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Design and Characterization of sustained release Microspheres of Acarbose

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Abstract

The present study was envisaged to reduce the dosing frequency and improve patient compliance by designing and evaluating sustained release microspheres of acarbose for effective control of type-II diabetes mellitus. Microspheres were prepared by emulsification solvent evaporation method using sodium alginate and HPMC K15M as sustained release agents. The prepared microspheres were evaluated for particle size, drug content, surface morphology, drug entrapment efficiency, flow properties, *in vitro* drug release and stability studies. The drug excipients compatibility was determined by FTIR studies. The surface morphology of prepared microspheres was measured by SEM and the particle size distribution was determined using an optical microscope. The particles were found to be discrete and spherical with the average particle size in the range of 91±1.24 to 207±1.49µm. The formed acarbose microspheres showed high drug entrapment efficiency of 74.01 to 88.9%. The effect of factors like concentration of polymer, emulsifying agent, stirring speed, alginate: HPMC ratio on drug entrapment efficiency, morphology and drug release was studied. *In vitro* results showed that the formulation F3 containing 1:1 ratio of sodium alginate and HPMC K15 M released maximum amount of drug i.e. 36.17% (pH 1.2) and 95.83% (pH 7.4) due to the proper cross linking between sodium alginate and HPMC K15 M.

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INTRODUCTION

The effect of a drug can now be reinforced as a result of the development of sustained release drug delivery system. Recently, dosage forms that can precisely control the release rates and target drugs to a specific body site have made an enormous impact in the formulation and development of novel drug delivery system[1]. Sustained release microspheres are one of the microparticulate delivery systems which are

widely accepted to achieve oral controlled drug delivery. Microspheres are solid spherical particles ranging in size from 1-1000µm. Microspheres offer advantages like limiting fluctuation within therapeutic range, reducing side effects due to decrease in dosing frequency and improved patient compliance[2].

Diabetes mellitus is a chronic disease that is characterized by impaired carbohydrate, protein and lipid metabolism. Its central disturbance appears to involve an abnormality either in the secretion of or effects produced by insulin although other factors may also be involved[3]. Acarbose is an oral α-glucosidase inhibitor and used in the management of type II diabetes mellitus. Acarbose inhibits enzymes glycoside hydrolases needed to digest carbohydrates, specifically, α-glucosidase enzyme in the brush border of the small intestines and pancreatic α-amylase. Pancreatic α-amylase hydrolyzes complex starch to oligosaccharides in the lumen of the small intestine, whereas the membrane-bound intestinal α-glucosidases hydrolyze oligosaccharides, trisaccharides and disaccharides to glucose and other monosaccharides in the small intestine. Inhibition of these enzymes systems reduces the rate of digestion of complex carbohydrates[4]. Because of its higher water solubility and shorter half life (2 h), drug requires frequent dosing by oral route. A sustained release formulation reduces the frequent drug administration and thus improves patient compliance. Sustained release formulation prolongs the action of the drug for a long period of time[5].

One of the very common and suitable method to prepare these polymeric microspheres is emulsification solvent evaporation method because it facilitates sustain release of a drug which has many clinical advantages as well as it provides compatibility to use more than one novel polymers like hydroxypropylmethylcellulose (HPMC K15 M) and sodium alginate as encapsulation matrix[6]. The main objective of this work was to investigate the possibility of obtaining sustained release microspheres of acarbose by using sodium alginate and HPMC K15 M as sustained release polymers in various ratios. The various physicochemical characteristics and the *in vitro* release rates from these microspheres were thus examined.

MATERIALS AND METHODS

Materials

Acarbose was obtained as gift sample from Windlass biotech Ltd. Dehradun, Uttranchal. Hydroxypropyl methyl cellulose (HPMC K 15M) procured from Central Drug House (P) Ltd., New Delhi. Sodium alginate was purchased from Thomas Baker Pvt. Ltd., Mumbai. Other materials used were of analytical grade, and procured from commercial sources.

Methods

Preparation of sustained release microspheres of acarbose

The sustained release microspheres of acarbose were prepared by emulsifications solvent evaporation method employing two different polymers, viz. sodium alginate and HPMC K15 M[7, 8,9,10]. For this, aqueous solution of drug and polymer is prepared. Then drug and polymer solution was added drop wise to the liquid paraffin containing 0.5 % span 20 as an emulsifying agent with constant stirring. The constant stirring was carried out using magnetic stirrer. The beaker and its content were heated at 80°C with constant stirring for 2 h until the aqueous phase was completely removed by evaporation. The liquid paraffin was decanted and collected microspheres were washed 5 times with n-hexane, filtered through Whatmann filter paper and dried in hot air oven at 50°C for 2 h. Seven batches of microspheres were prepared as per Table 1. Various variables like the polymer concentration, stirring speed, amount of emulsifying agent and sodium alginate-HPMC ratio were considered in the optimization of the formulation.

