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Evaluation of glibenclamide microspheres for sustained release

[Evaluación de microesferas de glibenclamida para liberación sostenida]

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Abstract

Context: Sustained release drug delivery systems are more preferred than the conventional drug delivery systems due to its enhanced bioavailability and patient compliance. Earlier studies reported on glibenclamide (GBCM) were not clear and hence, the step has been taken to explore the sustained release drug delivery system of GBCM.

Aims: To evaluate the sustained release microspheres obtained of GBCM.

Methods: Microspheres were prepared by ionic gelation method using the polymers like Eudragit RS 100 and xanthan gum. Polymers can sustain the drug release from microspheres. The prepared microspheres were subjected to micromeritic studies like Carr's index, Hausner's ratio and angle of repose.

Results: Micromeritic studies confirmed that the microspheres possessing acceptable flow properties. It was observed from the *in vitro* release studies, formulations F8 and F9 showed sustained drug release for desired time of 12 h and when compared to F9, formulation F8 showed maximum drug release for 12 h.

Conclusions: Results confirmed the formulation F8 consist of the polymers such as Eudragit RS 100 about 150 mg and xanthan gum about 100 mg showed desired sustained release of 12 h with 96.07% and kinetic studies confirmed that the release from microspheres followed non-Fickian diffusion mechanism. Due to its sustained release property, it could enhance the bioavailability of drug thereby improves the patient compliance and expect better treatment than conventional dosage forms.

Keywords: Eudragit RS 100; glibenclamide; ionic gelation method; sustained release; xanthan gum.

Resumen

Contexto: Los sistemas de suministro de fármacos de liberación sostenida son más preferidos que los sistemas convencionales de administración debido a su mejor biodisponibilidad y al cumplimiento del paciente. Los estudios anteriores sobre glibenclamida (GBCM) no fueron claros, por lo que se decidió explorar el sistema de liberación sostenida de fármacos de GBCM.

Objetivos: Evaluar las microesferas de acción sostenida obtenidas de GBCM.

Métodos: Las microesferas se prepararon mediante un método de gelificación iónica con polímeros como Eudragit RS 100 y goma xantano. Los polímeros pudieron sostener la liberación del fármaco a partir de microesferas. Las microesferas preparadas se sometieron a estudios micromeríticos como el índice de Carr, la relación de Hausner y el ángulo de reposo.

Resultados: Los estudios micromeríticos confirmaron que las microesferas poseen propiedades de flujo aceptables. Se observó, a partir de los estudios de liberación *in vitro*, que las formulaciones F8 y F9 mostraron una liberación sostenida del fármaco durante un tiempo deseado de 12 horas y cuando se comparó con F9, la formulación F8 mostró liberación máxima del fármaco durante 12 h.

Conclusiones: Los resultados confirmaron que la formulación F8 constituida de polímeros tales como Eudragit RS 100 (150 mg) y goma xantano (100 mg) mostró una liberación sostenida deseada de 12 h con 96,07% y estudios cinéticos confirmaron que la liberación de microesferas seguía mecanismo de difusión no Fickiano. Debido a su propiedad de liberación sostenida, esta podría mejorar la biodisponibilidad del fármaco, por lo tanto, mejorar el cumplimiento del paciente y se esperaría un mejor tratamiento que las formas de dosificación convencionales.

Palabras Clave: Eudragit RS 100; glibenclamida; goma xantano; liberación sostenida; método de gelificación iónica.

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INTRODUCTION

Oral drug delivery system is the most preferred route of drug administration due to its ease of administration, stability of formulation and improved patient compliance (Thirumalesh et al., 2016a). In the case of formulation development categories, sustained or controlled systems are more preferred than conventional systems due to its better treatment, efficacy and patient compliance (Thirumalesh et al., 2016b). There are a lot of systems developed for sustained or controlled drug release and amongst those, the prominent systems are matrix systems (Venkateswarlu and Shanthi, 2012), floating systems (Venkateswarlu and Chandrasekhar, 2016a) and microspheres (Vijayabhaskar et al., 2016).

Diabetes mellitus is a group of syndromes and a chronic metabolic disorder characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and proteins because of a lack of or ineffective use of the hormone insulin (Venkateswarlu and Shanthi, 2012). GBCM has actions and uses similar to that of sulfonylureas and it is more potent than tolbutamide on a weight basis, but the maximal hypoglycemic effect is similar to that of other sulfonylureas. GBCM stimulates the secretion of insulin but also increases peripheral sensitivity to insulin by a post-receptor mechanism. Inhibition of hepatic glucose production is an important factor in glycemic control (Rajkumar et al., 2010). Literature reported that emulsion solvent evaporation technique for the preparation of GBCM microspheres or microparticles (Kumar et al., 2013; Rashmi et al., 2014). Hence, the present study was aimed to develop the sustained release microspheres of GBCM by ionic gelation method using Eudragit RS 100, xanthan gum and sodium alginate.

