INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES

IMPACT FACTOR 4.018***
ICV 6.16***

| Pharmaceutical Sciences |

Research   Article……!!!

FORMULATION AND EVALUATION OF GASTRORETENTIVE MICROSPHERES OF AZILSARTAN

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ABSTRACT

By the use of solvent evaporation process and ionic gelation technique, an attempt has been made to produce GRDDS by using Ethyl cellulose and Hydroxypropyl methylcellulose as release retarded materials in this work. Three different concentrations of polymer were used to produce microspheres, as well as blends of both polymers. Infrared Spectroscopy, Differential Scanning Calorimetry, X-ray Diffractometry analysis were used to investigate the drug-polymer compatibility. The polymer and drug were compatible with each other. The microspheres' drug content, percentage yield, particle size analysis, surface morphology, and percent buoyancy were all investigated. The efficiency of entrapment improved as the concentration of ethyl cellulose was enhanced. The effect of polymer concentration on Azilsartan release from microspheres in vitro was also investigated. The rate of drug release from the microspheres is drastically reduced when the polymer concentration is increased. It is observed that the microspheres containing both the polymer i.e., Ethyl cellulose and Hydroxypropyl methylcellulose showed the best results.

1. INTRODUCTION:

Because of its convenience of administration, cost effective therapy, patient compliance, and flexibility of formulation, oral drug delivery is by far the most used modality of drug delivery. The stomach emptying time has some restrictions in oral sustained drug delivery formulations. Due to unpredictable and too speedy gastrointestinal transit, uncomplete drug release from the dosage form into the absorption window could result in diminished efficacy of the provided dose. According to recent studies and patent filings, there is an increasing interest in innovative dosage forms that stay in the stomach for a lengthy and predictable period [1].

The noesis to extend and manage the gastric emptying time is a critical asset for dosage forms that stay in the stomach for longer periods than conventional dosage forms. Developing controlled release systems for improved absorption and bioavailability is fraught with difficulties. One of these difficulties is containing the dosage form at the wanted area of the gastrointestinal system. Absorption of drug from the gastrointestinal tract is a complex process regulated by several factors. The amount of drug absorption in the gastrointestinal system is related to the amount of time the drug spends in contact with the small intestine mucosa, according to conventional wisdom. The small intestinal transit time is an important factor for drugs which are only partially absorbed [2].

Gastroretentive systems can stay in the stomach for several hours, considerably increasing the time drugs spend there. Prolonged stomach retention boost bioavailability, decreases drug waste, and increases solubility for drugs that are partially soluble at high pH. It can also carry drugs to the stomach and the proximal small intestine. Gastro retention makes it easier to design new medications with novel therapeutic alternatives and considerable patient benefits [3].

Controlling the insertion of a drug delivery system in a specific area of the GIT, i.e., gastroretention, as a technique of addressing local targeting in the stomach region, has several benefits, including [4,5].

- The longer the stomach residence time, the better the drug absorption.
- Enhancement of bioavailability.
- The dosing frequency is being reduced.
- Minimizing adverse effects in other parts of the body.
- Overall, cutting in the health care cost.
- Gastro retentive drug delivery system (GRDDS) has been advantageous especially for drugs.
- Drugs that have a local effect on the stomach.
- Which has a stomach absorption window.
- Drugs that are unstable in the intestine or colon.

- Drugs having poor solubility at high pH values [6]

In this study we have taken Azilsartan 2-[4-[4-methyl-6-(1-methyl-] Benzimidazole 1'-yl) methyl]-[1,1'-biphenyl]-2-carboxylic acid is a white, amorphous powder. Azilsartan is a non-peptide AIIRA that binds specifically to AT1 receptors, limiting angiotensin II's physiological effects. The Renin-Angiotensin system controls blood pressure, fluid balance, and electrolyte balance. Renin is a kidney enzyme that transforms the inactive plasma protein angiotensinogen into angiotensin I (Ang I). The angiotensin-converting enzyme (ACE) converts Ang I to Ang II, which subsequently binds to AT-receptors in the plasma. Increased cardiac contractility, salt reabsorption, and vasoconstriction are all caused by the AT1 receptor, resulting in elevated blood pressure. ARBs reduce blood pressure by blocking AT1 receptors [7,8,9].

