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FORMULATION AND DEVELOPMENT OF GLICLAZIDE MICROSPHERES FOR PHARMACEUTICAL EVALUATIONS

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ABSTRACT

Gliclazide microspheres were prepared by ionotropic gelation method using bioadhesive polymers such as sodium alginate, carbopol 934, carbopol 971, HPMC K4M in different ratios. Totally twelve different formulations of gliclazide were prepared by using the above polymers. The microspheres were characterized for drug content, entrapment efficiency, swelling index, mucoadhesive property by *In vitro* wash-off test and *in-vitro* drug release. The results of this investigation indicate that ionic cross linking technique Ionotropic gelation method can be successfully employed to fabricate Model drug microspheres. Micrometric studies revealed that the mean particle size of the prepared microspheres was in the size range of 512-903 µm and are suitable for bioadhesive microspheres for oral administration. The *in-vitro* mucoadhesive study demonstrated that microspheres of Model drug using sodium alginate along with Carbopol 934 as copolymer adhered to the mucus to a greater extent than the microspheres of Model drug using sodium alginate along with Carbopol 971 and HPMC K4Mas copolymers. Analysis of drug release mechanism showed that the drug release from the formulations followed non-Fickian diffusion and the best fit model was found to be Korsmeyer-Peppas. Based on the results of evaluation tests formulation coded T4 was concluded as best formulation.

Keywords: Bioadhesive Microspheres, Gliclazide, Ionotropic gelation method.

INTRODUCTION

The oral route for drug delivery is the most popula r, desirable, and most preferred method for administarting therapeutically agents for systemic effects because it is a natural, convenient and cost effective to manufacturing process. Oral route is the most commonly used for the drug administration [Patil D A]. Although different routes of administration are used for the delivery of drugs, oral route remain the preferred mode. Even for sustained release systems the oral route of administration has been investigated because of flexibility in designing dosage forms. Microspheres are small spherical particles, with diameters in the micrometer range (typically 1µm to 1000 µm). Microspheres are sometimes referred to as microparticles. Microspheres can be manufactured from various natural and synthetic materials [1].

Mucoadhesive drug delivery system are the systems which utilizes the property of bio adhesion of certain polymers which become adhesive on hydration and can be used for targeting a drug to a particular region of the body for extended periods of time. The term "mucoadhesion" was coined for the adhesion of the polymers with the surface of the mucosal layer. Bioadhesions are a phenomenon in which two materials at least one of which is biological and are held together by means of interfacial forces. In biological systems, bio adhesion can be classified into 3 types:

1. Adhesion between two biological phases, for example, platelet aggregation and wound healing.
2. Adhesion of a biological phase to an artificial substrate, for example, cell adhesion to culture dishes and bio film formation on prosthetic devices and inserts.
3. Adhesion of an artificial material to a biological substrate, for example, adhesion of synthetic hydrogels to soft tissues and adhesion of sealants to dental enamel.

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For drug delivery purposes, the term bio adhesion implies attachment of a drug carrier system to a specified biological location. The biological surface can be epithelial tissue or the mucus coat on the surface of a tissue. If adhesive attachment is to a mucus coat, the phenomenon is referred to as mucoadhesion/mucoadhesion as the interaction between a mucin surface and a synthetic or natural polymer. In bio adhesion, the polymer is attached to the biological membrane [2].

ADVANTAGES OF MUCOADHESIVE SYSTEMS

Mucoadhesive systems have three distinct advantages when compared to conventional dosage forms.

1. Readily localized in the region applied to improve and enhance the bioavailability of drugs. E.g. testosterone & its esters, vasopressin, dopamine, insulin and gentamycin etc.
2. Facilitate intimate contact of the formulation with underlying absorption surface. This allows modification of tissue permeability for absorption of macromolecules. E.g. peptides and proteins.
3. Prolong residence time of the dosage form at the site of application and absorption to permit once or twice a day dosing.

MATERIALS AND METHODS

Gliclazide was obtained as a gift sample from Chandra labs, hyderabad. Sodium alginate, HPMC K 100 M, Ethyl cellulose, Carbopol 940P, Methyl cellulose, Sodium CMC and Calcium chloride are purchased from SD fine-chem limited.

METHOD OF PREPARATION

Ionotropic Gelation Method

Batches of microspheres were prepared by ionotropic gelation method which involved reaction between sodium alginate and polycationic ions like calcium to produce a hydrogel network of calcium alginate. Sodium alginate and the mucoadhesive polymer were dispersed in purified water (10 ml) to form a homogeneous polymer mixture. The API, Model drug (100mg) was added to the polymer premix and mixed thoroughly with a stirrer to form a viscous dispersion. The resulting dispersion was then added through a 22G needle into calcium chloride (4% w/v) solution. The addition was done with continuous stirring at 200rpm. The added droplets were retained in the calcium chloride solution for 30 minutes to complete the curing reaction and to produce rigid spherical microspheres. The microspheres were collected by decantation, and the product thus separated was washed repeatedly with purified water to remove excess calcium impurity deposited on the surface of microspheres and then air-dried [3].