MATERIAL AND METHODS

Materials

GBCM was a gift sample from Hetero Drugs Pvt. Ltd., India. Xanthan gum, Eudragit RS 100, sodium alginate and Tween 80 were obtained from Yarrow Chem. Products, India. Remaining chemicals used were of analytical grade.

Compatibility studies

Compatibility of the drug with excipients used in the formulation was known by Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC).

Fourier Transform Infrared Spectroscopy studies

In order to check the integrity (compatibility) of drug with excipients was done by FTIR (Shimadzu FT-IR 8400 spectrophotometer, Japan) studies using KBr disc method. The samples were thoroughly blended with dry powdered potassium bromide crystals, compressed to form a disc, placed in a sample holder and then the spectrum was recorded from 4000 to 400 cm^{-1}. The IR spectrum of the pure drug was compared with the IR spectrum of the physical mixtures (Venkateswarlu and Chandrasekhar, 2016b).

Differential Scanning Calorimetry studies

The pure drug and optimized formulation were subjected to differential scanning calorimeter equipped with an intra cooler (NETZSCH, Japan). Indium/zinc standards were used to calibrate the DSC temperature and enthalpy scale. The samples were sealed in aluminum pans and heated at a constant rate of 10°C/min over a temperature range of 50-400°C. An inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 mL/min (Ashok and Desai, 2016).

Preparation of alginate microspheres

GBCM microspheres were prepared by ionic gelation method and ingredients were specified in Table 1. Sodium alginate and xanthan gum were dissolved in purified water (80 mL) to form a homogeneous polymer solution. GBCM was dissolved in methanol to form 5 mg/mL solution and to this solution; calculated amount of Eudragit RS 100 was added. Twenty mL of GBCM solution was added into the above polymer solution and mixed thoroughly with a magnetic stirrer to form a viscous dispersion. The resulting dispersion was then added drop by drop with the help of syringe and needle to the calcium chloride (10% w/v) solution and the addition was done with continuous stirring. The

added droplets were retained in the calcium chloride solution for 1 h to complete the curing reaction and to produce rigid spherical microspheres. The microspheres were collected by decantation and the product thus separated was repeatedly washed with water to remove excess calcium impurity and air dried (Bindu et al., 2009).

Characterization of the prepared microspheres

Derived properties of GBCM alginate microspheres

The flowability of the microspheres was determined by subjecting the microspheres to tapped density, bulk density (Venkateswarlu et al., 2016c), Hausner's ratio (Venkateswarlu et al., 2016d), Carr's index (Venkateswarlu et al., 2016e) and angle of repose (Thirumalesh et al., 2016c) studies and performed according to the standard methods reported in earlier studies.

Percentage yield

The practical percentage yield was calculated from the weight of dried microspheres recovered from each batch in relation to the sum of the initial weight of starting materials (Vijayabhaskar et al., 2016).

$$\text{Percentage yield} = \frac{\text{Weight of microspheres}}{\text{Weight of solid starting material}} \times 100$$

Drug entrapment efficiency

Microspheres equivalent to 10 mg of GBCM was weighed, crushed and then suspended in 100 mL of pH 7.4 phosphate buffer. After 24 h, the solution was filtered, 1 mL of the filtrate was pipette out, diluted to 10 mL and analyzed for the drug content using a UV-visible spectrophotometer (Elico, India) at 229 nm (Omar et al., 1987).

Swelling studies

The swellability of microspheres in physiological media was determined by swelling them in the phosphate buffer. Accurately weighed 100 mg of microspheres were immersed in little excess (25 mL) of phosphate buffer for 12 h, washed and the degree of swelling was calculated (Patil et al., 2012).

Particle size analysis

Particle size of the prepared microspheres was determined by optical microscopy. The optical microscope was fitted with an ocular micrometer and a stage micrometer. The eye piece micrometer was calibrated. The particle diameter of 200 microspheres was measured randomly by optical microscope (Tejraj et al., 1999).

Table 1. Formulation of glibenclamide (GBCM) microspheres.

