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Formulation of Mucoadhesive Microspheres of Irbesartan and Their Evaluation

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ABSTRACT

Mucoadhesive microspheres has been accepted as a process to achieve controlled drug delivery by prolonging the residence time of the dosage form at the site of absorption thereby improving and enhancing the bioavailability of drugs. Irbesartan is an Angiotensin receptor blocker (ARB) used mainly for the treatment of hypertension. It competes with Angiotensin II for binding at the AT1 receptor sub type. The mucoadhesive microspheres of Irbesartan were formulated by orifice ionic gelation technique employing polymers like Sodium Carboxy methyl cellulose and Carbopol along with Sodium alginate. The microspheres prepared were discrete, spherical and free flowing. Microspheres were evaluated for particle size, percentage yield, flow properties, drug content, and drug entrapment efficiency, percentage moisture loss, swelling property, in vitro drug release, drug release kinetics, in vitro wash-off test, stability study and drug polymer interaction study by FT-IR. The microencapsulation efficiency was found relatively high with 2% polymer. Average particle size was found in the range of 5.02 ± 0.36 to $9.45 \pm 0.43 \mu\text{m}$. Formulations F6 displayed the best results for. Entrapment efficiency was $85.26 \pm 0.43\%$, swelling-index was $194 \pm 3.45\%$ and drug release up to 8h was 94.97% . Drug release was diffusion controlled and followed first order kinetics. The in vitro wash-off test indicated that the microspheres had good mucoadhesive properties. Hence prepared mucoadhesive microspheres may be an effective strategy for the development of easy, reproducible and cost effective method for safe and effective oral drug therapy.

Keywords: Irbesartan, Angiotensin, Mucoadhesive Microspheres

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1. Introduction

The concept of bioadhesion or more specifically Mucoadhesion is one of them to increase gastric retention of drugs. Among the various approaches for controlled systems, microencapsulation process have gained good acceptance as a process to achieve controlled release and drug targeting. Though several studies reported Mucoadhesive drug delivery systems in the form of tablets, films, patches and gels for oral, buccal, nasal, ocular and topical routes, however, very few reports on Mucoadhesive Microspheres are available.[1-3]

The side effects of conventional form have been attenuated by designing the drug in the form of Mucoadhesive Microspheres which includes advantages like, maximized absorption rate due to intimate contact with the absorbing membrane, improved drug protection by polymer encapsulation, longer gut transit time resulting in extended periods for absorption. Irbesartan is an Angiotensin Receptor Blocker (ARB) used mainly for the treatment of hypertension. It competes with Angiotensin II for binding at the AT1 receptor subtype. Unlike ACE inhibitors,^[4] Irbesartan is chemically 2-butyl-3-({4-[2-(2H-1,2,3,4-tetrazol-5-yl)phenyl]phenyl}methyl)-1,3-diazaspiro [4.4] non-1-en-4-one, molecular mass: 428.53, bioavailability: 60-80% and half Life: 10-15 hrs.

The objective of this study is to prepare and evaluate the controlled release Mucoadhesive Microspheres of Irbesartan, thus reducing the frequency of dosing, side effects and increasing patient compliance. The novelty of this work is in combining the advantage of particulate system (microsphere) and mucoadhesive drug delivery system by taking Sodium alginate and Mucoadhesive polymers i.e. Sod CMC and Carbopol 934.

2. Material and methods

2.1 Materials:

2.2 Irbesartan was a gift sample from Aurobindo Pharma Ltd, Hyderabad. Sodium Alginate was obtained from Finar chemicals limited, Ahmadabad. Carbopol 934P was purchased from S.D. Fine chem. Ltd, Mumbai. Sod CMC was purchased from Yarrow chemicals ltd, Mumbai. All other reagents used were of analytical grade.

2.3 Compatibility Studies by IR-Spectroscopy: [5]

The drug polymer and polymer-polymer interaction was studied by the FTIR spectrometer using Shimadzu 8400-S, Japan. Two percent (w/w) of the sample with respect to a potassium bromide disc was mixed with dry KBr. The mixture was grind into a fine powder using an agate mortar and then compressed into a KBr disc in a hydraulic press at a pressure of 1000psi. Each KBr disc was scanned 16 times at 2 mm/sec at a resolution of 4 cm⁻¹ using cosine apodization. The characteristic peaks were recorded.