CHARACTERIZATION OF MICROSPHERES

Percentage Yield

The percentage of production yield was calculated from the weight of dried microspheres recovered from each batch and the sum of the initial weight of starting materials. The percentage yield was calculated using the following formula:

$$\% \text{ Yield} = \frac{\text{Practical mass (Microspheres)}}{\text{Theoretical mass (Polymer + Drug)}} \times 100$$

Drug entrapment efficiency

Microspheres equivalent to 15 mg of the drug Model drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres. The powder was transferred to a 100 ml volumetric flask and dissolved in 10ml of methanol and the volume was made up using simulated gastric fluid pH 1.2. After 24 hours the solution was filtered through Whatmann filter paper and the absorbance was measured after suitable dilution spectrophotometrically at 269 nm. The amount of drug entrapped in the microspheres was calculated by the following formula,

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Experimental Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Particle size analysis

Samples of the micro particles were analyzed for particle size by optical microscope. The instrument was calibrated and found that 1unit of eyepiece micrometer was equal to 12.5µm. Nearly about 100 Micro particles sizes were calculated under 45 x magnifications.

The average particle size was determined by using the Edm ondson's equation:

$$D_{mean} = \frac{nd}{n}$$

Where,

n – Number of microspheres observed

d – Mean size range

Swelling study

Swelling ratio of different dried microspheres were determined gravimetrically in simulated gastric fluid pH 1.2 .The microspheres were removed periodically from the solution, blotted to remove excess surface liquid and weighed on balance. Swelling ratio (% w/v) was determined [4]

From the following relationship:

$$\text{Swelling ratio} = \frac{(Wt - W0)}{(W0)} \times 100$$

Where W0 &Wt are initial weight and Final weight of microspheres respectively.

Evaluation of mucoadhesive property

The mucoadhesive property of microspheres was

evaluated by an *In vitro* adhesion testing method known as wash-off method. Freshly excised pieces of goat stomach mucous were mounted on to glass slides with cotton thread. About 20 microspheres were spread onto each prepared glass slide and immediately thereafter the slides were hung to USP II tablet disintegration test, when the test apparatus was operated, the sample is subjected to slow up and down movement in simulated gastric fluid pH 1.2 at 37ºC contained in a 1-litre vessel of the apparatus. At an interval of 1 hour up to 8 hours the machine is stopped and number of microspheres still adhering to mucosal surface was counted [5].

$$\% \text{ Mucoadhesion} = \frac{\text{Number of microspheres adhered}}{\text{Number of microspheres applied}} \times 100$$

***In vitro* drug release study**

The dissolution studies were performed in a fully calibrated eight station dissolution test apparatus (37 ± 0.5^0C, 50 rpm) using the USP type – I rotating basket method in simulated gastric fluid pH 1.2 (900ml). A quantity of accurately weighed micro spheres equivalent to 15mg Model drug each formulation was employed in all dissolution studies. Aliquots of sample were withdrawn at predetermined intervals of time and analyzed for drug release by measuring the absorbance at 269nm. At the same time the volume withdrawn at each time intervals were replenished immediately with the same volume of fresh pre-warmed simulated gastric fluid pH 1.2 maintaining sink conditions throughout the experiment.

***In-Vitro* Drug Release Kinetics**

The release data obtained was fitted into various mathematical models.

The parameters 'n'and time component 'k',the release rate constant and 'R',the regression coefficient were determined by KorsmeyerPeppas equation to understand the release mechanism.

To examine the release mechanism of model drug from microspheres, the release data was fitted into Peppa's equation,

$$\mathbf{Mt / M\infty = Kt^n}$$

Where, Mt / M∞ is the fractional release of drug, ' t' denotes the releasetime,'K'representsa constant incorporating structural and geometrical characteristics of the device, 'n' is the diffusional exponent and characterize the type of release mechanism during the release process [6,7].

Release exponent (n)	Drug transport mechanism	Rate as a function of time
0.5	Fickian diffusion	$t^{-0.5}$
0.5<n<1.0	Anomalous transport or non-Fickian	t^{n-1}
1.0	Case-II transport	Zero-order release
Higher than 1.0	Super Case-II transport	t^{n-1}

If n < 0.5, the polymer relaxation does not affect the molecular transport, hence diffusion is Fickian.
If n > 0.5, the solid transport will be non-fickian and will be relaxation controlled.