Formulation	GBCM (mg)	Sodium alginate (g)	Eudragit RS 100 (mg)	Xanthan gum (mg)	Total weight (g)
F1	100	2	50	50	2.20
F2	100	2	50	100	2.25
F3	100	2	50	150	2.30
F4	100	2	100	50	2.25
F5	100	2	100	100	2.30
F6	100	2	100	150	2.35
F7	100	2	150	50	2.30
F8	100	2	150	100	2.35
F9	100	2	150	150	2.40

Shape and surface morphology

The shape and surface characteristics of prepared microspheres were evaluated by means of scanning electron microscopy (SEM) (JEOL-JSM-840A, Japan). The samples for SEM were prepared by gently sprinkling the microspheres powder on a double adhesive tape, which was stuck to an aluminum stub. The stubs were then coated with gold using a sputter coater (JEOL Fine coat JFC 1100E, ion sputtering device) under high vacuum and high voltage to achieve a film thickness of 30 nm. The samples were then imaged using a 20 KV electron beam (Tejraj et al., 1999).

In vitro drug release studies

The *in vitro* release profile of the microspheres was evaluated by USP type II dissolution test apparatus (paddle type assembly) (Lab India 8 basket dissolution apparatus, India) using phosphate buffer (pH 7.4) and maintained at 37 ± 0.5°C with the speed of agitation at 100 rpm. Accurately weighed the amount of microspheres equivalent to 10 mg of drug were placed in a vessel containing dissolution medium and the experiment was performed. At the prefixed time of intervals (0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 h), 5 mL of solution was withdrawn and the same volume was replaced with pH 7.4 phosphate buffer. After suitable dilution, samples were assayed spectrophotometrically for the drug content at 229 nm using a UV-Visible spectrophotometer (Elico, India).

Kinetic studies

For determination of *in vitro* drug release mechanism, the obtained drug release data was fitted to zero order, first order, Higuchi's and Korsmeyer-Peppas models (Venkateswarlu, 2013).

Statistical analysis

One-way and two-way ANOVA was applied as the test of tool using GraphPad Prism 6 and significance was set at $p<0.05$. The results were expressed as mean ± standard deviation (SD).

RESULTS AND DISCUSSION

In the present study controlled delivery system of microspheres of GBCM was prepared by Ionic gelation method using different polymers like xanthan gum, Eudragit RS 100 and sodium alginate. The pre and post formulation parameters for all the formulations were evaluated. Compatibility studies were performed by FTIR spectrophotometer. The IR spectrum of the pure drug with its IR spectrum of the physical mixture was studied. The characteristic absorption peaks of GBCM were obtained at wave numbers 3315, 3367, 2989, 2931, 2848, 1715, 1618, 1523, 1450, 1341, 1306, 1244, 1159, 1035, 820, 685 cm^{-1} and corresponding to the functional groups of N-H stretching of CONH, N-H stretching of CONH, C-H stretching of CH_3, C-H stretching of CH_2, C-H stretching of OCH_3, C=O stretching, C=C ring stretching, C=C ring stretching, C-H bending, C-H bending, SO_2, SO_2, C-O, C-O-C, 1,4-disubstituted benzene, C-Cl, respectively. The obtained characteristic peaks of pure drug correlates with its peaks of physical mixture (Table 2). Hence, it was confirmed that the drug was compatible with the excipients used in the formulation. The DSC thermo gram study for drug and its formulations was also utilized for establishing physical characteristics. The DSC thermo gram of pure drug showed its sharp melting point at the temperature of 178.9°C, which indicates its sharp melting point. The DSC thermo gram of xanthan gum showed exothermic peak at 285.8°C, Eudragit RS 100 at 412°C and sodium alginate at 242.5°C. The DSC thermo gram of the best formulation (F8) showed drug peak at 176.1°C. Even though slightly differs in the nature and appearance, this endothermic peak is almost all near to 178.9°C. The comparative study of these two thermo grams, i.e. drug and its best formulation F8 showed the endothermic peak corresponding to the melting point of the drug. Hence, it indicated that there was no interaction between the drug with polymer and other excipients in best formulation (Fig. 1).