2.3 Preparation of Irbesartan Mucoadhesive Microspheres by Orifice-Ionic Gelation Method:

Sodium alginate (1%) and the Mucoadhesive polymer Carbopol 934 and Sod CMC were dissolved in Distilled water to form a homogeneous polymer solution. The active

core material Irbesartan (100mg) was added to the polymer solution and mixed thoroughly with a stirrer to form a smooth viscous dispersion. The resulting dispersion was then added drop wise into calcium chloride (2% w/v) solution through a syringe with a needle of size No: 18. The added droplets were retained in the calcium chloride solution for 30 minutes to complete the curing reaction and to produce spherical rigid microspheres. The microspheres were collected by decantation, and the product thus separated was washed repeatedly with water and dried at 45°C for 12 hours.

2.3 Evaluation of Irbesartan Mucoadhesive

Microspheres:

Micromeritic properties [6]

Bulk density, Tapped density and Hausner's ratio and Carr's index, were determined to assess the flow ability of the prepared microspheres.

Bulk density:

The product was tapped using bulk density apparatus for 1000 taps in a cylinder and the change in volume was measured. Bulk density of the formulations was determined using the formula

$$\text{Total weight/ Total bulk volume}$$

Tapped density:

Tapped density is used to investigate packing properties of microcapsules into capsules. The tapped density was measured by employing the conventional tapping method using a 10mL measuring cylinder and the number of tappings was 100 as sufficient to bring a plateau condition. Tapped density was calculated using the formula Total weight/ Total tapped volume.

Tapped density:

Tapped density is used to investigate packing properties of microcapsules into capsules. The tapped density was measured by employing the conventional tapping method using a 10mL measuring cylinder and the number of tappings was 100 as sufficient to bring a plateau condition. Tapped density was calculated using the formula Total weight/ Total tapped volume.

$$H = \text{Bulk Density/ Tapped Density}$$

Where, H = Hausner's ratio

Compressibility index:

It is indirect measurement of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials since all of them can influence the consolidation index. It is also called as compressibility index. It is denoted by CI and is calculated using the formula below.

$$\text{Compressibility index} = (1 - V_0/V) \times 100$$

Where, V₀ = volume of microspheres before tapping
V = volume of microspheres after 100 tappings.

The production 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 % production yields were calculated as per the formula mentioned below [7]

$$\% \text{ PY} = W_0 / W_T \times 100$$

PY = Production Yield;

WO=Practical mass (microspheres);

WT = Theoretical mass (Polymer +Drug)

2.5 Particle size analysis [8]

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 as diameter

2.6 Encapsulation efficiency [8]

To determine the amount of drug encapsulated in microspheres, a weighed amount (50 mg) of microspheres was suspended into 0.1N HCl and sonicated for 15 min in order to extract the entrapped drug completely. The solution was filtered through whatman filter paper and further dilutions were made. This solution was assayed for drug content by UV spectrophotometer at 244 nm.

$$EE (\%) = ED/AD \times 100$$

EE= Encapsulation efficiency;

ED= Amount of encapsulated drug;

AD= Amount of drug added.

2.7 Swelling Index [9-10]

The dynamic swelling property of microspheres in the dissolution medium was determined. Microspheres of known weight were placed in dissolution solution for 8 hr and the swollen microspheres were collected by a centrifuge and the wet weight of the swollen microspheres was determined by first blotting the particles with filter paper to remove absorbed water on surface and then weighing immediately on an electronic balance. The percentage of swelling of microspheres in the dissolution media was then calculated by using

$$\text{Swelling index: } SI = (W_t - W_0)/W_0 \times 100$$

$$\text{Swelling ratio: } W_t/W_0$$

Where SI = percentage of swelling of microspheres,

W_t = weight of the microspheres at time t,

W₀ = initial weight of the microspheres

2.8 Loose surface crystal study. [11]

The Irbesartan encapsulated microspheres prepared were evaluated for surface associated drug content on the surface of microspheres. From each batch, 100 mg of microspheres were shaken in 20 ml of 0.1N HCl for 5 min and then filtered through Whatman filter paper. The amount of drug present in filtrate was determined by spectroscopy and calculated as a percentage of total drug content