Other equationsto study thedrug releasekinetics from d osage forms

a. Zero Order: ***% R = kt***

This model represents an ideal release in order to a chieve prolonged pharmacological action. This is applicable to dosage forms like transdermal systems , coated forms, osmoticsystems, as well as Matrix tablets containing low soluble drugs.

b. First Order: ***log (fraction unreleased) = kt/2.303***

The model is applicable to hydrolysis kinetics and to study the release profiles of pharmaceutical dosage forms such as those containing water soluble drugs in porous matrices.

c. Matrix (Higuchi Matrix)*: % R = kt $^{0.5}$*

This model is applicable to systems with drug disp ersed in uniform swellable polymermatrix as in case of mat rix tablets with water soluble drug.

d. Peppas Korsmeyer Equation*: % R = kt ^{n}, log % R = logk + nlogt*

This model is widely used when release mechanis m is well known or when more than one type of release phenomenon could be involved. The 'n' values could be used to characterize different release mechanisms as:

Value of 'n'	Mechanism
0.5	Fickian Diffusion (Higuchi Matrix)
0.5<n<1	Anomalous Transport
1	Case – II transport (Zero Order Release)
n>1	Super Case Transport

PREFORMULATION STUDIES

Spectroscopic Studies Determination of λ max

A solution of 10µg/ml of Model drug was scanned in the range of 200 to 400nm. The drug exhibited a λ max at 269nm in simulated gastric fluid pH 1.2. Correlation between the concentration and absorbance was found to be near to 0.998, with a slope of 0.021 and intercept of 0.001.

Table 5 shows the calibration curve data of Model drug in simulated gastric fluid pH 1.2 at 269nm. Fig.1 shows the standard calibration curve with a regression value of 0.998, slope of 0.021 and intercept of 0.001 in simulated gastric fluid pH 1.2. The curve was found to be linear in the concentration range of 5-25µg/ml.

Compatibility Studies

Drug polymer compatibility studies were carried out using Fourier Transform Infra-Red spectroscopy to establish any possible interaction of Model drug with the polymers used in the formulation. The FT-IR spectra of the formulations were compared with the FTIR spectra of the pure drug. [Fig:2] The results indicated that the characteristic absorption peaks due to pure Model drug have appeared in the formulated microspheres, without any significant change in their position after successful encapsulation, indicating no chemical interaction between model drug and Polymers [6].

Evaluation and Characterisation of Microspheres

Percentage Yield

It was observed that as the polymer ratio in the formulation increases, the product yield also increases. The low percentage yield in some formulations may be due to blocking of needle andwastage of the drug polymer solution, adhesion of polymer solution to the magnetic bead and microspheres lost during the washing process. The percentage yield was found to be in the range of 80 to 88% for microspheres containing sodium alginate along with carbopol 934 as copolymer, 62.22 to87% for microspheres containing sodium alginate along with carbopol 971 as co-polymer and 80 to 87.5% for microspheres containing sodium alginate along with HPMCK4M as copolymer. The percentage yield of the prepared microspheres is recorded in Table 3.

Drug Entrapment Efficiency

Percentage Drug entrapment efficiency of Model drug ranged from 82.66 to 88.66% for microspheres containing sodium alginate along with carbopol 934 as copolymer, 53.2 to 76.66% for microspheres containing sodium alginate along with carbopol 971 as copolymer and 66.73 to 79.2% for microspheres containing sodium alginate along with HPMCK4M as copolymer. The drug entrapment efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. The % drug entrapment efficiency of the prepared microspheres is displayed in Table 3.

Particle Size Analysis

The mean size increased with increasing polymer concentration which is due to a significant increase in the viscosity, thus leading to an increased droplet size and finally a higher microspheres size. Microspheres containing sodium alginate along with carbopol 934 as copolymer had a size range of 512 µm to 826µm, microspheres containing sodium alginate along with carbopol 971 as copolymer exhibited a size range between 517µm to 834µm and microspheres containing sodium alginate along with HPMCK4 M as copolymer had a size range of 664µm to 903µm. The particle size data is presented in Tables 4. The particle size as well as % drug entrapment efficiency of the microspheres increased with increase in the polymer concentration.

Swelling Study

The swelling ratio is expressed as the percentage of water in the hydrogel at any instant during swelling. Swell ability is an important characteristic as it affects mucoadhesion as well as drug release profiles of polymeric drug delivery systems. Swell ability is an indicative parameter for rapid availability of drug solution for diffusion with greater flux. Swell ability data revealed that amount of polymer plays an important role in solvent transfer. It can be concluded from the data shown in Table 5 that with an increase in polymer concentration, the percentage of swelling also increases. Thus we can say that amount of polymer directly affects the swelling ratio. As the polymer to drug ratio increased, the percentage of swelling increased from 28 to 85% for microspheres containing sodium alginate along with carbopol 934 as copolymer, 24 to 64% for microspheres containing sodium alginate along with carbopol 971 as copolymer and 31 to 85 for microspheres containing sodium alginate along with HPMC K 4 M as copolymer. The percentage swelling of the prepared microspheres is displayed in Table no: 5