Table 1: Composition of drug loaded microspheres formulations

Sl. No.	Formulation Code	Amount of Drug (mg)	Polymer Ratio (w/w)	Amount of Polymer (mg)	
				Sodium Alginate	HPMC K15M
1	F1	150	--	1000	--
2	F2	150	--	--	1000
3	F3	150	1:1	500	500
4	F4	150	2:1	670	330
5	F5	150	1:2	330	670
6	F6	150	3:1	750	250
7	F7	150	1:3	250	750

All formulations were prepared at 2% polymer concentration.

Characterization of microspheres

Drug- Excipients compatibility study

Fourier Transform Infrared (FTIR) spectroscopy

Infrared spectra of acarbose, mixture of drug with sodium alginate and HPMC and optimized formulation were taken by using KBr pellet technique and were recorded on a Fourier Transform Infrared spectrophotometer (FTIR-8400S, Shimadzu, Japan)[11]. The pellets of drug and potassium bromide were prepared by compressing the powders at 20 psi for 10 min on KBr press and the spectra were scanned in the wave number range of 4000- 400 cm^{-1}

Percentage yield (%)

The percentage yield of microspheres of various batches were calculated using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation of microspheres and the percentage yield was calculated as per the formula mentioned below

% PY = WO / WT X 100

PY = Percentage Yield; WO = Practical mass (microspheres); WT = Theoretical mass (Polymer + Drug)[20].

Drug content

Microspheres formulation was dissolved in methanol and homogenized to break vesicles. Phosphate buffer pH 7.4 was then added to solution, filtered and the volume was made to 100 ml with phosphate buffer pH 7.4. The resultant solution was suitably diluted with phosphate buffer pH 7.4 and drug content was determined spectrophotometrically at λ_{max} of 625 nm.

Entrapment efficiency

The determination of entrapment efficiency was done by ultracentrifugation method. A known amount of microspheres formulation was weighed and dispersed in phosphate buffer pH 7.4. The microspheres dispersion so obtained was centrifuged at 10000 rpm for 40 min. The clear fraction (supernatant) was used for the determination of free drug. The drug concentration in the resulting solution was assayed spectrophotometrically at λ_{max} of 625 nm [12]. The percentage entrapment efficiency was calculated by the following equation:

$EE\ (\%) = [(C_t - C_f)/ C_t] \times 100$

Where C_t is the concentration of total drug and C_f is the concentration of unentrapped drug.

Degree of swelling

Swelling index was determined by measuring the extent of swelling of microspheres in phosphate buffer (pH 7.4). To ensure complete equilibrium, exactly weighed 100 mg of prepared microspheres were allowed to swell in simulated intestinal fluid pH 7.4 for 24 h. The excess surface adhered liquid drops were removed by blotting and swollen microspheres were weighed by using microbalance. The degree of swelling was then calculated by the following formula[13]:

Degree of swelling = $M_o - M_t / M_t \times 100$

Where M_t = initial weight of microspheres and M_o = weight of microspheres at equilibrium swelling in the media.

Particle size analysis

Particle size of different batches of microspheres was determined by optical microscopy. The projected diameter of microspheres from each batch was determined using ocular micrometer and stage micrometer equipped with optical microscope. Analysis was carried out by observing the slide containing microspheres under the microscope. The

average particle size of the microspheres was expressed in diameter[13].

Shape and surface morphology

Shape and surface morphology of microspheres was studied using scanning electron microscopy (SEM)[14]. The microspheres were mounted on metal stubs and the stub was then coated with conductive gold with sputter coater attached to the instrument. The photographs were taken using a Jeol scanning electron microscope (JEOL-JSM-AS430, Japan)[15].

Flow properties

Angle of repose

Angle of repose is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. It is calculated by the formula:

$\tan \theta = h / r$

$\theta = \tan^{-1}(h / r)$

Where, h = height of pile, r = radius of the base of the pile and θ = angle of repose

Bulk density

The microspheres were screened through sieve no. 18. The sample equivalent to 25g was accurately weighed and filled in 100 ml graduated cylinder, the powder was leveled, and the unsettled volume, V_0 was noted. The bulk density was calculated in g/cm^3 by the formula, Bulk density = M/V_0

Where M= mass of microspheres taken and V_0 = apparent volume

Carr's index

The bulk density and tapped density was measured and Carr's index was calculated using the formula:

Carr's index = Tapped density- Bulk density/Tapped density × 100

Hausner ratio

Packing factors is a measure of flow properties, which is calculated by finding Hausner ratio[14]. The formula is: Hausner ratio = Tapped density/ Bulk density

***In vitro* drug release studies**

The *in vitro* drug release studies were performed using USP Type II dissolution apparatus (paddle) at 100 rpm. The dissolution medium consisted of simulated gastric fluid (SGF) pH 1.2. The reading were taken for first 1 h in SGF and for subsequent 11 h in phosphate buffer pH 7.4 (900 ml), maintained at 37±0.5°C. The release studies were conducted in triplicate. Aliquot of samples (5ml) were withdrawn at specific time intervals and drug content was determined spectrophotometrically at 625 nm. Higuchi's equation ($Q= Kt^{1/2}$) and Korsmeyer-Peppas Equation are used to determine precisely the mechanism of drug release from the microspheres[16].