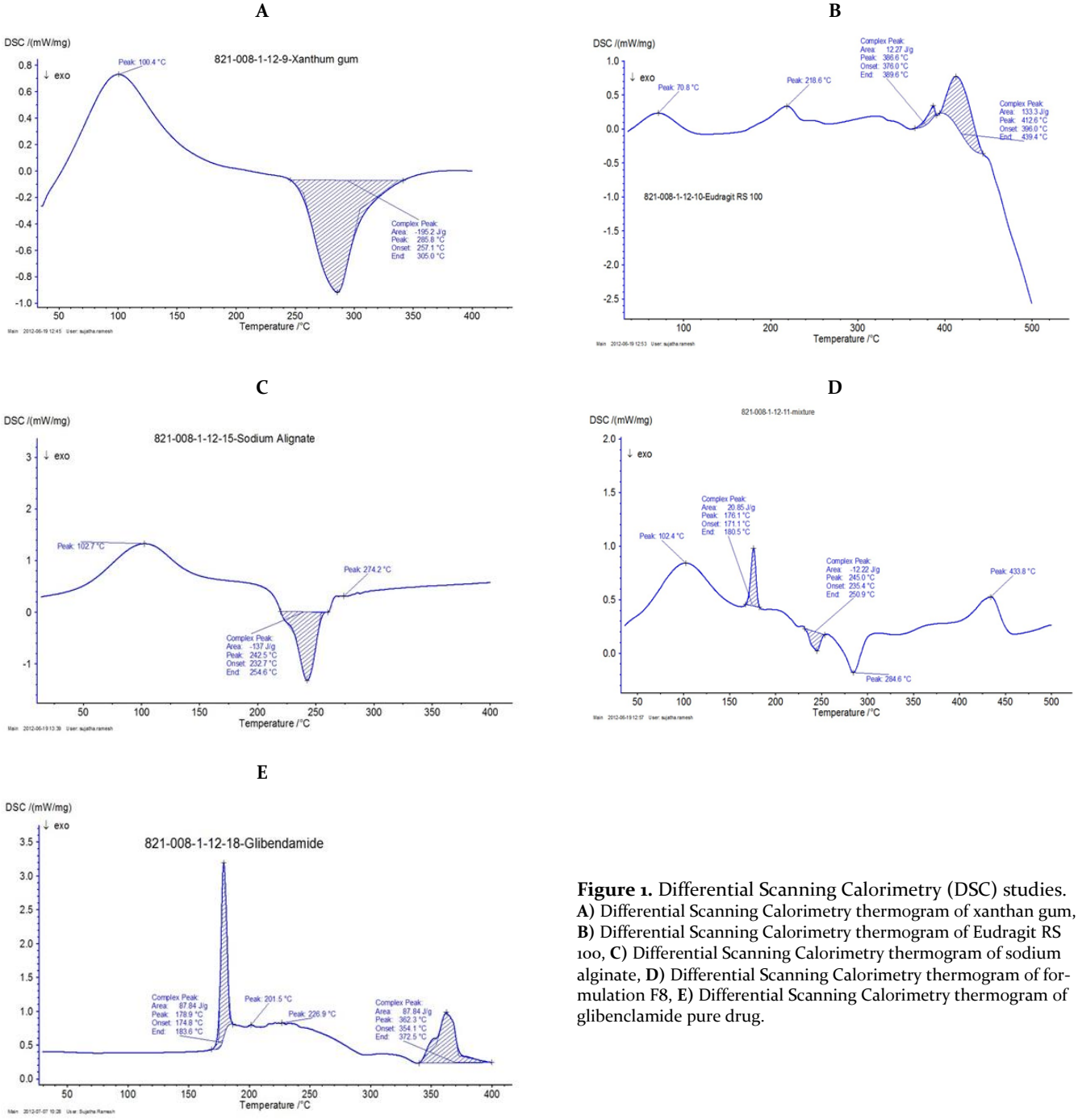

Figure 1. Differential Scanning Calorimetry (DSC) studies. **A)** Differential Scanning Calorimetry thermogram of xanthan gum, **B)** Differential Scanning Calorimetry thermogram of Eudragit RS 100, **C)** Differential Scanning Calorimetry thermogram of sodium alginate, **D)** Differential Scanning Calorimetry thermogram of formulation F8, **E)** Differential Scanning Calorimetry thermogram of glibenclamide pure drug.

Table 2. Infrared interpretation of pure drug along with its physical mixtures.

Functional groups	Glibenclamide pure drug	Formulation drug + Xanthan gum	Formulation drug + Eudragit RS 100	Formulation drug + Xanthan gum + Eudragit RS100 + Sodium alginate
N-H stretching of CONH	3315 and 3367	3314 and 3367	3314 and 3367	3315 and 3366
C-H stretching of CH_3, CH_2 and OCH_3	2989, 2931 and 2848	2989, 2929 and 2855	2988, 2931 and 2855	2989, 2933 and 2855
C=O	1715	1715	1716	1716
C=C ring stretching	1618 and 1523	1617 and 1520	1618 and 1523	1618 and 1523
C-H bending	1450 and 1341	1450 and 1341	1450 and 1341	1450 and 1342
SO_2	1244 and1306	1244 and 1306	1251 and 1305	1245 and 1306
C-O	1159	1158	1158	1157
C-O-C	1035	1035	1035	1035
1,4-disubstituted benzene	820	820	820	820
C-Cl	685	685	685	685

