Formulation and Evaluation of Microsphere Containing Telmisartan Drug by Ionotropic Gelation Method

[1]Himanshu C. Chaudhari, [2]Latesh Y. Chaudhari, [3]Pratik A. Chaudhari, [4]Shubham P Bhavsar, [5]Sandip A. Tadavi

PSGVP Mandal's College of Pharmacy
Shahada, Maharashtra, India 425409

Abstract: Microsphere is novel drug delivery system for improving therapeutic action of drug, increasing prolong action lowering dose frequency of dosage form and to improve patient complies. Microsphere are small micron size particle ranging from 1um to 1000 um and are free flowing particle prepared to acquired prolonged and controlled drug delivery to enhance the drug bioavailability and stability and target specific sites The main aim of the present study was to formulate Telmisartan microspheres by ionotropic gelation technique using various polymer such as Carbopol grade 940, sodium alginate, chitosan etc. where 8-10 % calcium chloride is used as a cross linking agent to form a discrete microsphere with sodium alginate for the effective use in the treatment of hypertension. Prepared microsphere was evaluated for entrapment efficiency, drug content. Microsphere size, morphology, FTIR, DSC, in vitro drug release and drug release kinetics. The prepared microsphere was bulky, free flowing, spherical and showed a drug entrapment ranging between 50 – 80 % and had a mean particle size ranging from as determined by optical microscopy and SEM (showed microsphere with spherical and rough surface) and the percent yield range between 80 to 98.94 %. The size of microsphere was increasing by increasing concentration of alginate and increasing concentration of polymer (Carbopol and chitosan). The in vitro drug release was carried out in Phosphate buffer (PH 7.8). Percent drug release was decreased and increased in concentration of sodium alginate and calcium chloride. The present study conclusively that telmisartan microsphere could be prepared successfully and formulation F4 shows satisfactory result. Telmisartan microspheres were developed to control the release rate of the drug and target to specific site of the body to make an enormous impact in the formulation and development of novel drug delivery system and also improve efficient absorption and enhances oral bioavailability of the drug due to high surface to volume ratio.

Keywords: Microsphere, Bioavailability, sustained release, Targeted drug delivery, Hypertension, Sodium alginate, Carbopol.

INTRODUCTION-

A drug is defined as the active pharmaceutical ingredient that upon formulation into dosage form using excipient is used to deliver drug into the body to exhibit a therapeutic effect. The drug administration to show the therapeutic effect in the body is known as drug delivery [1]. Novel drug delivery system means of improving the therapeutic effectiveness of incorporated drug by providing controlled delivery, targeted and sustained delivery [2]. The drug delivery system that can precisely control the release rate or targeted drug to specific body site have an enormous impact on the health care system [3]. Microsphere are mono or multinuclear materials embedded in spherical coating matrix [4]. Microsphere are small micron size particle ranging from 1um to 1000um and are free flowing particle made up of natural or synthetic polymer. These are prepared to acquired prolonged and controlled drug delivery to enhance the bioavailability, stability and target specific sites. By using novel advanced technologies and new dosage forms a Novel drug delivery system has been developed [1].

TARGETED DRUG DELIVERY SYSTEM –

In this system the specific site is targeted in the body and the drug is released in a controlled manner for a period so that drug fluctuations are minimized. this system is suitable for cancerous tissues in the body that can target the specific tumor tissue and release the drug at the targeted area. The drug become active only at the targeted site, hence the tissues in the other body parts are not affected by the drug, this minimizes side effect and toxicity [1].

CONTROLLED DRUG DELIVERY SYSTEM –

Now a days, very few drugs are coming out of research and development and already existing drugs suffering the problems of resistance due to their irrational use specifically in the case of drug like antibiotics. Hence for more effective way are formulated by slight alteration in drug delivery [5,6]. These dosage forms are modified in such a way that the drug is release over a long time, maintaining the drug in the effective therapeutic region for prolonged period. The dosage forms are modified in such a way that the drug can be sustained and maintained for a specific period for a slow and controlled release. They can be modified into delayed release form from which the drug is released after lag time and show action [1].

Frequent administration of a drug is necessary when those have a shorter half-life and all these leads to a decrease in a patient's compliance. To overcome the above problem various type of controlled release dosage forms are formulated and altered. The controlled release dosage form maintaining a relatively constant drug level in the plasma by releasing the drug at a predetermined rate for an extended period. There are significant challenges in developing controlled release formulations for drugs with poor aqueous solubility which required both solubilization and engineering of release profile [5,6].

 # TELMISARTAN-

Telmisartan is an angiotensin II receptor antagonist (angiotensin II receptor blocker) used in the management of hypertension. It is practically insoluble in water; A new oral drug delivery system was developed to utilized both the concept of sustained release and mucoadhesive Ness to obtain a unique drug delivery system that could remain in the intensive and control the drug release for a longer period. this drug also undergoes first pass metabolism. To overcome this problem telmisartan mucoadhesive microspheres were developed to controlled the release rate of the drug and target to the specific site of the body [5].