Stability studies

Stability is defined as the ability of particular drug or dosage form in a specific container to maintain its physical, chemical, therapeutic and toxicological specifications[17]. To determine the stability of microspheres the selected formulation of microspheres was kept at 4 ± 1°C (Refrigerated Temperature), 25± 2°C and 60 ± 5% RH (Room Temperature) and 37± 2°C and 65 ± 5% RH (Incubator Temperature) for two months and after two months, percentage entrapment efficiency and drug content was carried out.

RESULTS AND DISCUSSION

Fourier Transform Infrared (FTIR) Spectroscopy

The FTIR spectra of acarbose, physical mixture of acarbose and sodium alginate, physical mixture of acarbose and HPMC K15M and optimized formulation of microspheres are shown in Figure 1 to 4. IR Spectrum of acarbose shows prominent peaks of hydroxyl stretching at 3445 cm^{-1}, C=C stretching at 1624 cm^{-1}, C-O stretching at 1032 cm^{-1} and hydroxyl bending vibrations at 1424 cm^{-1}. It was found that the peaks characteristics of the drug were preserved in all scan done in combination with polymers and optimized formulation of microspheres. It indicates that drug and excipients (polymers) interaction was not seen in the formulation.

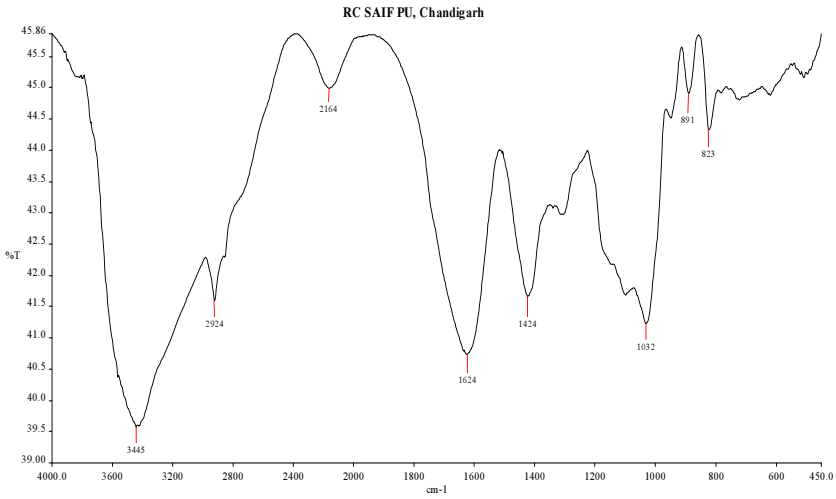

Figure 1: Infra-red spectra of pure drug acarbose

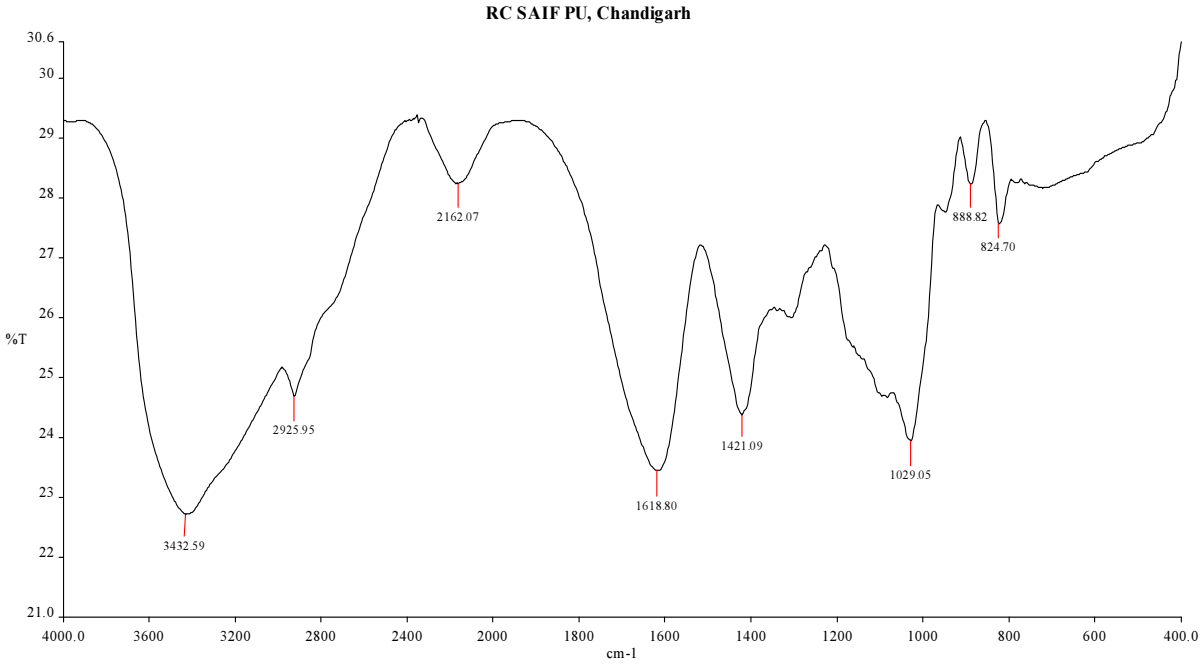

Figure 2: Infra-red spectra of acarbose- sodium alginate mixture

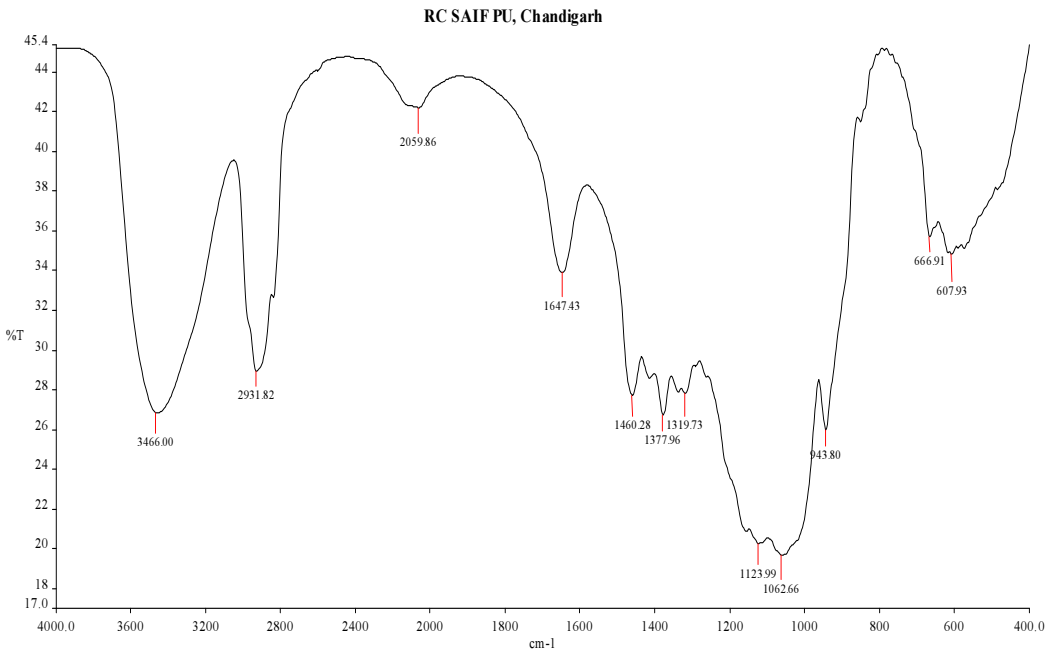

Figure 3: Infra-red spectra of acarbose- HPMC K15M mixture

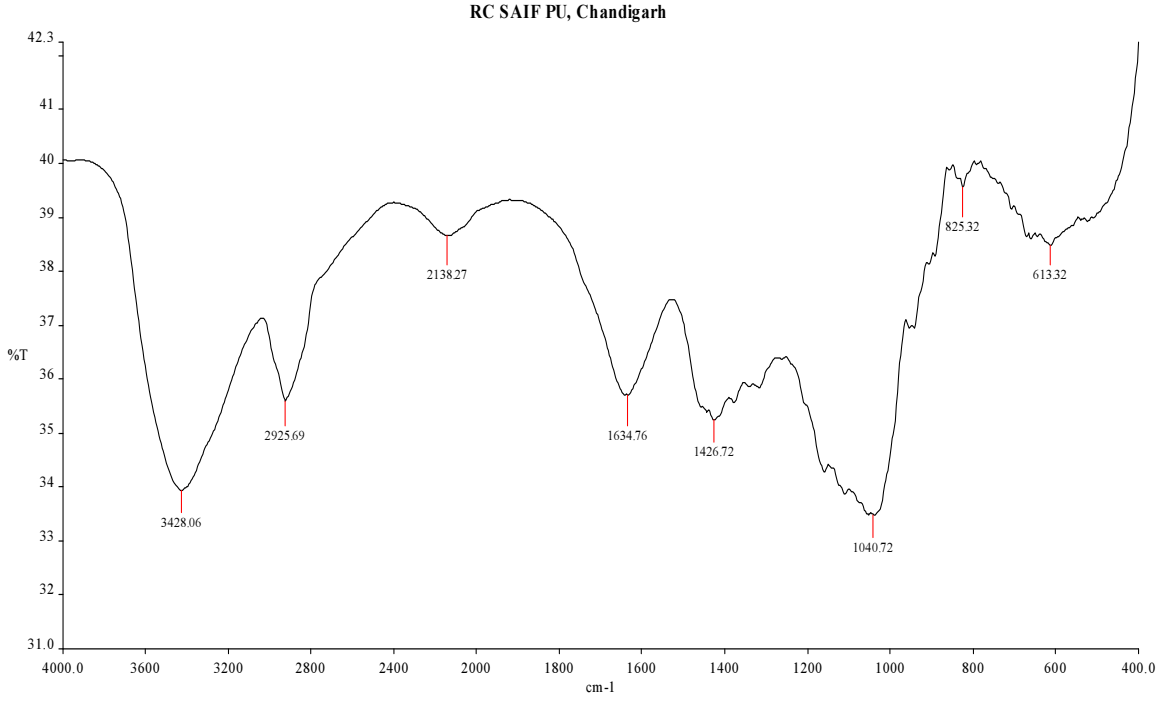

Figure 4: Infra-red spectra of optimized formulation of microspheres F3

Percentage yield

The percentage yield of prepared sustained release microspheres was in the range of 74%-86% approximately (Table 2, Figure 6). Results demonstrated that microspheres formulation F3 having optimized sodium alginate and HPMC K15M ratio had highest percentage yield i.e. 86.67±0.4%. The yield of solvent evaporation method is relatively high for acarbose microspheres, considering the preparation method employed. The loss of material during preparation of microspheres is due to process parameters as well as during filtration of microspheres. The yield of microspheres was affected by stirring speed, polymer concentration and their ratio used in the formulation.