The percentage yield of all the formulations represented in Table 3 was in the range of 87-95% and formulation F5 showed highest percentage yield of 95.3%. Formulations F3 and F9 showed greater than 90% of the yield but other formulations like F7 and F8 showed approximately 90% of the yield. The percentage of drug entrapment was calculated for all the formulations and F6 showed high entrapment efficiency of 90%. Other formulations like F4-F5 and F8-F9 showed greater than 80% of the drug entrapment. The swelling index of all the formulation was calculated and varied from 83-115%. F6 showed highest swelling index whereas F1 showed least swelling index. The particle size analysis of the microspheres showed the average particle size in the range of 668-1075 µm (Table 3) and mean particle size of the microspheres is directly proportional to the polymer concentration.

Flow properties of the microspheres were known by the evaluation tests namely Hausner's ratio, Carr's index and angle of repose and values varied from 1.04 to 1.16, 5.5-15.1% and 9°.01'-15°.99' respectively (Table 4). Results from evaluation tests confirmed that the microspheres blend possessing acceptable flow properties (Venkateswarlu et al., 2016a) and indicates microspheres were dried enough to give sufficient flowability. The *in vitro* dissolution studies of formulations F1 to F9 were carried out in phosphate buffer (pH 7.4) and the percentage of drug release was calculated. Formulations F8 and F9 showed desired sustained release with maximum drug release of 96.07% and 87.58% in 12 h, respectively. Remaining formulations failed to sustain the drug release for 12 h but F6 and F7 were sustained the drug release for 11 h. Hence the formulation F8 was selected as the best formulation. Polymers ratio of 3:2 (Edragit and xanthan gum - F8) and 3:3 (Edragit and xanthan gum - F9) showed sustained release and it indicates that the increase in the concentration of the polymers showed increased sustained release but increase in the concentration of xanthan gum showed less drug release compared to the Eudragit (Table 5). It was evident from drug release studies that the drug release was indirectly proportional to the polymer concentration i.e. increase in polymer concentration cause decrease in drug release rate. All the formulations except F8 and F9 failed to sustain the drug release for 12 h but the formulations F6 and F7 sustained drug release up to 11 h and the formulation F8 showed more drug release than F9 for 12 h study. From the significant studies, it was found that there was no significant difference in drug release from F6 and F7 with p value more than 0.05 but the formulation F8 showed significant difference ($p<0.05$) in drug release rate compared to F6 and F7. Hence, the for-

mulation F8 was selected for further studies such as kinetics studies. Kumar et al. (2013) reported that microparticles prepared with Eudragit RL PO couldn't sustain the drug release for 12 h but expected to get stable microparticles. Another work reported by Mohit et al. (2015) showed the drug release of 76% only for 24 h due to the presence of ethyl cellulose and guar gum along with Eudragit RS 100. In above both cases, they failed to sustain the optimum drug release for desired time period and it is expected that the patients cannot be treated for optimum level. But in the present study, the microspheres proved to sustain the drug release for 12 h with the concentration of 96%, hence it is expected that the patients can get optimum level of treatment.

Surface morphology of the microspheres was studied by SEM analysis. SEM studies showed almost spherical in shape with a rough surface and slight depressions and elevations (Fig. 2). When compared to formulation F8 microspheres, the microspheres without active principle appearing more spherical with homogeneity.

Table 3. Percentage yield, drug entrapment efficiency, swelling index and average particle size of all the formulations.

Formulation	Percentage yield (%)	Drug entrapment efficiency (%)	Swelling index (%)	Average particle size (µm)
F1	87.4 ± 0.13	65.18 ± 0.43	83.01 ± 0.17	668.8 ± 0.10
F2	89.5 ± 0.31	75.08 ± 0.64	87.60 ± 0.63	734.34 ± 0.28
F3	90.3 ± 0.30	78.88 ± 0.37	89.8 ± 0.38	783.75 ± 0.37
F4	85.8 ± 0.14	80.70 ± 0.40	92.9 ± 0.34	853.1 ± 0.46
F5	95.3 ± 0.18	85.59 ± 0.67	98.65 ± 0.39	968.80 ± 0.59
F6	85.1 ± 0.17	90.07 ± 0.84	115.9 ± 0.53	1028.4 ± 0.64
F7	89.1 ± 0.51	79.01 ± 0.35	91.04 ± 0.58	885.0 ± 0.76
F8	89.3 ± 0.64	82.60 ± 0.54	97.89 ± 0.84	984.6 ± 0.84
F9	91.3 ± 0.34	83.09 ± 0.19	109.7 ± 0.15	1075.4 ± 0.18

Results were expressed in mean ± SD (n=3).