2.9 Moisture loss.[12]

The Irbesartan loaded microspheres was evaluated for % of moisture loss which sharing an idea about its hydrophilic nature. The microspheres weighed initially kept in desiccators containing calcium chloride at 37°C for 24 hour. The final weight was noted when no further change in weight of sample

$$\% \text{ Moisture loss} = \frac{\text{initial weight} - \text{final weight}}{\text{Final weight}} \times 100$$

2.10 In-vitro wash off test [12]

The mucoadhesive property of microspheres was evaluated by an *in vitro* adhesion testing method known as the wash-off test. Freshly excised pieces of intestinal mucosa from

sheep were mounted onto glass slide. About 100 microspheres were spread onto wet rinsed tissue specimen and immediately thereafter the slides were hung onto the arm of a tablet disintegrating machine. Then the machine was operated. The tissue specimen was given a slow, regular up and down movement in the test fluid at about 37°C contained in a vessel of the machine. At the end of 1, 2, 3, 4, 5, 6, 7,8 hrs the machine was stopped and the number of microspheres still adhering to the tissue was counted. The test was performed at 0.1N hydrochloric acid solution.

$$\% \text{ Mucoadhesion} = (N_a - N_l) / N_a \times 100$$

Where, N_a = number of microspheres applied;

N_l = number of microspheres leached out.

2.11 In-vitro drug release studies.[13-14]

900mL of 0.1N HCL was placed in the dissolution vessel and the USP dissolution apparatus I (Basket method) was assembled. The medium was allowed to equilibrate to temperature of 37°C ±0.5°C. Microspheres were placed in the dissolution vessel and the vessel was covered, the apparatus was operated for 8hrs at 50 rpm. At definite time intervals the 5mL of the dissolution fluid was withdrawn, filtered and again 5mL blank sample was replaced. Suitable dilutions were done with the dissolution fluid and the samples were analyzed spectrophotometrically at 244 nm using a UV-spectrophotometer (Lab India).The cumulative drug release was calculated by using standard curve.

2.12 In-vitro drug release kinetics:

In order to study the exact mechanism of drug release from microcapsules, drug release data was analyzed according to Zero order, First order, Higuchi square root and Korsmeyer-Peppas model. The analysis of the drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of mucoadhesive controlled release systems. The order of drug release from mucoadhesive controlled release systems was described by using Zero order kinetics or First orders kinetics. The mechanism of drug release from the mucoadhesive controlled systems was studied by using the Higuchi equation and the Korsmeyer - Peppas equation

Zero order release

It defines a linear relationship between the fractions of drug released versus time

$$Q = k_0 t$$

Where, Q is the fraction of drug released at time t and k₀ is the zero order release rate constant. A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First order release

Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics. The equation that describes first order kinetics is

$$\ln(1-Q) = -K_1 t$$

Where, Q is the fraction of drug released at time t and k₁ is the first order release rate constant. Thus, a plot of the logarithm of the fraction of drug un dissolved against the

time will be linear if the release obeys the first order release kinetics.

Higuchi equation: It defines a linear dependence of the active fraction released per unit of surface (Q) and the square root of time.

$$Q = K_2 t^{1/2}$$

Where, K_2 is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependant.

Korsmeyer - Peppas equation

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by Peppas's and Korsmeyer equation (Power law).

$$M_t/M = K.t^n$$

The drug release, the value of n can be used as abstracted. A plot between logs of M_t/M against log of time will be linear if the release obeys Peppas's and Korsmeyer equation and the slope of this plot represents "n" value.