***In-Vitro* Mucoadhesion Test**

As the polymer to drug ratio increased, microspheres containing sodium alginate along with carbopol 934 as copolymer exhibited % mucoadhesion ranging from 65to 85%, microspheres containing sodium alginate along with carbopol 971 as copolymer exhibited % mucoadhesion ranging from 60 to 75% and microspheres containing sodium alginate along with HPMC K 4 M as copolymer exhibited % muco adhesion ranging from 60 to 80%. The rank of order of mucoadhesion is carbopol 934 > HPMC K4M > carbopol 971. Effect of polymer proportion on % mucoadhesion is depicted in table no: 6

***In-Vitro* Drug Release Studies**

Dissolution studies of all the formulations were ca rriedout using dissolution apparatus USP type I. The dissolution studies were conductedby usingdissolutio nmedia, pH1.2. The results of the in-vitro dissolution studies of formulations T_1 to T_4, T_5 to T_8 and T_9 to T_{12} are shown in table no.7 to 8. The plots of Cumulative percentage d rug release Vs Time. Figure: 3 shows the comparison of % CDR for formulations T_1 to T_4, figure5.23 for formulations T_5 to T_8 and figure: 5 for

formulations T_9 to T_{12}. Korsmeyer-Peppas plots of Model drug microspheres formulations T_1 to T_{12} are displayed in figures 3 and 4.

The formulations T_1,T_2, T_3 and T_4 containing Sodium alginate along withCarbopol 934 as copolymer showed a maximum release of 92.66% after 9 hours, 90.66% after10hours, 90.6% after 11 hours and 94.66% after 12 hours respectively.

The formulations T_5,T_6, T_7 and T_8 containing Sodium alginate along with Carbopol 971 as copolymer showed a maximum release of 92.22% after 9 hours, 91.33% after10hours, 89.55% after 11 hours and 90.66% after 12 hours respectively.

The formulations T_9,T_{10}, T_{11} and T_{12} containing Sodium alginate along with HPMCK4M as copolymer showed a maximum release of 92.6% after 9 hours, 91.3% after 10hours, 90% after 11 hours and 92.44% after 12 hours respectively.

This shows that more sustained release was observed with the increase in percentage of polymers. As the polymer to drug ratio was increased the extent of drug release decreased. A significant decrease in the rate and extent of drug release is attributed to the increase in density of polymer matrix that results in increased diffusion path length which the drug molecules have to traverse. The release of the drug has been controlled by swelling control release mechanism. Additionally, the larger particle size at higher polymer concentration also restricted the total surface area resulting in slower release.

In-Vitro Drug Release Kinetics [Chowdary K P R]

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the in-vitro drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, and Krosmeyer-Peppas model. The values are compiled in Table 5.21. The coefficient of deter mination (R^2) was used as an indicator of the best fitting for each of the models considered. The kinetic data analysis of all the formulations reached higher coefficient of determination with the Korsmeyer-Peppas model (R^2 = 0.914 to 0.996) whereas release exponent value (n) ranged from 0.498 to 0.743. From the coefficient of determination and release exponent values, it can be suggested that the mechanism of drug release follows Korsmeyer-Peppas model along with non-Fickian diffusion mechanism which leading to the conclusion that a release mechanism of drug followed combination of diffusion and spheres erosion.

Table 1. Prepared formulation of Bioadhesive Microspheres

S.no.	Formulation code	Drug: Polymer ratio	Polymer ratio
1	F1	Drug: Sod. Alginate : HPMC (K100 M)	**1:1**
2	F2	Drug: Sod. Alginate : Carbopol **(**940**)**	**1:1**
3	F3	Drug: Sod. Alginate: Ethyl cellulose	**1:1**
4	F4	Drug: Sod. Alginate : Sod.CMC	**1:1**
5	F5	Drug: Sod. Alginate : HPMC (K100 M)	**1:2**
6	F6	Drug: Sod. Alginate : Carbopol **(**940**)**	**1:2**
7	F7	Drug: Sod. Alginate: Ethyl cellulose	**1:2**
8	F8	Drug: Sod. Alginate : Sod.CMC	**1:2**
9	F9	Drug: Sod. Alginate : HPMC (K100 M)	**1:3**
10	F10	Drug: Sod. Alginate : Carbopol **(**940**)**	**1:3**
11	F11	Drug: Sod. Alginate: Ethyl cellulose	**1:3**
12	F12	Drug: Sod. Alginate : Sod.CMC	**1:3**