The objectives of proposed research work are to formulate and evaluate the regiospecific floating microspheres of antihypertensive drug and study the effect of different polymers and different concentration of individual polymers on the floating behavior of microspheres. To enhance patient compliance and minimize dosing frequency.

2. Materials and methods:

2.1. Reagents and Chemicals:

Watson pharma Ltd, Mumbai, provided Azilsartan as a gift sample; Rajesh Chemicals, Mumbai, provided hydroxypropyl methylcellulose K100M; and Loba Chemical, Mumbai, provided Ethyl-cellulose. Tween 80, Dichloromethane, Methanol, Acetone, and Dichloromethane were obtained from Research Lab, Islampu.

2.2. Pre-formulation study

The assessment of the drug's physical and chemical properties is known as a pre-formulation study. It's the initial step toward logical dosage form development.

1.1.1. Identification of the drug by FTIR

Infrared spectra of the pure drug were recorded by using Fourier Transform Infrared Spectrophotometer (Alpha E Bruker). A small number of samples was taken and mixed with KBr, and disc was formed and directly put on the IR platform. Then spectra of dried mixtures of pure drug and polymer were recorded for compatibility study Scanning was done from 2000 to 400 cm-1[10].

1.1.2. Solubility profile

Understanding a drug's solubility in the aqueous environment was critical since therapeutic responses require some aqueous solubility. To identify an appropriate solvent solution to dissolve the drug and various excipients for the formulation, a preformulation solubility analysis was performed. Also, the solubility of the drugs in the dissolution medium which was to be used was tested [11]. According to the solubility

characteristics of drugs, 0.1 N Hydrochloric acid was selected as a solvent for analysis. Determination of λ max. Since most drugs are aromatic or contain double bonds, they absorb light in the ultraviolet region of 400-200 nm. Using a double beam UV spectrophotometer, a solution containing 10 g/ml of Azilsartan was prepared in 0.1 N Hydrochloric acid and scanned in the UV range of 400-200 nm against 0.1 N Hydrochloric acid as a blank. The maximum obtained in the graph was considered as λmax for the pure drug[12] (Figure No.1).
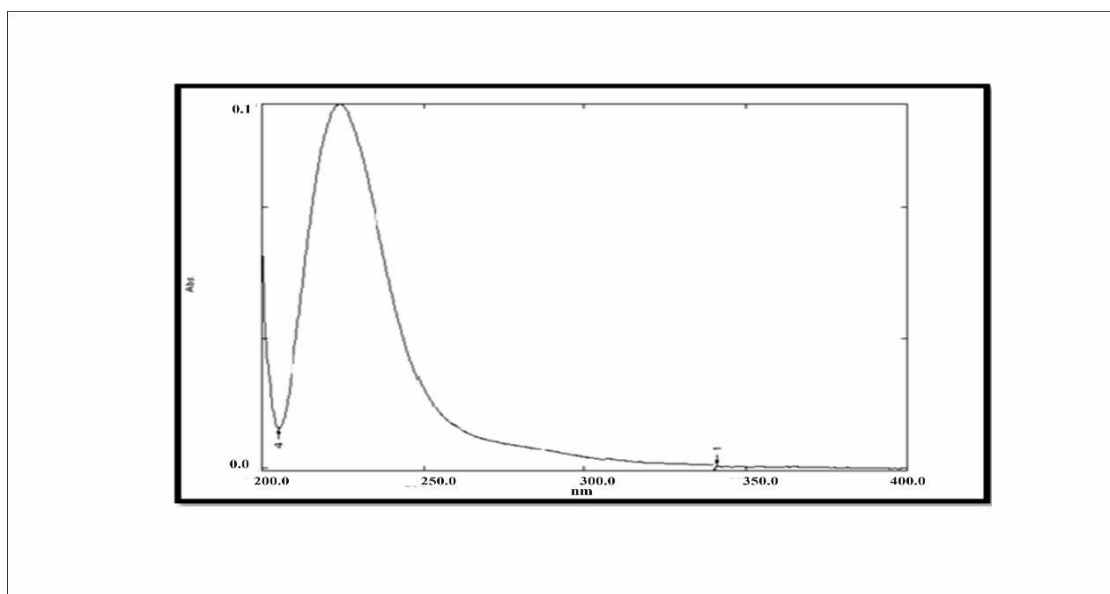

Figure no. 1: Absorbance spectrum of Azilsartan.