A. Undried microsphere **B. Dried microsphere**

FIG 1. Formulated Microsphere

 # MATERIAL AND METHOD-

 # MATERIAL- Telmisartan drug was given by the guide teacher MR. Tadvi sir, Associate professor at PSGVP Mandal's College of Pharmacy, Shahada, Maharashtra 425409. And remaining all material like, chitosan, Carbopol, sodium alginate, Calcium chloride etc. was already available in college.

 # METHOD- Preparation of microsphere by Ionotropic gelation method.

PROCEDURE-

Microsphere were prepared by ionotropic gelation technique. In this method a homogeneous polymer solution is prepared by dissolving a mixture of sodium alginate and mucoadhesive polymers like, Chitosan, Carbopol into the purified water with continuously stirring on magnetic stirrer for 10 min at 1000 RPM. To this solution the active ingredient is added into the purified water (500 mg) and stirred continuously for 15-20 min until a viscous dispersion is obtained. A 5 – 10 % Calcium Chloride solution is prepared and to this solution the viscous solution of drug dispersion is added manually dropwise manner by using 20 – 22 syringe needle gauge. The added droplet is left in the solution for 15 – 20 min with continuous stirring (300 RPM) to complete the curing process and thereby proceeding spherical and rigid microspheres. Then the solution containing the microsphere is get filtered out to obtained the microsphere and collected microsphere is dried at 45°C for 12-24 hr., [1,5]. The prepared dried microsphere containing the drug were stored in desiccator until used [5].

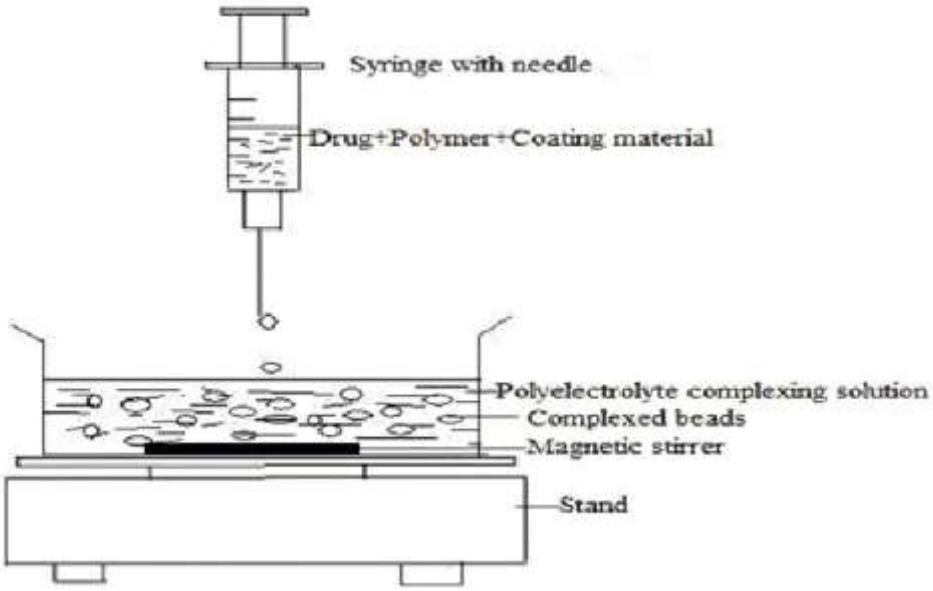

FIG. 2 Process of formation of microsphere

 # DRUG EXCIPIENT COMPATIBILITY STUDY-

FTIR spectroscopy was used to determine the functional group present in pure drug sample. The FTIR spectra of pure telmisartan was showed the characteristic peaks at 740 cm^{-1}, 1128 cm^{-1}, 1268 cm^{-1}, 3057 cm^{-1}, 1695 cm^{-1}, 1695 cm^{-1}, and 862 cm^{-1} were due to aromatic C-H stretching, C=N stretching aromatic C-H stretching, C=O stretching and OH stretching, IR spectra of Telmisartan is as follows [5,7].