Table 2. Calibration curve data for Gliclazide in simulated gastric fluid pH 1.2

Concentration (µg /ml)	Absorbance
0	0
5	0.108
10	0.224
15	0.339
20	0.423
25	0.552

Table: 3 Percentage yield and percentage drug entrapment efficiency of the prepared microspheres

S.No.	Formulation code	% yield	%Drug entrapment efficiency
1	F_1	78.2	80.14
2	F_2	80.45	81.58
3	F_3	81.63	83.45

4	F_4	85.2	85.18
5	F_5	80	82.66
6	F_6	82.33	84.4
7	F_7	83	84.66
8	F_8	88	88.66
9	F_9	75	76.66
10	F_{10}	77	80.73
11	**F_{11}**	**83.78**	**85.98**
12	F_{12}	84.32	87.21

Table 4. Particle size data

S.No	Formulation Code	Particle Size (µM)
1	F1	680
2	F2	792
3	F3	823
4	F4	912
5	F_5	664
6	F_6	774
7	F_7	814
8	F_8	903
9	F_9	512
10	F_{10}	617
11	**F_{11}**	711
12	F_{12}	826

Table 5. Percentage swelling of the prepared microspheres

S.No.	Formulation Code	Initial (Wt)	Final (Wt)	Percentage Swelling
1	F_1	10	13.7	37
2	F_2	10	15.4	54
3	F_3	10	16.2	62
4	F_4	10	16.3	63
5	F_5	10	14.2	42
6	F_6	10	15.8	58
7	F_7	10	16.2	62
8	F_8	10	16.5	65
9	F_9	10	14.9	49
10	F_{10}	10	16.0	60
11	**F_{11}**	**10**	**16.5**	**69**
12	F_{12}	10	17.4	74

Table 6. Percentage mucoadhesion of the prepared microspheres

S.no.	Formulation code	No. Of microspheres		Percentage Mucoadhesion
		Initial	Final	
1	F_1	20	13	65
2	F_2	20	15	75
3	F_3	20	16	80
4	F_4	20	17	85
5	F_5	20	12	60
6	F_6	20	13	65
7	F_7	20	14	70
8	F_8	20	15	75
9	F_9	20	12	60
10	F_{10}	20	14	70
11	**F_{11}**	**20**	**15**	**75**
12	F_{12}	20	16	80

Table 7. *In-Vitro* drug release data of Model drug microspheres

Time(h)	Cumulative Percent of Drug Released			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
1	26.68	23.12	20.62	18.54
2	35.53	34.56	31.21	26.17
3	48.42	42.78	39.34	35.42
4	57.45	50.67	48.26	43.58
5	64.20	57.56	57.60	52.66
6	72.64	69.43	65.23	61.30
7	80.54	77.54	70.01	68.21
8	89.38	86.32	81.61	75.17
9	95.67	90.60	85.73	80.35
10	95.67	94.17	90.69	86.63
11	95.67	94.17	94.21	90.56
12	95.67	94.17	94.21	93.58

Table 8. *In-Vitro* drug release data of Model drug microspheres

Time (h)	Cumulative Percent of Drug Released			
	F5	**F6**	**F7**	**F8**
0	0	0	0	0
1	24.88	21.11	18.66	16.88
2	31.55	31.55	28.11	25.22
3	42.44	39.77	37.44	35.66
4	53.55	47.77	44.66	39.33
5	60.21	56.66	54.67	52.55
6	68.54	65.44	63.33	55.77
7	77.55	75.55	73.11	61.77
8	86.33	83.33	78.11	69.55
9	92.66	84.66	82.33	77.55
10	92.66	91.06	86.66	85.55
11	92.66	91.06	92.66	90.66
12	92.66	91.06	93.55	92.66

Table 9. *In-Vitro* drug release data of Model drug microspheres

Time(h)	Cumulative Percent of Drug Released			
	F9	**F10**	**F11**	**F12**
0	0	0	**0**	0
1	27.77	22.44	**18.44**	17.11
2	36.44	32.22	**29.33**	26.44
3	43.77	40.88	**39.55**	37.55
4	54.66	48.66	**45.55**	46.88
5	64.01	57.55	**56.33**	55.77
6	75.77	63.55	**61.33**	63.55
7	84.65	70.44	**69.55**	71.33
8	90	76.55	**75.56**	75.77
9	92.22	85.55	**81.55**	79.77
10	92.22	91.33	**86.33**	82.44
11	92.22	91.33	**89.55**	86.88
12	92.22	91.33	**96.55**	90.66