Stability studies of microspheres

Stability studies of Irbesartan microspheres were performed at $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{RH}$ and $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{RH}$ for a period of 3 months. The samples were withdrawn at the intervals of 0, 30, 60 and 90 days and were analyzed for its appearance, Drug entrapment efficiency, swelling index and *in-vitro* drug release.

2.13 Surface electron microscopy [16]

Shape and surface morphology of microspheres was studied using scanning electron microscopy (SEM). 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).

3. Results and discussion

3.1 Drug compatibility studies: The IR spectral studies of pure Irbesartan, Sodium Carboxy Methyl Cellulose, Carbopol, Sodium alginate and combination of drug and polymers containing highest proportion were carried out. When the characteristic peaks of Irbesartan were compared with the combination of Irbesartan and polymers, it was found that the same fundamental peaks were also present in the drug-polymer combinations indicating there was no interaction between Irbesartan and polymers used and the spectral data are presented in [Fig 1-5].

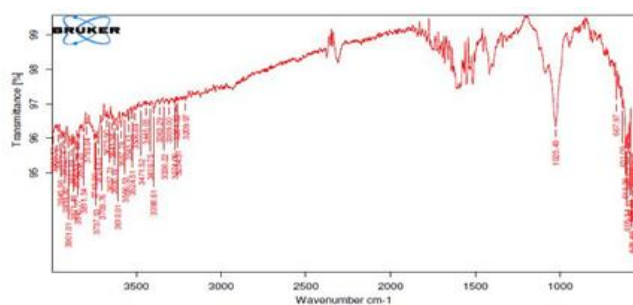


Figure 1: IR spectrum of pure Sodium alginate

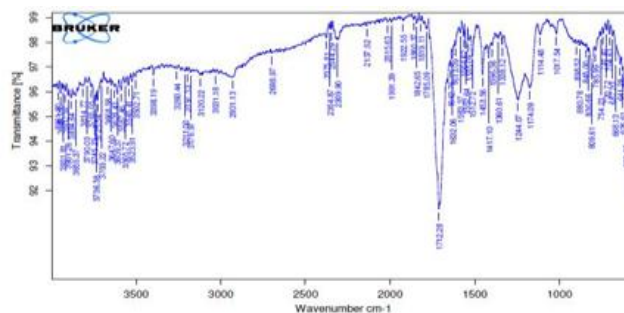


Figure 2: IR spectrum of pure Carbopol 934

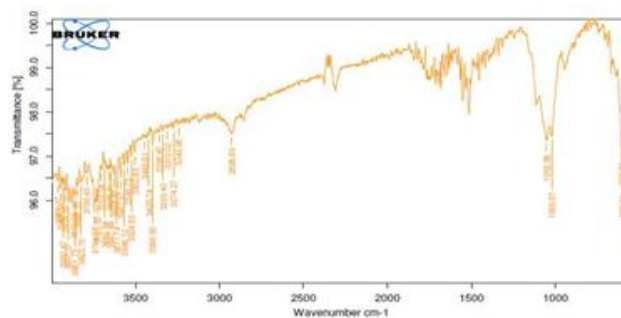


Figure 3: IR spectrum of pure Sod CMC

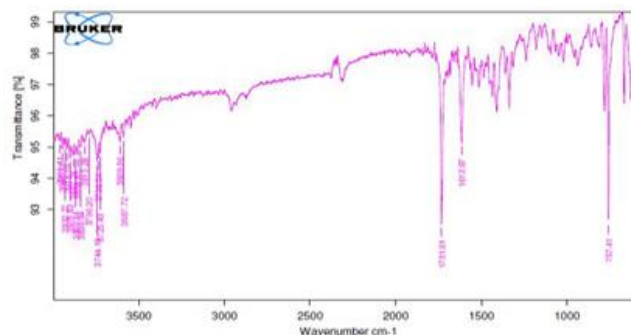


Figure 4: IR spectrum of pure Irbesartan drug

3.2 Micromeritic properties: The Micromeritic studies revealed that the microspheres have better flow property which indicates the microspheres produced are spherical and non- aggregated. The, Bulk density, Tapped density, Carr's index and Hausner's ratio for all formulations i.e.F1 to F10 were found to be in the range of 0.27 ± 0.07 to 0.48 ± 0.05 , 0.41 ± 0.08 to 0.59 ± 0.03 , 1.15 to 1.18 and 11.55 to 15.21 respectively. All the formulations showed excellent flow ability as expressed in term of Micromeritic parameters. The results are shown in Table 2.