Table 4. Derived properties of all the formulations.

Formulation	Compressibility index (%)	Hausner's ratio	Angle of repose (°)
F1	6.4 ± 0.46	1.04 ± 0.38	15°.09′ ± 0.34
F2	15.1 ± 0.41	1.10 ± 0.47	11°.04′ ± 0.19
F3	5.9 ± 0.10	1.08 ± 0.56	14°.80′ ± 0.27
F4	11.9 ± 0.56	1.13 ± 0.48	10°.29′ ± 0.28
F5	5.5 ± 0.35	1.09 ± 0.14	11°.80′ ± 0.21
F6	10.7 ± 0.58	1.11 ± 0.18	9°.01′ ± 0.27
F7	14.7 ± 0.86	1.14 ± 0.04	11°.09′ ± 0.20
F8	7.5 ± 0.79	1.07 ± 0.07	15°.99′ ± 0.62
F9	9.8 ± 0.60	1.16 ± 0.08	13°.86′ ± 0.35

Results were expressed in mean ± SD (n=3).

Kumar et al. (2013) reported the micro particles of GBCM made from Eudragit RLPO exhibited rough surface along with slight elevations and depressions but Rashmi et al. (2014) reported that microspheres made from ethyl cellulose exhibited smooth surface and also minute elevations and depressions. It can observe from previous studies that the microspheres prepared with ethyl cellulose exhibits smooth surfaced microspheres than Eudragits.

To investigate the mechanism of drug release from microspheres, *in vitro* release data of selected formulation F8 was subjected to various mathematical models like zero order, first order, Higuchi's and Korsmeyer-Peppas equations. The 'r²' values were considered to evaluate the drug release behavior from the optimized formulation and release exponent (n) value was considered for determining the drug release mechanism from its dosage form. From the observations (Table 6), it was concluded that the order of release was as per zero order equation, indicating that the dissolution rate of the drug was independent of the concentration of available drug for dissolution. Linear plot was obtained from the Higuchi's model with 'r²' value of 0.959 indicated that the drug release from microspheres was diffusion controlled. The release data obtained were also put in Korsmeyer-Peppas model in order to find out 'n' values, which describe the drug release mechanism. The diffusion exponent (n) value of formulation F8 showed above 0.5 indicating non-Fickian type transport mechanism. Hence, above observations led us to conclude that, all the microspheres followed diffusion controlled zero-order kinetics with non-Fickian type transport mechanism.

CONCLUSIONS

Microspheres of GBCM using different polymers were successfully prepared and evaluated. The concentration of polymers influence the drug release as the polymer level was increased, the drug release rates were found to be decreased (F9). It was observed that xanthan gum possessing more retaining capacity than the Eudragit. *In vitro* drug release studies revealed that the formulation F8 was found to be finest formulation. The mechanism of drug release for formulation F8 was found to be non-Fickian diffusion controlled zero order process. The aim of this study was achieved by sustaining the drug release for 12 h thereby it improves the bioavailability of drug followed by patient compliance and gives better treatment. Hence, it is recommended that there is a lot of scope for future *in vivo* studies.