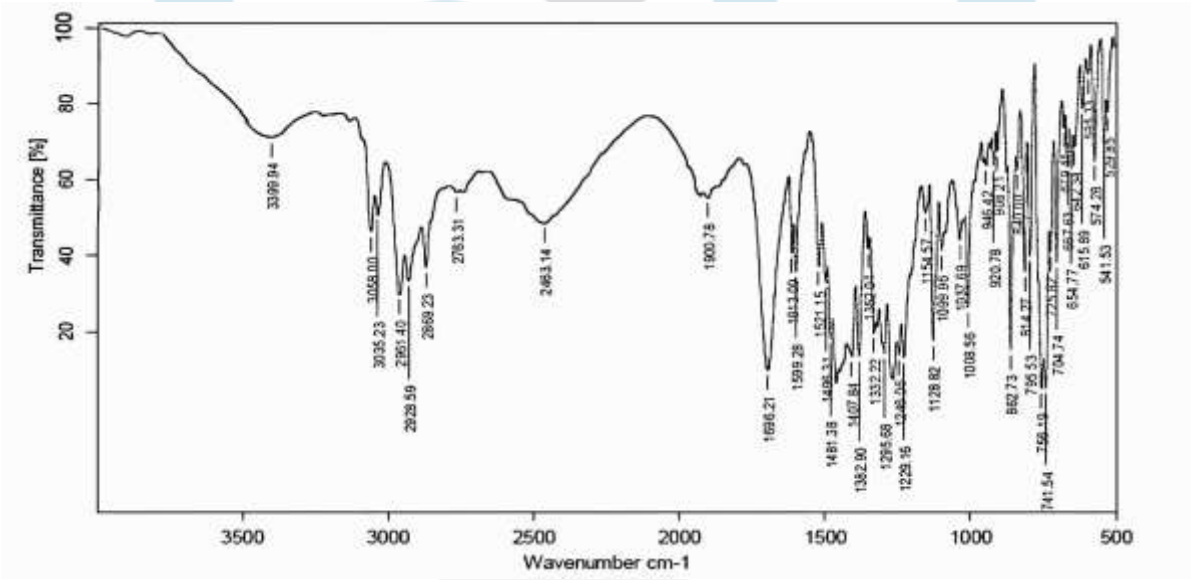

FIG. 3 IR Spectra of Telmisartan

Similarly, the IR Spectra of Telmisartan + Carbopol and Telmisartan + Chitosan is given below to show the drug compatibility of Telmisartan with another ingredient.[5]