Determination of drug content

The values of percentage drug content for the formulated microspheres were shown in Table 2. Formulation F3 containing optimized concentration of sodium alginate and HPMC K15M showed maximum percentage drug content of 95.2 % due to higher entrapment efficiency. The drug content was generally higher for the formulation containing sodium alginate cross-linked with HPMC K15M as compared to the sodium alginate used alone in the formulation.

Determination of percentage drug entrapment

The values for entrapment efficiency were in the range of 74.01±1.5% to 88.9±0.86%. The method adopted for the preparation of microspheres could also be responsible for the high entrapment efficiency. Formulation F3 containing optimized concentration of sodium alginate and HPMC K15M showed maximum percentage drug entrapment efficiency of about 88.9%. Drug entrapment was attributed to the permeation characteristics of polymers used, that could facilitate the diffusion of part of entrapped drug to the surrounding medium during preparation of microspheres. The entrapment efficiency was generally higher for the formulation cross-linked with HPMC K15M as compared to the sodium alginate used alone in the formulation. Optimized concentration of HPMC K15M in formulation F3 caused increase in the entrapment efficiency (Table 2, Figure 8). However, further increase in HPMC K15M concentration resulted in increase in the particle size and decrease in the entrapment efficiency.

Table 2: Percentage yield, Particle size and percent drug entrapment of formulated microspheres

S. No.	Formulation Code	Percentage Yield (%)	% Drug content	Particle size (µ m)	% Drug entrapment	Degree of swelling
1	F1	78.9±0.2	89.2±1.6	207±1.49	76.06±1.45	1.43±0.01
2	F2	75.13±0.4	85.2±0.8	91±1.24	75.01±1.23	1.31±0.02
3	F3	86.67±0.4	95.2±0.7	110±1.84	88.9±0.86	1.17±0.01
4	F4	85.45±0.25	92.1±1.5	107±0.21	80.02±0.75	1.26±0.03
5	F5	82.4±0.36	86.4±0.9	103±1.02	86.9±1.84	1.06±0.04