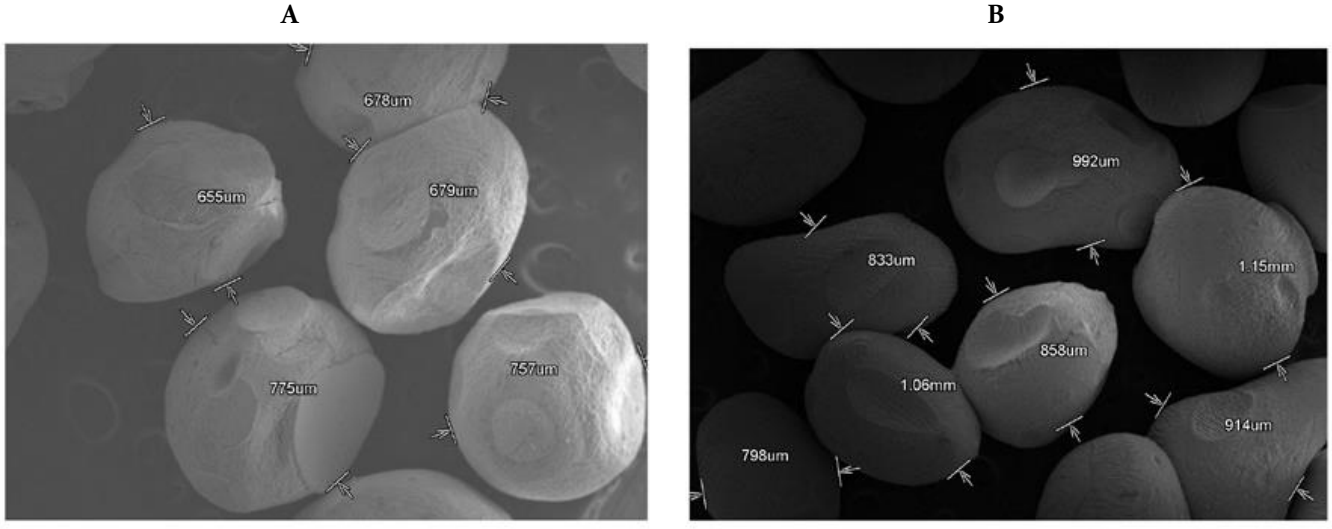

Figure 2. Scanning electron microscopy studies.

A) Scanning electron microscopy picture of microspheres without drug, **B)** Scanning electron microscopy picture of formulation F8.

Table 5. *In vitro* drug release data of all the formulations.

Time (h)	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	27.37 ± 0.28	27.88 ± 0.04	33.74 ± 0.02	23.48 ± 0.03	21.67 ± 0.26	23.88 ± 0.04	16.94 ± 0.06	16.13 ± 0.05	14.54 ± 0.04
1	35.02 ± 0.04	34.74 ± 0.07	36.80 ± 0.13	31.32 ± 0.2	27.78 ± 0.32	29.52 ± 0.13	24.51 ± 0.12	24.18 ± 0.03	20.45 ± 0.12
2	49.88 ± 0.23	45.64 ± 0.23	45.69 ± 0.16	36.34 ± 0.13	35.58 ± 0.06	37.46 ± 0.15	28.33 ± 0.06	31.35 ± 0.12	23.76 ± 0.07
3	57.03 ± 0.12	51.02 ± 0.11	54.04 ± 0.2	47.60 ± 0.15	46.53 ± 0.13	45.51 ± 0.23	35.45 ± 0.15	36.07 ± 0.14	29.87 ± 0.11
4	64.67 ± 0.15	58.45 ± 0.05	58.63 ± 0.13	53.87 ± 0.03	53.09 ± 0.04	49.86 ± 0.06	41.74 ± 0.07	43.97 ± 0.05	35.06 ± 0.2
5	73.86 ± 0.06	64.82 ± 0.13	66.74 ± 0.04	61.73 ± 0.06	60.17 ± 0.07	54.68 ± 0.05	47.05 ± 0.03	49.53 ± 0.23	41.04 ± 0.13
6	86.06 ± 0.26	72.09 ± 0.21	73.62 ± 0.09	68.88 ± 0.13	67.03 ± 0.04	61.03 ± 0.12	56.67 ± 0.15	55.86 ± 0.21	45.40 ± 0.22
7	97.07 ± 0.31	81.59 ± 0.11	77.52 ± 0.03	78.03 ± 0.25	76.58 ± 0.13	65.34 ± 0.23	65.70 ± 0.23	60.98 ± 0.15	49.76 ± 0.1
8		92.01 ± 0.06	87.31 ± .13	85.59 ± 0.11	82.61 ± 0.11	71.95 ± 0.19	74.37 ± 0.3	66.87 ± 0.12	55.43 ± 0.08
9			97.01 ± 0.24	90.05 ± 0.08	86.36 ± 0.1	75.45 ± 0.07	81.07 ± 0.13	75.98 ± 0.25	61.03 ± 0.9
10				96.38 ± 0.21	91.08 ± 0.05	86.34 ± 0.21	87.07 ± 0.11	83.07 ± 0.08	69.06 ± 0.15
11						93.72 ± 0.2	94.06 ± 0.02	90.58 ± 0.04	78.87 ± 0.21
12								96.07 ± 0.14	87.58 ± 0.2

Results were expressed in mean ± SD (n=3).

Table 6. *In vitro* drug release kinetics of formulation F8.

Formulation	Zero order	First order	Higuchi	Korsmeyer-peppas	Drug release mechanism
	r^2	r^2	r^2	n	
F8	0.977	0.856	0.959	0.572	Non-Fickian transport

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPLEMENTARY DATA

Supplementary data associated with this article can be found at http://jppres.com/jppres/pdf/vol5/jppres16.156_5.2.78.suppl.pdf

REFERENCES

Ashok AA, Desai GB (2016) Formulation and evaluation of liposomal transdermal patch for targeted drug delivery of tamoxifen citrate for breast cancer. Indian J Health Sci 9: 40-48.