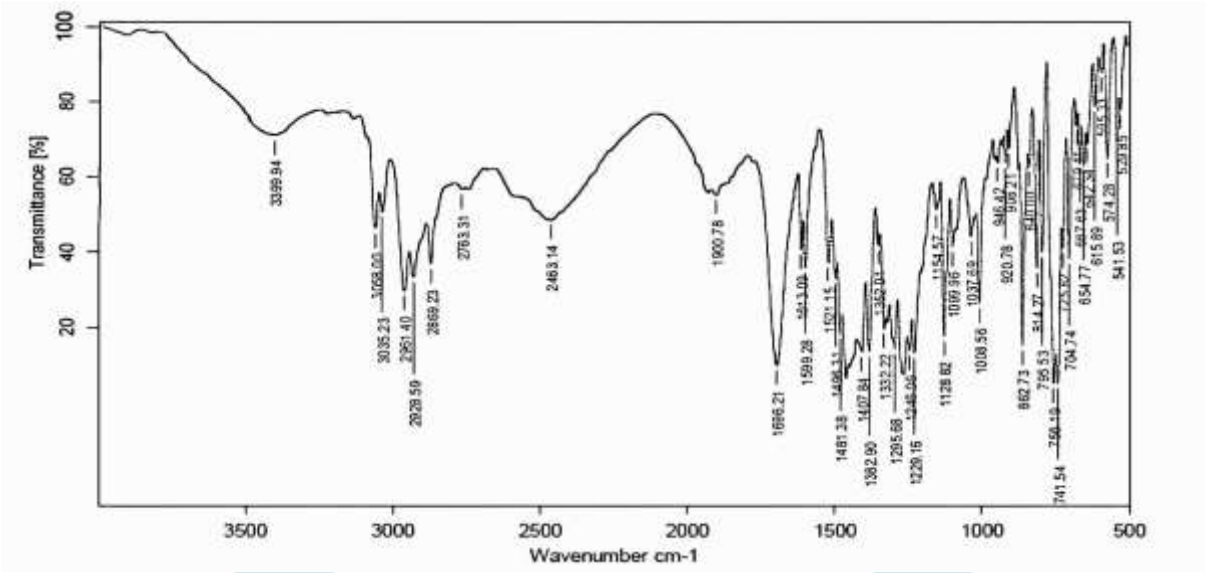

FIG.4 IR Spectra of Telmisartan + Carbopol

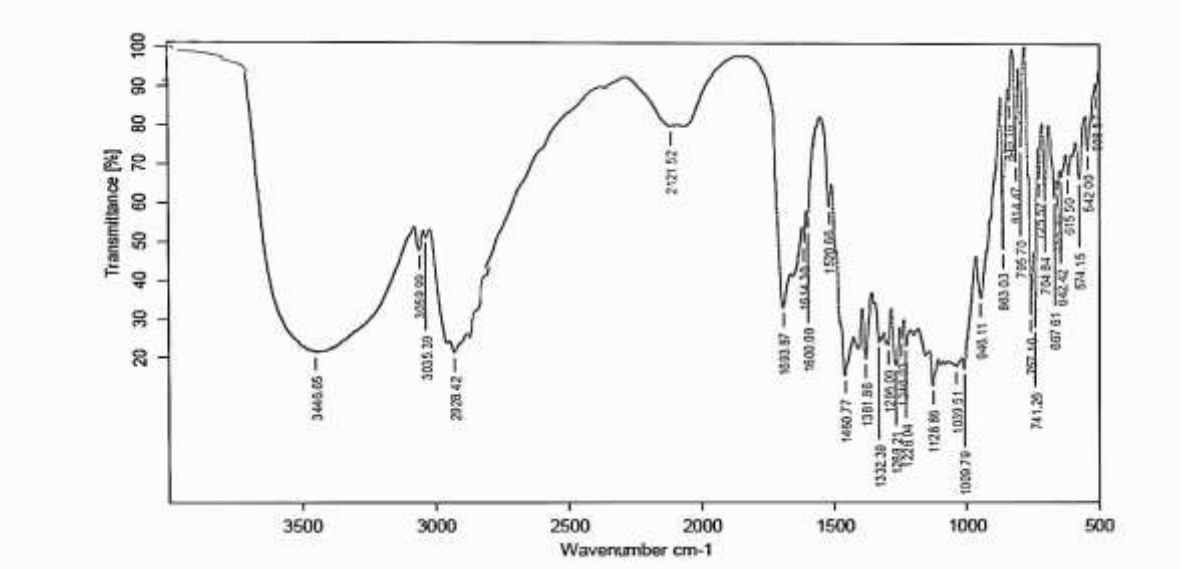

FIG.5 IR Spectra of Telmisartan + Chitosan

The sample of pure drug and formulas were dispersed in KBR powder and compressed into pellets at a pressure of 600 kg/cm^2. Spectral measurement was obtained by powder diffuse reflectance on the infrared spectrophotometer.

Inference – the FTIR spectra for the pure drug and formulation were shown in fig 3-5. The spectra of drug and polymers were showed a broad peak at the same place as the peak observed at the same place as the peak observed at the spectrum of the pure drug has been observed which indicated that there was no chemical interaction with the polymer [5].

Importance of Drug Compatibility study-

1) Stability of dosage form can be maximized.
2) It helps to avoid the surprise problems.
3) It bridges the drug discovery and drug development.
4) Drug excipient compatibility study data is essential for investigational new drug submission.

CALIBRATION CURVE OF TELMISARTAN –

Calibration curve was determined for the use of telmisartan as API and in pharmaceutical dosage form. It is done by using the UV Spectroscopy. Here the absorbance was taken by using ethanol(95%) and 0,1N $NaHCO_3$in the ratio 60:40 as a solvent in the range of λ max 200 - 400 using UV Spectrophotometer.

Preparation of standard stock solutions -

Weigh accurately 10 mg of the drug with the help of digital balance and transfer it into beaker containing the solution of ethanol (60 ml) and 0.1 N $NaHCO_3$ (40ml) after dissolving the solution keep it for ultra-sonification to obtain a clear solution. After completion of sonification process for 15 - 20 min. This solution contained 100ug/ml drug.

Determination of absorbance of Telmisartan-

For the determination of absorbance, the solution of 10ug/ml were prepared by taking 10ml of 100ug/ml in 100ml measuring cylinder and diluted with ethanol(95%) and 0.1N $NaHCO_3$ in the ratio 60:40 up to 100 ml. The absorbance of this solution was scanned in the UV range of 200 to 400 nm against water as blank. and the absorption maxima was found to be noted at 295 nm which is shown in Fig.6 .

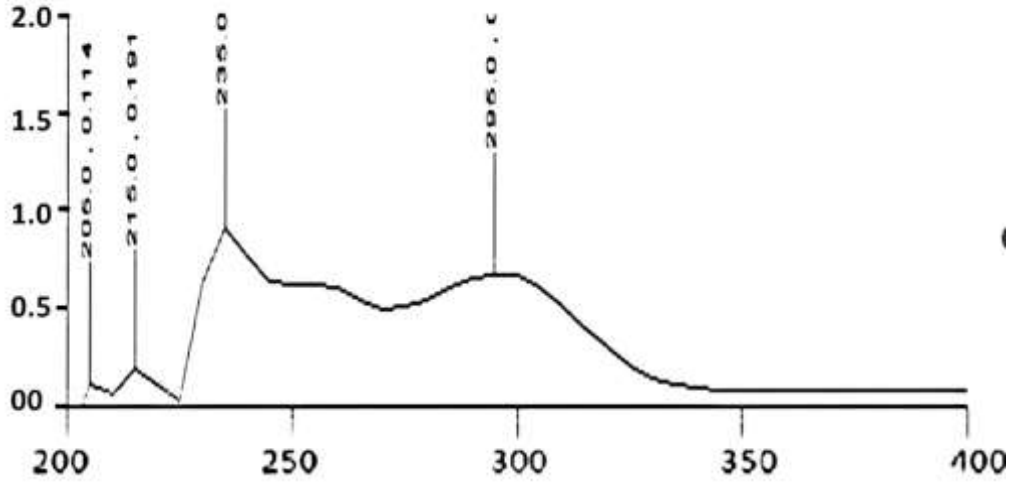

Fig 6. Scan of Telmisartan.