6	F6	76.27±1.72	87.5±0.6	145±1.26	79.45±0.68	1.13±0.02
7	F7	74.03±0.3	90.4±1.2	97±2.04	74.0±1.5	0.99±0.01

All values are expressed as Mean ± SD, n=3. All formulations were prepared at 2% polymer concentration.

Degree of swelling

The formulation F1 showed higher degree of swelling of alginate microspheres than HPMC microspheres due to higher molecular weight of alginate than HPMC (Table 2). In formulation F3 with optimized concentration of HPMC, the overall swelling of polymer decreases significantly due to crosslinking of HPMC to sodium alginate[20]. The cross-linking of the sodium alginate formulation depends on the HPMC concentration, but the optimal concentration of the

cross-linking agent was a compromise between swelling ability and *in vitro* digestion of microspheres. However in formulation F5 and F7, at higher concentration of HPMC the degree of swelling of microspheres decreases. It may be due to tight or close packing of alginate matrix in presence of HPMC.

Particle size analysis

Particle size analysis of different formulations was done by optical microscopy. The average particle size was found to be in the range of 91±1.24 to 207±1.49µm (Table 2, Figure 7). The mean particle size was significantly varied according to the type of polymer used for the preparation of microspheres due to the differences in the viscosity of the polymer solution. The results indicated that the proportional increase in the mean particle size of microspheres with increasing amount of sodium alginate in the formulation F1, F4 and F6 could be due to an increase in the relative viscosity at higher concentration of sodium alginate. HPMC K15M solution has low viscosity than sodium alginate at the same concentration.

Surface morphology

Surface morphology of the microspheres was examined by scanning electron microscopy (SEM) (Figure 5). The SEM showed that the microspheres obtained from all the formulations were discrete, uniform and spherical with a smooth surface. The high shearing rate required for emulsification caused the breakdown of the viscous aqueous alginate solution to fine globules resulting in small microspheres.