Table 10. Release Kinetics Studies of The Prepared Formulations

Formulation code	Release model			
	Zero order	First order	Higuchi matrix	Koresmeyer-peppas
	R^2	R^2	R^2	R^2
F_1	0.908	0.844	0.859	0.831
F_2	0.933	0.984	0.779	0.568
F_3	0.956	0.906	0.924	0.992
F_4	0.973	0.946	0.987	0.987
F_5	0.921	0.876	0.934	0.876
F_6	0.938	0.965	0.923	0.934
F_7	0.962	0.876	0.932	0.912
F_8	0.982	0.765	0.976	0.923
F_9	0.960	0.878	0.876	0.987
F_{10}	0.971	0.745	0.876	0.967
F_{11}	**0.967**	**0.970**	**0.972**	**0.992**
F_{12}	0.948	0.765	0.879	0.897

Figure 1. Standard graph of Model drug in simulated gastric fluid pH 1.2

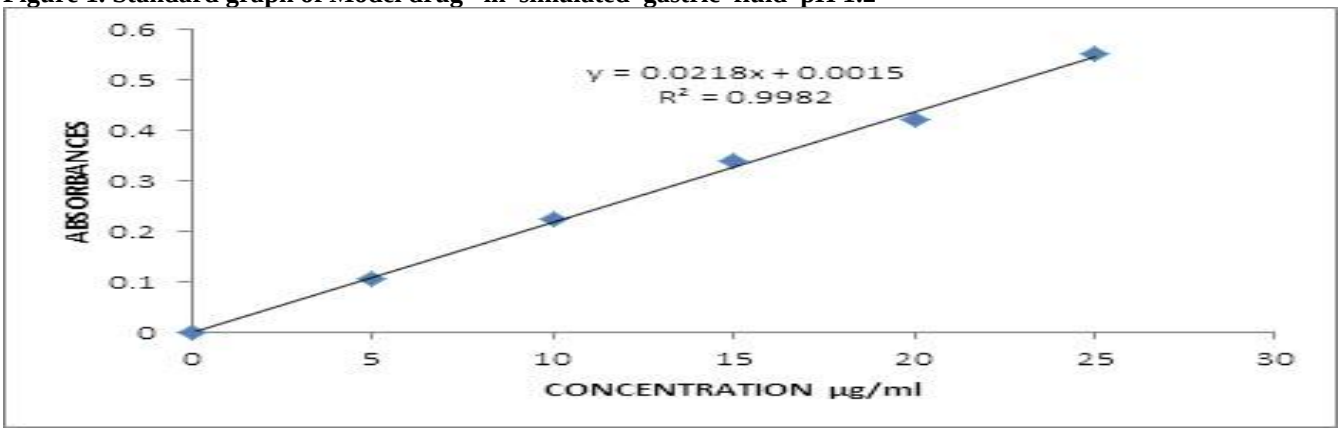
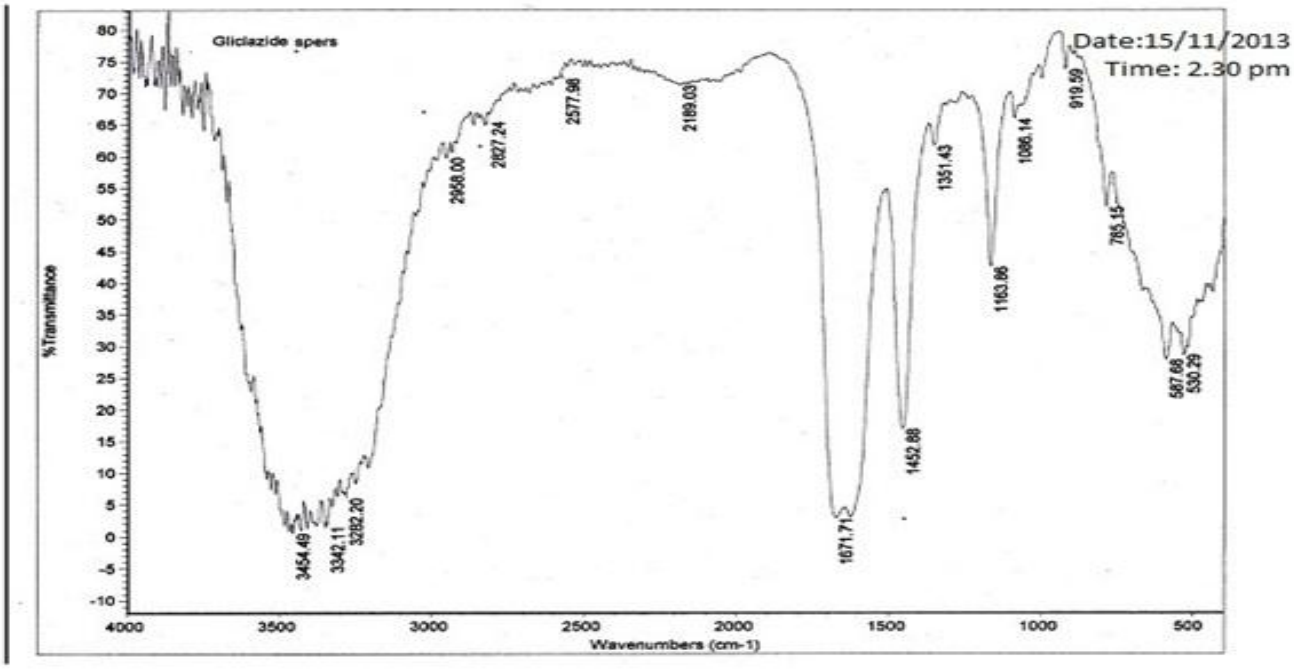