Preparation of calibration curve –

0.2, 0.4, 0.6, 0.8, 1.0, 1.2 and 1.4 ml of the solution from stock solution were pipette out into series of 10 ml measuring cylinder. The volume was made up to the marks with ethanol and 0.1 N $NaHCO_3$ solution (60:40) and mixed to obtain solutions in the concentration range of 0.2, 0.4, 0.6, 0.8, 1.0, 1.2 and 1.4 ug/ml of the drug.

Concentration(ug/ml)	Absorbance
0.2	0.223
0.4	0.322
0.6	0.443
0.8	0.549
1.0	0.688
1.2	0.827
1.4	0.921

TABLE 1. ABSORBANCE OF DRUG AT DIFFERENT CONCENTRATION.

The absorbance of these resultant solution was measured at 295 nm against ethanol and 0.1 N sodium carbonate solution (60:40) as blank and the graph was plotted between absorbance obtained and the concentration of the solutions. The beer's lamberts law obeyed in concentration range of 0.2 t0 1.4 ug/ml at 295 nm, results were shown in Fig.7[8,9]

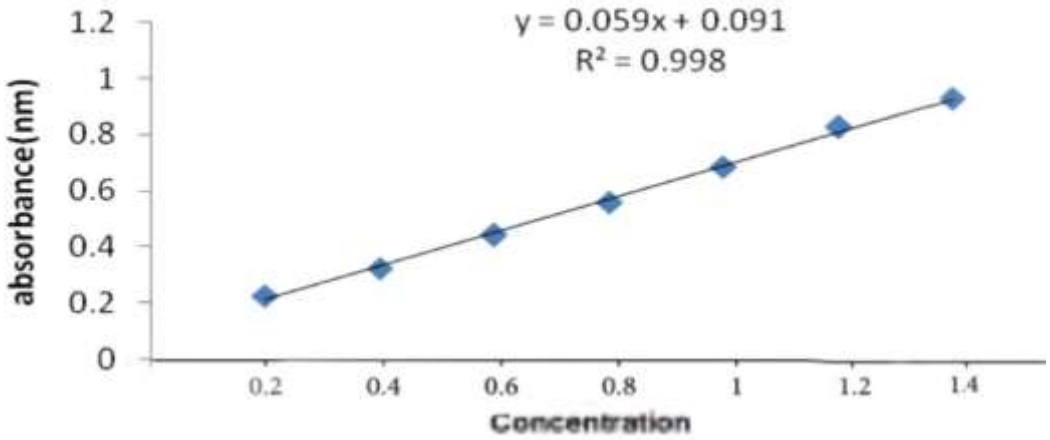

Fig. 7 Calibration curve of Telmisartan at 295 nm

 # FORMULATION OF TELMISARTAN MICROSPHERE BY IONOTROPIC GELATION METHOD –

The microsphere was prepared by using the ingredient like, Drug, Sodium alginate and polymer like Chitosan and Carbopol and sodium chloride used for curing process. All the material which are used in the formulation are used in different quantities to make different formulation i.e., F1 to F6 as shown in Table. 2

(DRUG + SODIUM ALGINATE + POLYMER)

INGREDIENT	F1	F2	F3	F4	F5	F6
Telmisartan	500 mg	500 mg	500 mg	500 mg	500 mg	500 mg
Sodium alginate	1 g	1 g	1.5	1.5	2 g	2 g
Chitosan	0.5 g	-	0.5 g	-	0.5 g	-
Carbopol	-	0.5 g	-	0.5	-	0.5
Calcium chloride	8 %	8 %	8 %	8 %	8 %	8 %
Dist. water	QS.	QS.	QS.	QS.	QS.	QS.

TABLE.2 FORMULATION DESIGN OF MICROSHERE

FIG. 8 FORMULATED MICROSPHERE

 # EVALUATION OF PREPARED MICROSPHERE-

1) **Percent yield –** In the percentage yield of microsphere the obtained microsphere is dried throughout and accurately weighted and calculated as.

% yield = (mass of microsphere obtained /weight of drug and polymer) x 100

The production yield of microsphere prepared by the ionic gelation technique were found to be as follows [1,5].

FORMULATION	% YIELD
F1	36.60 ± 0.02
F2	38.30 ± 0.01
F3	46.52 ± 0.03
F4	48.52 ± 0.02
F5	46.38 ± 0.01
F6	48.12 ± 0.04

(n = 3)

TABLE.3 PERCENT YIELD OF THE MICROSPHERE

2) **Micromeritics properties of the prepared microsphere –**

The flow property of microspheres such as angle of repose, Car's index and Hausner's ratio are to be evaluated in the micromeritics properties.

a) **Angle of Repose** – The angle of repose should be calculated by conventional fixed funnel method. The free flowing powdered is poured from the funnel onto the paper funnel is adjusted in a such a way that the heap of the poured powder touches the funnel tip. The area of the powder that is fallen on the paper is circled and its diameter is noted and the angle of repose is calculated as-

The angle of repose (θ) = $Tan^{-1}(h/r)$

Were,

θ = Angle of repose in degree
h = Height of the heap
r = Radius of the base

the angle of repose of all formulations shows excellent flow property ranged from 17.02 to 22.30

b) **Car's Index** – It is the measurement of flow property and is obtained from the bulk volume and tapped volume.