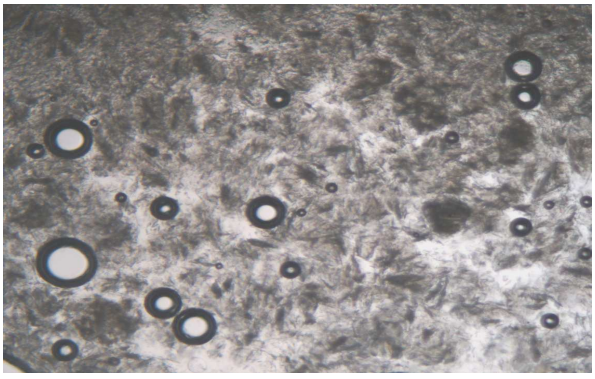

Figure 5: Scanning electron micrograph of formulation F3.

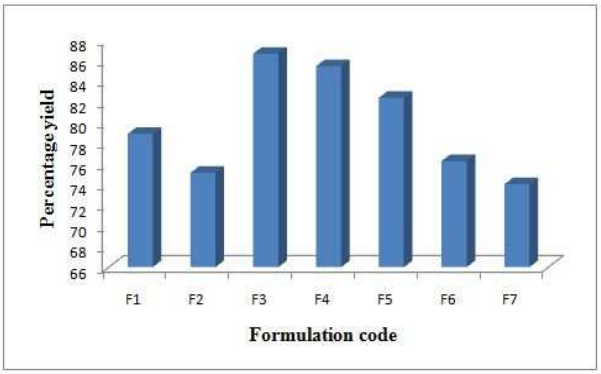

Figure 6: Comparative percentage yield of Formulation F1 to F7

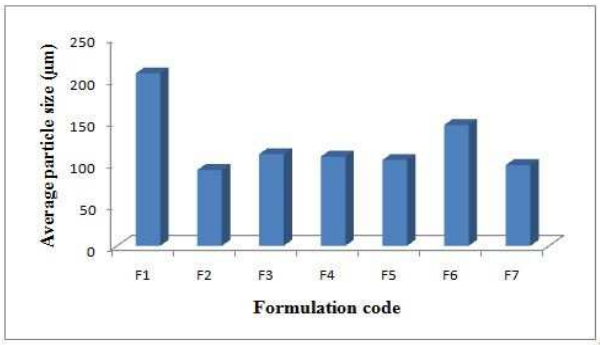

Figure 7: Comparison of average particle size of Formulation F1 to F7

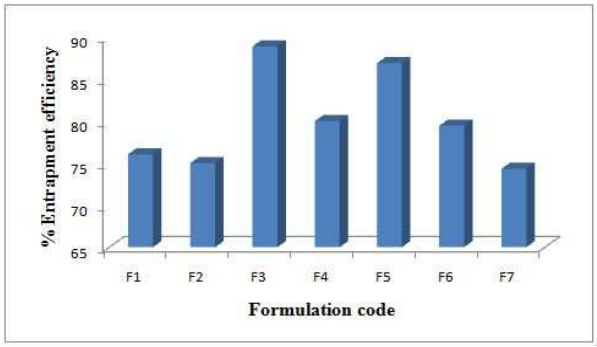

Figure 8: Comparative entrapment efficiency of Formulation F1 to F7

Flow properties

The values of angle of repose were between 24˚ to 31˚ which are within the normal acceptable range of 20˚ to 40˚. Formulation F1 had lowest angle of repose and larger particle size as compared to the formulation F2 having highest angle of repose and smaller particle size. It showed that decrease in the

particle size leads to a higher angle of repose (Table 3).

Table 3: Flow properties of acarbose microspheres

Formulation Code	Angle of repose (θ°)	Bulk density (g/cm³)	Tapped density (g/cm³)	Carr's index (%)	Hausner ratio
Pure drug	36° 40'±0.11	0.296±0.02	0.359±0.2	17.5±0.1	1.212±0.1
F1	23° 20'±0.23	0.603±0.01	0.675±0.1	10.67±0.2	1.120±0.2
F2	31° 40'±0.21	0.742±0.01	0.873±0.1	15.58±0.1	1.176±0.3
F3	26° 20'±0.13	0.662±0.01	0.758±0.2	12.66±0.3	1.145±0.1
F4	27° 10'±0.19	0.673±0.01	0.790±0.1	12.27±0.1	1.173±0.2
F5	28° 30'±0.21	0.701±0.02	0.821±0.3	14.61±0.2	1.171±0.1
F6	29° 10'±0.23	0.642±0.02	0.720±0.2	10.83±0.1	1.121±0.1
F7	29° 60'±0.13	0.689±0.02	0.832±0.1	16.10±0.2	1.191±0.3

All value are mean ± SD, n = 3

The bulk densities of formulated microspheres were found to be in the range 0.603 to 0.742 g/cm³. Formulation F1 having low bulk density 0.603 g/cm³ had larger particle size whereas formulation F2 having high bulk density 0.742 g/cm³ had smaller particle size. It can be concluded that as the particle size increases, the bulk density decreases, due to increase in the intraparticulate space.

