with increasing amount of polymers in the hollow microspheres. Formulation F3 & F6, showed the relatively higher encapsulation efficiency as these formulations composed of high concentration of polymer.

Scanning electron microscopy (SEM) revealed the discrete, spherical shaped spheres with rough surface and presence of holes /hollow cavity on floating microspheres. Porous structure was observed on the surface of microspheres shell. Microspheres were floated more than 12 h because of presence of hollow cavity.

In vitro drug release
In vitro dissolution studies of RSM from floating hollow microspheres were carried out for all formulations in pH 1.2 Hydrochloric acid buffer for 12 hours using electrolab dissolution test apparatus 1. It was found that formulations F1, F2, F3, F4, F5,
F6, F7, and F8 showed 43.0% - 80.76% of release at 8 hour and 75.3% - 105 % of release at 12 hour.
The increasing in the concentration of the polymer with the drug gives the maximum release. The combination of water soluble polymer and a controls release polymer in the formulation F3 produced maximum sustain release. The in vitro release showed the maximum release of more than 105 % in 12 hours. Among the formulated hollow microspheres, those prepared from blend of polymer showed optimum release. In 6 to 8 hours, the 43 % to 80 % of drug was released in 0.1N HCl buffer. It was observed that as the concentration of ethyl cellulose increased the % cumulative release of RSM increasing.

Conclusion:
The Accuracy Of The Formulation Was Established On The Basis Of Significantly Affects In Drug Entrapment Efficiency, Drug Release At 8 Hour, Floating Ability And Particle Size Of The Floating Drug Delivery System Promises To Be A Potential Approach For Gastric Retention. Hollow Microspheres Of Rosiglitazone Maleate Having A Spherical Structure Were Prepared Successfully In One Step Using Modified Quasi Emulsion Solvent Diffusion Technique. The Microspheres Of The Optimum Batch (F3) Exhibited 89±1.9 % Drug Entrapment Efficiency, Mean Particle Size Of 312±4.1µm And 80% Rel8h 82% Floating Ability. In Vivo Of Floatation Behaviour Evidences By Taking The X-Ray By At 4h, 8h & 12h It Can Be Concluded The Floatation Behaviour Of Hollow Microsphere. The In Vitro Release Showed The F3 Formulation Was Maintain Up To The 12th Hour And Blood Glucose Was Found To Be 88.9 Mg/Dl. Results Of The Stability Studies Showed That There Were No Significant Changes In The Drug Content And Physical Appearance. It May Be Concluded That Dosage Form Can Control The Release, Avoid Dose Dumping, And Extend The Duration Of Action Of A Drug With Prolonged Floating Time.

References:
5. Chaurasia H, Jain K, Prajapatis K,Chaurasia D, Gupter, Arya R,


15. Perumal D, Dangor Cm, Alcock Rs, Hurbons N, Moopanar Kr. Effect Of Formulation Variables On In-Vitro Drug Release And Micromeritic Properties Of Modified Release


Table 1: Formulation chart of hollow microspheres

<table>
<thead>
<tr>
<th>INGREDIENTS</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
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<tr>
<td>Ethyl cellulose (gm)</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>polyethylene oxide (gm)</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Eudragit L 100 (gm)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Solvent ratio * (ml)</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
</tr>
<tr>
<td>Drug (gm)</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
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<tr>
<td>Tween 80 (ml)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
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</table>

* Ethanol and dichloromethane of 30 ml each
Table 2: Physicochemical characterization of hollow microspheres