Car's compressibility index = (Vb – Vt)/ Vb x 100

Were,

Vb = Bulk Volume

Vt = Tapped Volume

The cars index of all formulation exhibited excellent flow properties and ranged from 9.62 to 14.60

c) **Hausner's ratio** – The Hauser's ratio is a number that is corelated to flowability of a powder or granular material and it can be calculated as-

Hausner's ratio = Vt / Vb

Were,

Vt = Volume tapped

Vb = Volume bulked

Hausner's ratio of all the formulated microsphere exhibited good properties which is ranged from 1.01 to 1.3 [1,5]

FORMULATION	ANGLE OF REPOSE	CARS INDEX	HAUSNERS RATIO
F1	17.80 ± 0.03	11.85 ± 0.01	1.1 ± 0.02
F2	17.02 ± 0.01	11.98 ± 0.03	1.02 ± 0.04
F3	21.30 ± 0.03	9.62 ± 0.04	1.04 ± 0.01
F4	17.20 ± 0.02	14.60 ± 0.02	1.02 ± 0.03
F5	19.02 ± 0.04	12.20 ± 0.05	1.01 ± 0.05
F6	21.84 ± 0.02	11.46 ± 0.03	1.3 ± 0.03

(n = 3)

TABLE. 4 MICROMERITICS PROPERTIES OF MICROSPHERE

3) Size distribution of microsphere -

The size distribution in terms pf the average diameter of the microsphere was determined by an optical microscopy method. A compound microscope fitted with a calibrated ocular micrometer and stage micrometer was used to count at least 50 microspheres. The mean at the particle was taken into account. The microspheres were uniform in size in each formulation and the mean size ranged from 184.5 ± 0.01 to 1002.5 ± 0.02 um which was in the arbitrary particle size range of 10 – 1000 um. The particle size range are shown in Table 5.[5]

FORMULATION	PARTICLE SIZE (um)
F1	622 ± 0.02
F2	184.5 ± 0.04
F3	428.4 ± 0.01
F4	580 ± 0.05
F5	648.5 ± 0.02
F6	1002.5 ± 0.03

(n = 3)

TABLE. 5 PARTICLE SIZE DISTRIBUTION TABLE

4) Percentage moisture content-

The percent moisture content study was carried out for a period of 24 h. The percentage of moisture loss was found to be in the range of 5.14 to 10.22 % for the formulation F1 to F6 as shown in the Table 6. During this drying process percent moisture loss increases with increase in time. [5]

FORMULATION	% MOISTURE LOSS					
	1hr	2hr	3hr	6hr	12hr	24hr
F1	4.5	5.3	5.8	5.14	8.3	9.2
F2	4.09	4.53	5.20	5.90	5.97	6.13
F3	4.16	5.4	5.9	6.3	8.4	9.6
F4	4.14	4.67	4.80	5.04	5.10	5.14
F5	4.92	5.30	6.78	7.54	8.9	10.22
F6	4.32	4.80	5.07	5.30	5.56	5.91

(n=3) TABLE 6. PERCENTAGE OF MOISTURE LOSSES OF MICROSPHERE

5) Drug content and entrapment efficacy –

The required amount of the prepared microsphere is weighted accurately and crushed into powder using a mortar and pestle. This powder is dissolve in 100 ml of water and kept aside for 12 hours. The next day supernatant is collected and filtered and finally analyses [1]. The drug content and entrapment efficacy of all formulation have been summarized in Table 7 and 8. The drug content range from 58.87 to 93.86 and entrapment range from 55.48 to 68.82 respectively [5,10].

FORMULATION	THEORETICAL DRUG CONTENT (Mg)	PRACTICLE DRUG CONTENT (Mg)
F1	100	58.87 ± 0.03
F2	100	62.98 ± 0.01
F3	100	68.38 ± 0.04
F4	100	79.22 ± 0.02
F5	100	82.91 ± 0.05
F6	100	93.86 ± 0.01

(n = 3) TABLE. 7 DRUG CONTENT OF MICROSPHERE

% Entrapment efficacy = (Actual Drug Content / Drug Content)

FORMULATION	ENTRAPMENT EFFICACY (%)
F1	59.68 ± 0.04
F2	68.82 ± 0.02
F3	55.48 ± 0.01
F4	64.24 ± 0.03
F5	67.45 ± 0.02
F6	63.79 ± 0.05

(n = 3)

TABLE. 8 ENTRAPMENT EFFICACY OF MICROSPHERE

6) Loose surface crystal study –

The loose surface crystal studies were performed to estimate the excess amount of drug attached to the surface of microsphere after a successful drug entrapment. This study was executed with all the formulation and the result are showed in Table 9. It was found in the range of 34.18 to 44.94 for formulation F1 to F6 which is the attribute to the initial burst of expelled medication from the sphere surface [5,10].