The values of Carr's index and Hausner ratio of formulated microspheres were found to be in the range of 10.83-17.5 and 1-1.2 respectively, indicating good flow characteristics of the microspheres as compared to the pure drug (Table 3). The improved micromeritic properties of the prepared microspheres suggest that they can be easily handled and filled into capsule for effective delivery.

In vitro drug release studies

The *in-vitro* release data of all the formulations are tabulated in Table 4. The cumulative percent drug release after 12 h was found to be 78.21%, 86.52%, 95.83%, 94.12%, 91.41%, 91.88% and 88.21% respectively for the formulations F1 to F7. Figure 9 and 10 shows the plot of cumulative percentage drug release as a function of time for the formulation F1 to F7. Although the drug possessed higher solubility at pH 1.2, despite the increased solubility; the release rate of acarbose at pH 1.2 was slow and sustained, which may be due to the stability of alginate in acidic pH[17] and the conversion of alginate to the insoluble but swelling alginic acid[18]. Approximately, 36.17% of the drug was released in the SGF, pH 1.2 over a period of 1 h and 95.83% in phosphate buffer, pH 7.4 in 12 h. The microspheres of hydrophilic polymers when immersed in water swell and form a gel diffusion layer that hinders the outward transport of the drug, hence, producing a sustained release effect. However, at acidic pH the alginate microspheres shrink due to tightening of the gel meshwork. The polymer is eroded at alkaline pH and the contents are released in a sustained manner by both diffusion and slow erosion of polymer matrix[19]. Although the release profile was found to be sustained in all the cases reported, sodium alginate cross linked with HPMC in the ratio of 1:1 (F3) resulted in the highest extent of drug release (Table 4) up to 12 h. *In vitro* drug release studies showed that in formulation F5 and F7 with increase in concentration of HPMC K15 M, the release of drug from microspheres was decreased, due to an increase in density of the polymer matrix at higher concentration of HPMC K15 M which results in larger microspheres and in turn increased diffusional path length. This may decrease the drug release from the polymer matrix.

The *in vitro* release data obtained were fitted to zero order, first order, Higuchi, Korsmeyer-Peppas kinetic models to determine the mechanism of drug release from the microspheres (Table 5)[20]. Formulation F1,

F6 and F7 followed first order kinetics which indicates rate of drug release depends upon concentration. However drug release was also found to follow zero order kinetics in case of formulation F2, F3, F4 and F5 which indicated that the concentration was independent of drug release. The formulations F2, F3, F4 and F5 best fitted into Higuchi model and their corelation coefficient (r) were 0.989, 0.991, 0.989 and 0.992 respectively (Table 5). On the other hand, the formulations F1, F6 and F7 best fitted into the Peppas model. Mechanism of drug release from formulations was determined by Korsmeyer–Peppas equation where exponent n indicated mechanism of drug release. The value of release exponent (n) for all formulations was less than 1, *i.e.* between ($0.43 < n < 0.85$) indicating anomalous transport (non fickian). Non fickian release kinetics is indicative of drug release mechanisms involving a combination of both diffusion and chain relaxation mechanisms. Therefore, the release of the drug from the formulated microspheres was sustained by swelling of the polymer, followed by drug diffusion through the swelled polymer and slow erosion of the polymer**.**

Table 4: *In vitro* release profile of acarbose from microspheres formulation F1 to F7

Time (h)	Cumulative percentage drug released						
	F1	F2	F3	F4	F5	F6	F7
0.5	23.5±0.2	25.5±0.2	26.2±0.4	28.2±0.3	21.7±0.6	28.9±0.4	26.4±0.2
1	29.7±0.5	31.9±0.3	36.1±0.3	33.6±0.4	28.3±0.2	44.2±0.5	33.8±0.4
2	36.1±0.8	40.8±0.4	42.2±0.2	42.1±0.4	35.9±1.0	51.5±0.2	41.6±0.4
3	42.2±0.3	49.1±0.5	50.2±0.6	47.3±0.5	44.4±0.6	57.3±0.3	48.3±0.5
4	49.9±0.2	55.9±1.2	57.0±0.7	54.5±0.3	50.2±0.7	71.1±0.4	55.3±0.5
5	57.5±0.4	62.9±1.3	64.4±0.7	60.7±0.4	56.2±0.8	74.7±0.6	60.9±0.6
6	68.1±0.6	68.4±0.9	69.8±0.6	65.2±0.5	65.3±0.9	81.3±0.9	65.6±0.7
8	72.3±0.7	83.1±0.9	84.8±0.2	76.2±0.6	75.9±1.2	87.7±1.0	79.5±0.8
10	77.1±0.8	86.2±1.5	91.1±0.9	88.1±0.8	85.4±0.9	91.2±1.4	87.4±0.9
12	78.2±0.9	86.5±1.6	95.8±0.9	94.1±0.8	91.4±1.3	91.8±1.6	88.2±1.1

Each value represents Mean ± S.D. (n=3)

Table 5: Kinetic values from *in vitro* release profile of formulated microspheres