<table>
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<tr>
<th>Formulation</th>
<th>Mean size (µm)</th>
<th>Angle of repose</th>
<th>CI%</th>
<th>Tapped density gm/cm³</th>
<th>% Yield ± SD*</th>
<th>Encapsulation efficiency (%)</th>
<th>Floating Ability (%)</th>
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<tbody>
<tr>
<td>F1</td>
<td>257±5.7</td>
<td>25±0.7</td>
<td>20.8±1.1</td>
<td>0.201±1.03</td>
<td>56.5±0.2</td>
<td>53±2.2</td>
<td>83±1.2</td>
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<tr>
<td>F2</td>
<td>306±2.3</td>
<td>28±1.2</td>
<td>16.2±1.6</td>
<td>0.197±1.2</td>
<td>69.2±2.1</td>
<td>72±2.1</td>
<td>72±1.4</td>
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<tr>
<td>F3</td>
<td>312±4.1</td>
<td>28±0.9</td>
<td>13.7±1.1</td>
<td>0.225±0.9</td>
<td>94.3±0.9</td>
<td>89±1.9</td>
<td>82±1.9</td>
</tr>
<tr>
<td>F4</td>
<td>308±3.7</td>
<td>28±2.1</td>
<td>18.6±2.0</td>
<td>0.166±1.3</td>
<td>88.3±1.8</td>
<td>69±1.4</td>
<td>76±0.9</td>
</tr>
<tr>
<td>F5</td>
<td>347±4.1</td>
<td>28±1.5</td>
<td>25.8±1.3</td>
<td>0.228±1.12</td>
<td>78.1±2.2</td>
<td>74±2.1</td>
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<tr>
<td>F6</td>
<td>393±1.9</td>
<td>27±1.1</td>
<td>18.8±2.4</td>
<td>0.154±1.3</td>
<td>85.4±1.7</td>
<td>89±1.3</td>
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<tr>
<td>F7</td>
<td>377±2.8</td>
<td>26±2.3</td>
<td>21.7±1.7</td>
<td>0.174±1.0</td>
<td>67.6±2.1</td>
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<tr>
<td>F8</td>
<td>302±1.7</td>
<td>26±1.9</td>
<td>20.8±0.7</td>
<td>0.281±0.9</td>
<td>79.0±0.9</td>
<td>88±1.7</td>
<td>65±0.9</td>
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*mean ± SD, n = 3

Table 3: Data of various parameters of model fitting of RGM-Hollow microsphere

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Zero Order</th>
<th>Matrix</th>
<th>Peppas</th>
<th>Hix Crow</th>
<th>n</th>
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<td>K</td>
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<td>K</td>
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<tr>
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<td>7.4852</td>
<td>0.9001</td>
<td>20.6745</td>
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<td>0.9580</td>
<td>6.0171</td>
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<td>16.6972</td>
<td>0.9167</td>
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<tr>
<td>F3</td>
<td>0.7415</td>
<td>-0.0726</td>
<td>0.8856</td>
<td>30.6762</td>
<td>0.9870</td>
<td>51.2435</td>
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<td>F4</td>
<td>0.7537</td>
<td>-0.0680</td>
<td>0.9137</td>
<td>29.3030</td>
<td>0.9756</td>
<td>47.5736</td>
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<td>F5</td>
<td>0.9659</td>
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<td>0.9621</td>
<td>24.7344</td>
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<td>F6</td>
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<td>F8</td>
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<td>0.9214</td>
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Fig 1: FT-IR overlaps spectra of pure drug and formulation F3

Fig 2: FT-IR overlaps spectra of pure drug and formulation F8
Fig 3: DSC curves of pure RGM and RGM loaded hollow microspheres F3

Fig 4: DSC curves of pure RGM and RGM loaded hollow microspheres F8
Fig 5: SEM Photographs of microsphere formulations (a) F3 & (b) F8

Fig 6: X-ray photographs showing floating ability hollow microspheres.
Fig 7: In vitro release rate profile of hollow microsphere formulations of F1-F8

Fig 8: Comparison of in vivo plasma glucose level in alloxan-induced diabetic albino rat following oral administration of pure drug (group III) and Rosiglitazone hollow microsphere F3 (group IV) with plasma glucose level of normal rat (group I) and alloxan-induced diabetic rat without drug (group II)