FORMULATION	LOOSE SURFACE CRYSTAL
F1	44.94 ± 0.01
F2	43.28 ± 0.04
F3	38.86 ± 0.03
F4	40.92 ± 0.05
F5	35.82 ± 0.02
F6	34.18 ± 0.04

(n = 3)

TABLE. 9 LOOSE SURFACE CRYSTAL STUDY OF MICROSPHERES

7) In vitro wash off test –

The adhesion time of microsphere followed the rank order F4 > F6 > F3 > F2 > F5 > F1. Result indicated that the viscosity of the polymer was strongly associated with the mucoadhesive property. The microsphere consisting of sodium alginate in combination with various mucoadhesive polymers exhibited good property as observed in the invitro wash off test [5,11].

FORMULATION	% MICROSPHERE ADHERING TO TISSUE AT VARIOUS TIME INTERVAL						
	0.5 hr.	1 hr.	2 hr.	3 hr.	4 hr.	5 hr.	6 hr.
F1	81	77	66	63	37	16	-
F2	85	79	81	65	43	20	18
F3	86	88	82	70	43	24	20
F4	97	91	83	72	51	32	28
F5	81	72	61	58	43	21	16
F6	88	80	74	67	41	27	22

(n = 3)

TABLE. 10 IN VITRO WASH OFF TEST OF MICROSPHERE IN PHOSPHASTE BUFFER PH 6.8

8) In vitro drug release study-

The in-vitro drug release studies of Telmisartan were initially carried out in phosphate buffer pH 6.8 for 22 hrs. Sodium alginate-based microspheres not significantly retarded the drug released at the examined time points throughout up to 24 hrs. The release of Telmisartan was mainly driven by the permeation of the drug through the hydrophobic polymer membrane. All these formulations show an initial burst effect which was due to the presence of drug particles on the surface of the microspheres as also inferred from loose surface crystal study. Sodium alginate is widely regarded as a sustained-release matrix because of its properties of water-insoluble and low permeability. Its effect on drug release could be influenced by various grades of Carbopol, and chitosan as a polymer, which forms hydrophilic passages inside the microspheres which helps the drug to diffuse out easily as compared to other mucoadhesive polymers.

From the in vitro dissolution data, It is seen that after 24 hr. study, formulation F4 showed better drug release retardation as compared based formulation shows less to other formulations. In the case of F4 might be 94% it's swelling as well as excellent mucoadhesion properties. The viscosity of the mucoadhesive polymer has the main role in both bioadhesion and sustained action[5].

Time (hr)	Formulation						
	Pure drug	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0	0
0.5	50.46 ± 0.02	20.80 ± 0.04	30.47 ± 0.01	5.76 ± 0.03	4.47 ± 0.02	7.14 ± 0.01	5.90 ± 0.05
1	53.20 ± 0.04	25.17 ± 0.02	36.20 ± 0.03	8.66 ± 0.05	6.70 ± 0.06	9.80 ± 0.03	8.87 ± 0.01
2	56.69 ± 0.01	39.25 ± 0.05	43.56 ± 0.02	15.30 ± 0.02	23.65 ± 0.04	16.48 ± 0.04	13.45 ± 0.04
4	70.34 ± 0.02	54.76 ± 0.01	56.88 ± 0.05	48.78 ± 0.04	38.88 ± 0.01	38.12 ± 0.01	33.90 ± 0.02
6	88.60 ± 0.03	64.23 ± 0.03	71.35 ± 0.02	65.44 ± 0.03	45.65 ± 0.04	52.30 ± 0.02	48.30 ± 0.06
8	99.46 ± 0.05	78.46 ± 0.06	80.40 ± 0.01	79.83 ± 0.01	55.60 ± 0.02	64.70 ± 0.05	59.94 ± 0.02
10		88.90 ± 0.02	90.33 ± 0.04	84.40 ± 0.05	71.80 ± 0.02	78.65 ± 0.06	76.20 ± 0.04
12		92.87 ± 0.04	98.76 ± 0.02	91.12 ± 0.06	82.20 ± 0.01	83.17 ± 0.03	78.88 ± 0.03
14		98.37 ± 0.03	99.49 ± 0.01	96.20 ± 0.02	86.47 ± 0.03	91.30 ± 0.01	88.70 ± 0.01
18				99.47 ± 0.03	89.18 ± 0.04	99.93 ± 0.02	95.57 ± 0.03
22					95.47 ± 0.02		99.67 ± 0.04
24					99.91 ± 0.01		

(n=3)

TABLE. 11 DRUG IS OF FORMULATION F1 TO F6

9) Scanning electron microscopy-

The scanning electron microscopy (SEM) is used to observed the shape and surface morphology of optimized chitosan based mucoadhesive microspheres. SEM study revealed that the microspheres were spherical in shape with rough outer surface. Some drug particles may be deposited on the outer surface of the microspheres.[2]