S. No.	Formulation Code	Zero Order R^2	First Order R^2	Higuchi R^2	Korsemeyer and Peppas		Release Order and Main Transport Mechanism
					n	R^1	
1	F1	0.916	0.963	0.971	0.734	0.983	First order, Anamalous
2	F2	0.992	0.977	0.989	0.787	0.982	Zero order, Anamalous
3	F3	0.996	0.966	0.991	0.776	0.986	Zero order, Anamalous
4	F4	0.987	0.909	0.989	0.978	0.979	Zero order, Case II
5	F5	0.978	0.958	0.992	0.989	0.957	Zero order, Case II
6	F6	0.854	0.993	0.954	0.725	0.989	First order, Anamalous
7	F7	0.959	0.970	0.980	0.723	0.988	First order, Anomalous

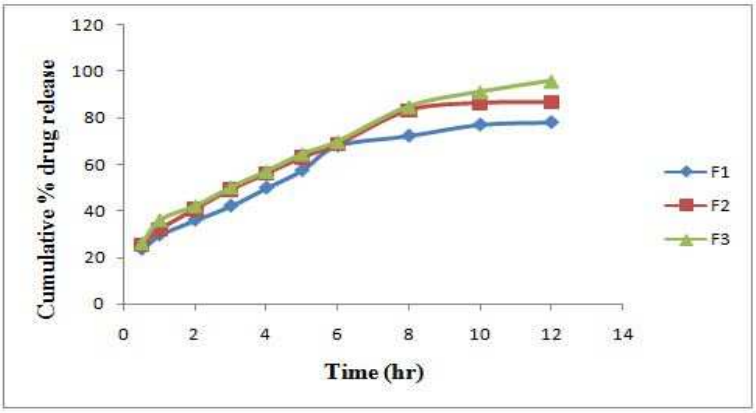

Figure 9: Cumulative percentage drug release from microspheres formulation F1-F3

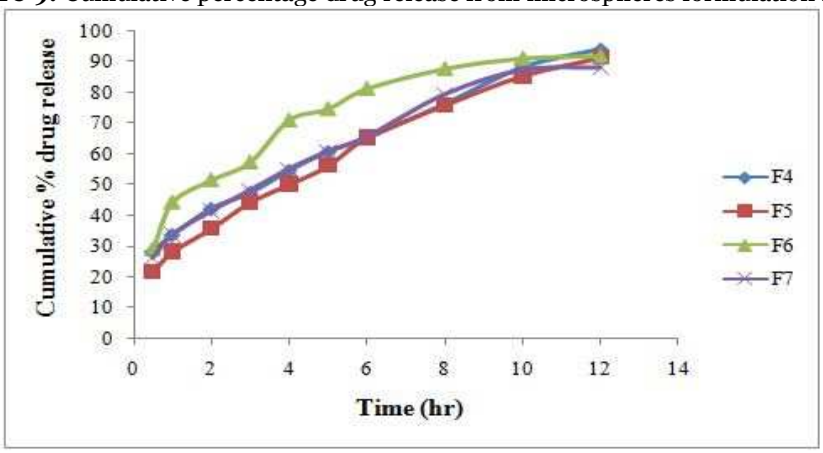

Figure 10: Cumulative percentage drug release from microspheres formulation F4-F7

Stability studies

The stabilty studies results revealed no changes in the physical appearance of the formulation after two months study. The drug content of fomulation F3 was found to be 95.01% and 94.92% at refrigerated temperature (4±2°C) after one and two months respectively. A marked reduction in the residual drug content was found when formulation was stored at 25 ± 2°C and 37 ± 2°C . Formulation stored at 4 ± 1°C was found to be stable as the drug content results was found to be satisfactory in this case. Formulation F3 stored at refrigrated temperature (4±2°C) showed 87.16% and 87.01% entrapment efficiency after one and two month respectively (Table 6).

Table 6: Stability Studies – Drug content and entrapment efficiency (% EE) of formulation F3 after 30 days and 60 days storage

Parameter	At refrigerated temperature 4±2°C		At room temperature 25±2°C & 60±5% RH		At incubator temperature 37±2°C & 65±5% RH	
(%) Drug content	95.01±0.2	94.92±0.4	94.01±0.2	93.11±0.4	92.03±0.5	91.09±0.2
% EE	87.16±0.3	87.01±0.5	86.03±0.7	85.02±0.3	84.79±0.4	83.01±0.9

All values are expressed as Mean ± SD, n=3.

CONCLUSION

The sustained release microspheres of acarbose were prepared by emulsification solvent evaporation method to obtain high entrapment efficiency (88.9%). The drug release from the microspheres was affected by the pH of the dissolution medium. *In vitro* drug release of 95.83% over the period of 12 h was obtained. The finding of all the investigations have conclusively demonstrated that loading of acarbose into microspheres improves therapeutic response, patient compliance by reducing the dosing frequency and considerable reduction in side effects associated with the sudden release of drug from conventional dosage form in the systemic circulation by providing sustained release from the polymer matrix. From this study, it is concluded that acarbose can be loaded to sustained release microspheres for the treatment of diabetes with better patient compliance and improved efficacy.

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