Figure 2. FT-IR spectra of Model drug



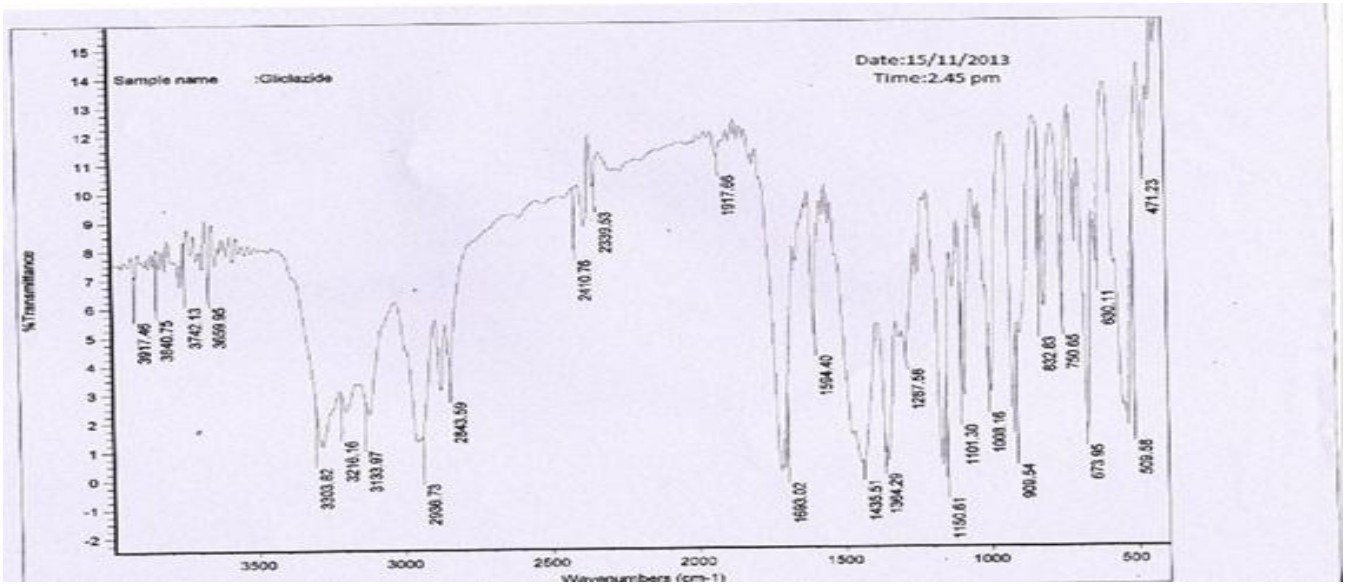


Figure 3. Comparison of In-Vitro drug release profile of Model drug microspheres

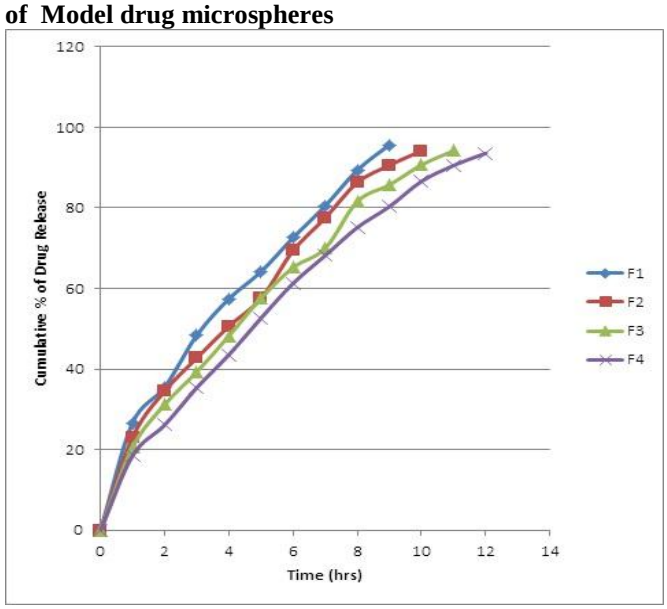


Figure 4. Comparison of In-Vitro drug release profile of Model Drug microspheres

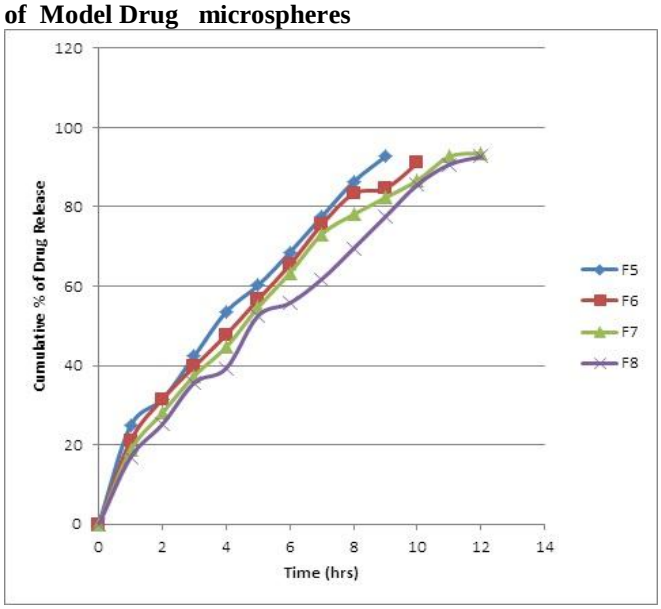
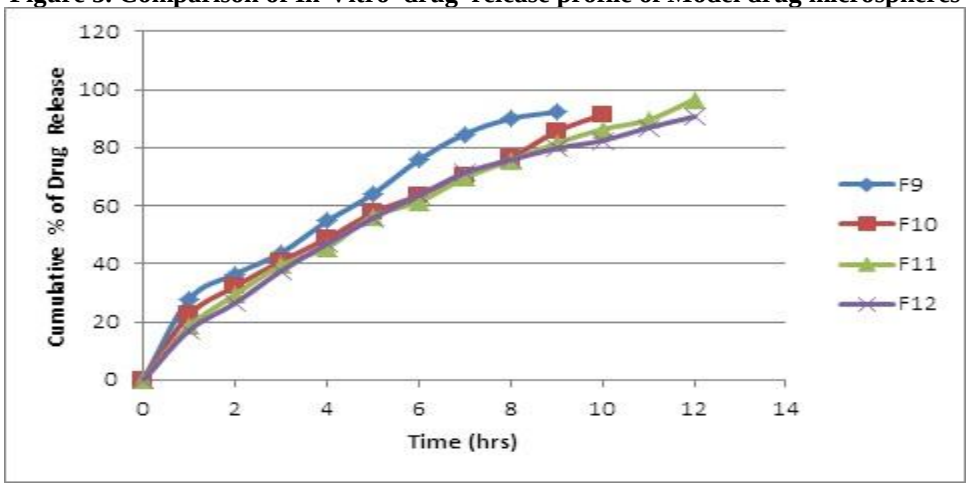


Figure 5. Comparison of In-Vitro drug release profile of Model drug microspheres



DISCUSSION AND CONCLUSION

In the present work, bioadhesive microspheres of model drug using Sodiumalginate along with Carbopol934, Carbopol 971, HPMCK4M as copolymers were formulated to deliver model drug via oral route.

Details regarding the preparation and evaluation of the formulation shave been discussed in the previous chapter. From the study following conclusions could be drawn:-

- The results of this investigation indicate that ionic cross linking technique Ionotropic gelation method can be successfully employed to fabricate Model drug microspheres. The technique provides characteristic advantage over conventional microsphere method, which involves an "all-aqueous" system, avoids residual solvents in microspheres. Other methods utilize larger volume of organic solvents, which are costly and hazardous because of the possible explosion, air pollution, toxicity and difficult to remove organic solvent completely.
- FT-IR spectra of the physical mixture revealed that the drug is compatible with the polymers and copolymers used. [Fig-2]
- Micrometric studies revealed that the mean particle size of the prepared microspheres was in the size range of 512-903µm and are suitable for bioadhesive microspheres for oral administration.
- Increaseinthepolymerconcentrationledtoincrease in % Yield, % Drug entrapment efficiency, Particle size, % swelling and % Mucoadhesion.
- The *in-vitro* mucoadhesive study demonstrated that microspheres of Model drug using sodium alginate along with Carbopol934 as copolymer adhered to the mucus to a greater extent than the microspheres of Model drug using sodium alginate along with Carbopol 971 and HPMC K4Mas copolymers.
- The *invitro* drug release decreased with increase in the polymer and copolymer concentration.
- Analysis of drug release mechanism showed that the drug release from the formulations followed non-Fickian diffusion and the best fit model was found to be Korsmeyer-Peppas and shown in fig 3 and 4.
- Based on the results of evaluation tests formulation coded T_4 was concluded as best formulation.

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