The size of the microspheres increased with increase in the alginate concentration which may be due to the increase in viscosity, resulting in increase in droplet size during addition of the polymer dispersion to the harvesting medium. The SEM of prepared microspheres (F1 and F4) is shown in Figure 9 and 10. Formation of cracks on the surface of the microspheres were observed which may be due to the penetration of the dissolution medium into the microspheres and the sub-sequent dissolution of the drug and hence its diffusion through the polymer matrix.[12]

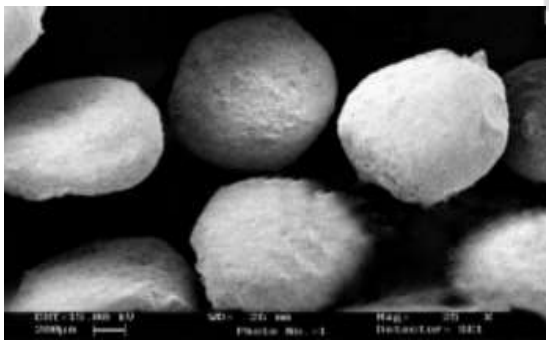

Figure. 9 SEM scanning of F1

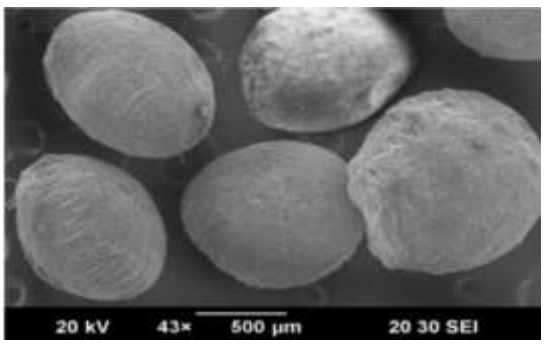

Figure. 10 SEM Scanning of F4

CONCLUSION-

Telmisartan loaded microsphere were successfully prepared by ionic gelation method for the sustained or controlled drug delivery. By evaluating all the parameter of all formulation F4 showed best drug release retardation as compared to other formulation. The drug release of F4 formulation is 99.91 % at 24 hrs., because its swelling property and mucoadhesive properties. From the above research we concluded that Telmisartan is suitable drug to formulate a mucoadhesive drug delivery system (microsphere) for better treatment and result of hypertension rather than another delivery system.

REFERENCE –

1. R. Prasantha, B. Haarika, S. Selvamuthukumar; Gastro retentive microspheres-drugs for Parkinson's disease; Journal of Drug and Alcohol Research; Vol-10 (2010); Page 1-7.

2. Priya P. Mane Deshmukh, Archana. N. Barhate; formulation and evaluation of microsphere of Glibenclamide by ionotropic gelation method; Indo American Journal of Pharmaceutical Research ;7(09) 2017.

3. Maya Sharma, Choudhury PK, Suresh Kumar Dev; Formulation and evaluation pf alginate chitosan microspheres of glipizide by ionic gelation method; Asian Journal of Pharmaceutical and Clinical Research; Vol 10(7),2017.

4. M., Sowjanya Battu, K. Jothshna Devi, C. Madhusudhana Chetty, M. Alagusundaram and K. Malikarjuna Rao; Purushothaman Formulation and characterization of ofloxacin microsphere prepared by ionotropic gelation method; Research Journal of Pharmacy and Technology; 3(4)2010.

5. A. V. S Hima Bindu, MD. Mehrej. K. padmalatha; Formulation design and evaluation of telmisartan mucoadhesive microspheres; International Journal of Pharmacy and Pharmaceutical Research; Vol 19(3), oct 2010.

6. Prasanth V.V, Moy A C, Mathew M, Mathapan R; Microspheres-An Overview, International Journal Research in Pharmaceutical Biomedical Science; 2011, 2(2).

7. Punitha S, Girish Y; Polymers in mucoadhesive buccal drug delivery system, International Journal Research in Pharmaceutical Science 2010, 1(2): 170-186.

8. Niranjan D. Chivate, Siddharth M. Patil, Jagdish K. Saboji, Anuradha N. Chivate; Development of UV spectrophotometric method for estimation and validation of Telmisartanas a pure API; Journal of Pharmacy Research; vol 5(6),2012.

9. Khushboo Rawat, Praveen Kumar, and Meenu Chaudhary; Validated method development and validation for estimation of telmisartan as API and in Pharmaceutical dosage form by UV spectroscopy; Research Journal of pharmaceutical, Biological and chemical Science; vol 5(4) 2014.

10. Gupta S, Singh RP, Sharma R, Kalyanwat R, Lokwani P; Osmotic Pumps: Review, Pharmacie Globale (IJCP) 2011, 6(1): 212-221.

11. Muthukumaran M, Dhachinamoorthi D, Chandra Sekhar KB, Sriram N; A Review on Polymers Used in Mucoadhesive Drug Delivery System, International Journal of Pharmacy & Indian Research. 2011, 1(2): 123-127.

12. Akanksha Garud · Navneet Garud; Formulation of mucoadhesive microspheres of rosiglitazone maleate and its in vitro evaluation using ionotropic gelation technique; Ars Pharmaceutica 2015; 56(2): 101-107