Bindu BM, Ravinder AN, David B, Ramalingam R, Madhu MN, Arjun G, Sriharsha V (2009) Formulation and evaluation of venelafaxine hydrochloride enclosed in alginate microbeads prepared by iontophoretic gelation method. Int J Pharm Res Dev 8(4): 45-52.

Kumar BP, Chandiran IS, Jayaveera KN (2013) Formulation development and evaluation of glibenclamide loaded Eudragit RLPO microparticles. Int Curr Pharm J 2(12): 196-201.

Mohit S, Ajay B, Mahesh KK (2015) A research on formulation and evaluation of floating microspheres of glimepiride. World J Pharm Pharm Sci 4(9): 1298-1317.

Omar S, Sadeq O, Ibrahim J, Abdulla A, Walid Al-T (1987) Comparison of pharmacokinetics and pharmacodynamics of a conventional and a new rapidly dissolving glibenclamide preparation. Int J Pharm 38: 123-131.

Patil SS, Hiremath D, Basha KM, Udupi RH (2012) Design and *in vitro* evaluation of gastro retentive bilayer floating tablets of rosiglitazone Maleate. Int J Pharm Bio Archiv 3(1): 204-210.

Rajkumar AM, Kumar IK, Nagaraju T, Sowjanya L, Srikanth B, Venkateshwarulu G, Sandeep P (2010) Design and *in vitro* evaluation of drug release and bioadhesive properties of

from bucoadhesive tablets of glibenclamide for systemic delivery. J Chem Pharm Res 2(4): 291-303.
Rashmi RK, Yogesh SC, Suresh DK, Harshal AP (2014) Development and evaluation of sustained release microspheres of glibenclamide by emulsion solvent evaporation method. Clin Pharmacol Biopharm 4(1): 1-3.
Tejraj MA, Anandro RK, Kumaresh SS (1999) Controlled release of diclofenac sodium from sodium alginate beads cross-linked with gluteraldehyde. Pharm Acta Helvet 74(9): 29-26.
Thirumalesh NSB, Venkateswarlu K, Chandrasekhar KB (2016a) Formulation and *in vitro* evaluation of orodispersible tablets of olanzapine for the improvement of dissolution rate. J Chem Pharm Res 8(1): 177-181.
Thirumalesh NSB, Venkateswarlu K, Chandrasekhar KB (2016b) Formulation and evaluation of oxybutynin chloride extended release matrix tablets. Indo Am J Pharm Res 6(01): 4179-4184.
Thirumalesh NSB, Venkateswarlu K, Chandrasekhar KB (2016c) Formulation and *in vitro* evaluation of pregabalin mini tablets for sustained release. Pharm Lett 8(2): 277-283.
Venkateswarlu K, Chandrasekhar KB (2016a) Development and statistical optimization of sustained release gastro retentive floating tablets of cephalexin. Marmara Pharm J 22(2): 172-183.
Venkateswarlu K, Chandrasekhar KB (2016b) Formulation and *in vitro* evaluation of lacidipine oral disintegrating tablets: enhancement of solubility and dissolution rate. Int J Life Sci Pharm Res 6(2): 16-26.
Venkateswarlu K, Chandrasekhar KB, Ramachandra R (2016c) Development and *in vitro* evaluation of reconstitutable suspension of flucloxacillin. Marmara Pharm J 20(3): 280-287.
Venkateswarlu K, Preethi JK, Chandrasekhar KB (2016d) Enhancement of loperamide dissolution rate by liquisolid compact technique. Adv Pharm Bull 6(3): 385-390.
Venkateswarlu K, Shanthi A (2012) Formulation and evaluation of sustained release Glipizide matrix tablets. IOSR J Pharm BiolSci 2(5): 17-23.
Venkateswarlu K, Thirumalesh NSB, Chandrasekhar KB (2016e) Formulation and *in vitro* evaluation of orlistat orodispersible tablets for enhancement of dissolution rate. Int J Pharm PharmSci 8(4): 236-241.
Venkateswarlu K (2013) *In vitro* stability testing of syrup dosage form for hepatitis. Am J Phytomed Ther 1(6): 491- 497.
Vijayabhaskar K, Venkateswarlu K, Thirumalesh NSB, Kiran Jyothi R, Nethra Vani G, Chandrasekhar KB (2016) Preparation and *in vitro* Evaluation of ranitidine mucoadhesive microspheres for prolonged gastric retention. Br J Pharm Res 10(2): 1-12.

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Concepts or Ideas	X
Design	X
Definition of intellectual content	X
Literature search	X
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Data analysis	X
Statistical analysis	X
Manuscript preparation	X
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