3.3 Percentage yield:

It was observed that percentage yield of all formulations i.e.F1 to F10 was ranging from 84.43% to 90.12%. The formulation F9 showed maximum yield i.e. 90.12%. Due to higher concentration of polymers which indicates that this orifice ionic gelation method was very useful for adoption in the formulation of Irbesartan Mucoadhesive Microspheres. The results are shown in Table 3.

3.4 Drug encapsulation efficiency:

The drug content was determined by UV spectrophotometry. The standard deviations among the values were found to be less. This indicates that the drug

was distributed almost uniformly throughout the batch of microspheres. The microencapsulation efficiency was in the range of $74.78 \pm 0.56\%$ to $85.26 \pm 0.43\%$. This improved encapsulation efficiency simply by due to the greater proportion of polymer with respect to amount of drug. The results are shown in the Table 3.

3.5 Particle size:

The particle size of Irbesartan Microsphere was analyzed by optical microscopy. The average particle size was found to be in the range of $5.02 \pm 0.36 \mu\text{m}$ to $9.45 \pm 0.43 \mu\text{m}$. The average particle size of microspheres was found to be increased as the concentration of the polymer was increased. This may be due to increased coat thickness with increasing polymer proportion. Particle size of the microspheres was large. The results are shown in Table 3.

3.6 Swelling Index:

The degrees of swelling of formulations F1-F10 were $162 \pm 2.48\%$ to $194 \pm 3.45\%$ which indicates the hydrophilic property of the polymers with establishing the fundamentals that the increase in degree of swelling depends on the polymer concentration in formulation. The formulation F6 showed good degree of swelling. The results are shown in the Table 3.

3.7 Loose surface crystallography:

Loose surface crystal study done showed relative amount of drug encapsulated in outer layers. Formulations F1, F2, F3, F4 and F5 showed $24.32 \pm 0.12\%$, $25.52 \pm 0.31\%$, $24.13 \pm 0.22\%$, $20.69 \pm 0.15\%$ and $23.69 \pm 0.28\%$ respectively and F6, F7, F8, F9, F10 showed $12.32 \pm 0.34\%$, $20.95 \pm 0.18\%$, $16.63 \pm 0.16\%$, $15.35 \pm 0.32\%$ and $24.59 \pm 0.16\%$ respectively. Surface drug content of microspheres decreased with increase in the concentration of the polymer. Initially in batches with low polymer concentration the surface associated drug content was more due to the lower encapsulation efficiency. As the polymer concentration increased from F1-F5, F6-F10 it showed increased encapsulation efficiencies and hence decreased surface drug contents. The results are shown in the Table 3.

3.8 Moisture loss:

The percentage moisture loss of formulations F1 to F5 were 10.76%, 8.68%, 7.02%, 11.58%, and 9.16% respectively and formulations F6 to F10 were 7.06%, 9.45%, 8.32%, 7.91% and 11.26% respectively. The results ensure the presence of diminutive water content which can be due to the involvement of water in process and hydrophilic property of mucoadhesive polymers shown in Table 3.

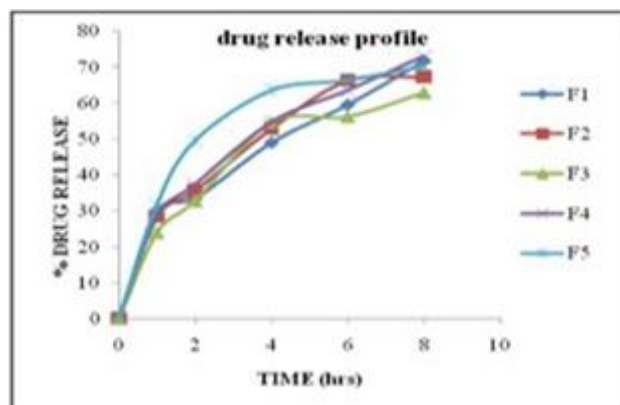
3.9 In-vitro wash off test:

Microspheres with a coat consisting of alginate and a mucoadhesive polymer exhibited good mucoadhesive property in the *in vitro* wash off test. The rapid wash-off, observed may be due to ionization which increases their solubility and reduces adhesive strength. The results of wash off test indicated that the microcapsules had fairly good mucoadhesive properties. The *in vitro* study results revealed that Irbesartan release from the microspheres was slow and spread over extended period of time shown in Table 4 and Fig 6.

3.10 In-vitro drug release studies

The percentage drug release from formulations, F1-F10 was observed for 8 hours in 0.1 N HCl. The formulations F1-F5

drug release was found to be 78.3% to 85.75%, by using 2% polymer. The maximum drug release was found in F2 due to equal proportion of concentration of polymers i.e. Carbopol 934P and Sod CMC (0.5:0.5). The formulations F6-F10 was found to be 75.45% to 94.97% by using 2.5% polymer. The maximum drug release was found in F6 due to increase in concentration of primary polymer and decrease in concentration of secondary polymer Carbopol 934p to Sod CMC (1:0.5). Among all formulation F6 was found to be best i.e. 94.97% drug release. The results of *in-vitro* dissolution studies are shown in the Fig 5-6.



Cumulative % drug release of formulations F1-F5

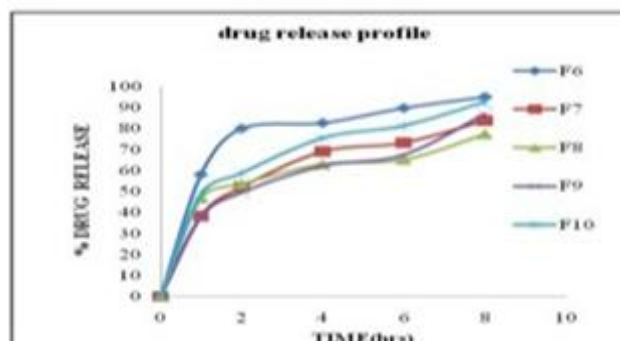


Figure 5: Cumulative % drug release of formulations F6-F10

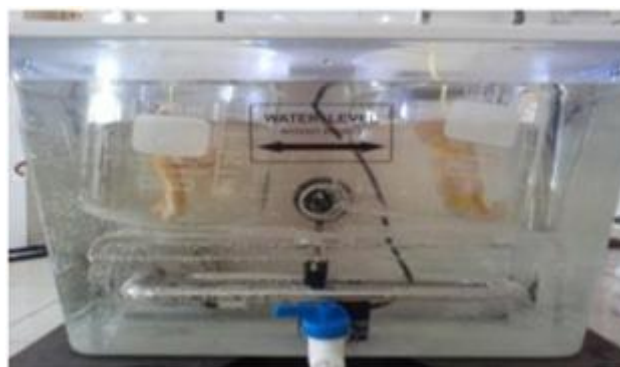


Figure 6: *in-vitro* washes off test for Mucoadhesive Microspheres of Irbesartan

3.11 Kinetics of Drug Release

The drug release data was subjected for mathematical treatment to check the release order kinetics. Plots of log cumulative percent drug remaining Vs time were found to

be linear with all the microsphere formulations indicating that the drug release was according to the first order kinetics. To evaluate the drug release mechanism from microsphere Peppas's plot were constructed and these plots were found to be linear with all microspheres indicating that the drug release mechanism from the microspheres was diffusion controlled. The results of all microspheres showed 'n' values less than 0.5 which indicates that it follows fickian diffusion. The Kinetic data of release profiles of Irbesartan microspheres are shown in Table 5.

3.12 Stability Studies:

The stability studies were conducted on the selected formulation F6 as per the ICH guidelines i.e. 25°C/60% RH and 40°C/75% RH. The stability studies were done at the intervals of 0, 30, 60 and 90 days. The parameters studied were entrapment efficiency, swelling index and *in-vitro* drug release. The results are shown in Table 6.

3.13 Scanning Electron Microscopy:

Scanning electron micrographs of formulations is shown in Fig.09. The microspheres were found to be discrete, uniform and spherical in shape. The surface of the microspheres was found to be smooth and the core was completely covered by the coating as evidenced by the SEM photographs.

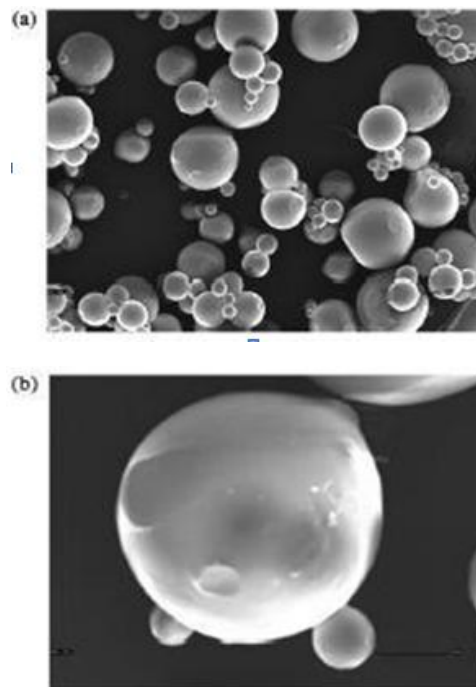


Figure 7: Scanning electron micrograph of F6 formulation (a) group of microspheres and (b) single microsphere

Table 1: Preparation of Irbesartan Mucoadhesive Microspheres

FORMULATION CODE	DRUG(mg)	SODIUM ALGINATE	CARBOPOL(934)	NACMC
F1	100	1	0.25	0.75
F2	100	1	0.5	0.5
F3	100	1	0.75	0.25
F4	100	1	0	1
F5	100	1	1	0
F6	100	1	1	0.5
F7	100	1	0.5	1
F8	100	1	0.75	0.75
F9	100	1	0.25	1.25
F10	100	1	1.25	0.25

Table 3: Results of evaluation parameters of Irbesartan Mucoadhesive Microspheres for formulations F1-F10

Formulation code	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Compressibility index (%)	Hausner's ratio
(Mean \pm s.d; n=3)				
F1	0.32 \pm 0.02	0.52 \pm 0.06	1.15	13.46
F2	0.28 \pm 0.05	0.47 \pm 0.09	1.16	14.28
F3	0.45 \pm 0.08	0.59 \pm 0.03	1.15	13.2
F4	0.32 \pm 0.01	0.49 \pm 0.02	1.17	15.1
F5	0.42 \pm 0.03	0.55 \pm 0.05	1.16	14
F6	0.34 \pm 0.04	0.49 \pm 0.05	1.18	11.55
F7	0.48 \pm 0.05	0.52 \pm 0.09	1.17	12.58
F8	0.31 \pm 0.08	0.47 \pm 0.04	1.15	13.46
F9	0.27 \pm 0.07	0.41 \pm 0.08	1.15	13.72
F10	0.38 \pm 0.08	0.42 \pm 0.05	1.18	11.55

Formulation code	Percentage yield (%)	Drug encapsulation (%)	Particle size (μm)	Degree of swelling (%)	Loose surface crystal stud (%)	Moisture loss (%)
F1	86.19	77.66 \pm 0.67	5.02 \pm 0.36	170 \pm 1.52	24.32 \pm 0.12	10.76 \pm 0.32
F2	89.64	74.78 \pm 0.56	6.21 \pm 0.46	185 \pm 2.68	23.52 \pm 0.31	8.68 \pm 0.41
F3	85.91	76.22 \pm 0.48	6.00 \pm 0.55	189 \pm 3.64	24.13 \pm 0.22	7.02 \pm 0.56
F4	86.33	78.58 \pm 0.64	5.57 \pm 0.49	176 \pm 2.98	20.69 \pm 0.15	11.58 \pm 0.28
F5	87.29	76.16 \pm 0.52	6.23 \pm 0.39	182 \pm 2.88	23.69 \pm 0.28	9.16 \pm 0.31
F6	88.15	85.26 \pm 0.43	7.65 \pm 0.37	194 \pm 3.65	12.32 \pm 0.34	7.06 \pm 0.45
F7	84.43	76.45 \pm 0.65	8.36 \pm 0.51	162 \pm 2.48	20.95 \pm 0.18	9.45 \pm 0.25
F8	87.65	84.32 \pm 0.46	7.68 \pm 0.38	172 \pm 1.68	16.63 \pm 0.16	8.32 \pm 0.36
F9	90.12	79.91 \pm 0.58	9.45 \pm 0.43	186 \pm 3.20	15.35 \pm 0.32	7.91 \pm 0.38
F10	86.89	78.26 \pm 0.67	8.52 \pm 0.46	193 \pm 2.51	24.59 \pm 0.16	11.26 \pm 0.43

Table 4: *In-vitro* wash off test of Irbesartan Mucoadhesive Microspheres for formulations F1-F10

Formulation code / time in hrs	1 hr	2 hr	4 hr	6 hr	8 hr
F1	78	74	68	61	55
F2	81	82	73	68	63
F3	88	87	84	72	77
F4	79	75	71	64	52
F5	74	68	63	58	50
F6	93	89	86	83	81
F7	94	87	82	76	74
F8	93	88	83	79	77
F9	92	86	81	77	77
F10	93	85	81	78	75

Table 5: *In-vitro* drug release kinetics studies of prepared Irbesartan microspheres

Formulation code	First order (R ² value)	Zero order (R ² value)	Higuchi (r ²)	Peppas		Hixson n crowel
				(R ²)	n	
F1	0.79	0.69	0.96	0.99	0.35	0.79
F2	0.9	0.71	0.92	0.97	0.25	0.85
F3	0.94	0.81	0.95	0.97	0.42	0.9
F4	0.85	0.66	0.89	0.96	0.21	0.79
F5	0.88	0.69	0.91	0.99	0.25	0.83
F6	0.83	0.58	0.84	0.85	0.21	0.74
F7	0.92	0.77	0.96	0.97	0.35	0.86
F8	0.67	0.54	0.81	0.96	0.14	0.62
F9	0.92	0.78	0.96	0.99	0.32	0.88
F10	0.95	0.74	0.94	0.99	0.29	0.9

Table 6: Stability studies of formulation F6 as per ICH guidelines

Characteristics	Initials	30 days	60 days	90 days
	25 \pm 2 $^{\circ}$ C 60 \pm 5 % RH	25 \pm 2 $^{\circ}$ C 60 \pm 5 %RH	25 \pm 2 $^{\circ}$ C 60 \pm 5 % RH	40 \pm 2 $^{\circ}$ C 75 \pm 5 % RH
Entrapment efficiency	85.26 \pm 0.4	83.01 \pm 0.5	82.75 \pm 0.1	82.50 \pm 0.2
Swelling index	3	3	2	1
<i>In vitro</i> drug release	194 \pm 3.65	191 \pm 0.24	188 \pm 0.73	185 \pm 0.92
	94.97 \pm 0.8	93.80 \pm 0.3	92.98 \pm 0.7	94.15 \pm 0.6

4. Conclusion

The Mucoadhesive Microspheres of Irbesartan were successfully prepared by orifice Ionic Gelation Technique using polymers Sodium alginate, Carbopol and Sod CMC. Higher percentage of entrapment was obtained by

increasing the concentration of polymer. The particle size of microspheres was determined by optical microscopy and all the batches of microspheres show uniform size distribution. The *in-vitro* dissolution studies showed that

Irbesartan Mucoadhesive Microspheres formulation F6 (94.97%) showed better sustained effect over a period of 8 hours than other formulations. Hence, prepared Mucoadhesive Microspheres may be an effective strategy for the development of easy, reproducible and cost effective method for safe and effective Mucoadhesive drug delivery.

5. References

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