1.1.3. Standard calibration curve for Azilsartan

Accurately weighed the quantity of 100 mg of the drug transferred to the 100 ml volumetric flask containing 0.1 N Hydrochloric acid, sonicated for 10 min to dissolve it completely. The Hydrochloric acid is added to the flask to make up the volume. 10 ml of the above solution is withdrawn and diluted to 100 ml. From the above stock solution aliquots of 0.1,0.2, 0.3,0.4, and 0.5 were taken in a 10 ml volumetric flask and diluted with 0.1 N Hydrochloric acid; which gave the concentrations of 1-5 μg/ml. Using a UV spectrophotometer, absorbance values were measured against a blank at max 230 nm. And then plotted the graph of absorbance vs. Concentration [12,13].

1.2. Preparation of floating microspheres

Two approaches were used to make microspheres using Azilsartan as the core material:

i. Solvent evaporation method

ii. Ionic gelation method

1.2.1. Solvent evaporation method

Microspheres containing Azilsartan as core material prepared by taking drug and polymer in different proportions i.e., 1:1, 1:2,1:3. Drug and polymer were mixed in DCM: Methanol mixture (70:30). This solution was slowly introduced in the 70 ml of light liquid paraffin containing 1% tween 80. Over 2 hours,

the system was agitated at 1000 rpm with a propeller-type agitator, and the solvent was allowed to evaporate completely. The paraffin was then decanted out like a light liquid. Filtration and washing were used to separate the microspheres [14] (Table No. 1).

Table No. 1: Preparation batches by solvent evaporation technique: -

Batch code	Drug	EC	HPMC
E1(s)	250	250	
E(S)	250	500	
E3(S)	250	750	
HE1(S)	250	250	250
HE2(S)	250	250	500
HE3(S)	250	500	250
H(s)	250		250

1.2.2. Ionic gelation technique

The 1% sodium alginate solution was prepared in distilled water. Ethyl cellulose and Hydroxypropyl methyl cellulose were added to that stated amount of the drug. A 20gauge hypodermic needle was used to put the prepared -polymer solution into 100 ml of 1% w/v crosslinking agents, i.e., calcium chloride solution. The formed microspheres were kept in solution for 2 hrs.; to improve the mechanical strength of microspheres. Following that, these are filtered and rinsed with distilled water [15,16].

Nine formulations by each technique were prepared; formulations E1(s), E2(s), E3(s) were formulated and prepared with EC and Azilsartan in the ratio of 1:1, 1:2, 1:3. Same formulations were prepared by ionic gelation coded as E1(g), E2(g), E3(g). Similarly, Hydroxypropyl methyl cellulose microspheres were also prepared with a drug to polymer ratio of 1:1, 1:2, 1:3 coded as; H1(s), H2(s), H3(s), and H1(g), H2(g), H3(g). Another 6 batches were prepared by using a combination of Ethyl cellulose and Hydroxypropyl methyl cellulose polymer by using the drug: Ethyl cellulose: Hydroxypropyl methyl cellulose ratio as; 1:1:1, 1:1:2 and 1:2:1coded as HE1(s), HE2(s), HE3(s), HE1(g), HE2(g), HE3(g) (Table No. 2). All the batches prepared were taken further for evaluation Study.

Table No. 2: Preparation batches by ionic gelation technique: -

Batch code	Drug	EC	HPMC
E1 (g)	250	250	
E2(g)	250	500	
E3(g)	250	750	
H1(g)	250		250
H2(g)	250		500
H3(g)	250		750
HE1(g)	250	250	
HE2(g)	250	500	
HE3(g)	250	750	

1.3. Evaluation of floating microspheres

1.3.1. % Practical yield

The ready-to-use microspheres were collected and weighed. The total amount of nonvolatile chemicals in the formulation was divided by the measured weight [17,18,19]. The following formula was used to compute the percent yield:

% Practical yield = weight of microspheres /weight of drug + excipient × 100

1.3.2. Entrapment efficiency

50 mg microspheres were weighed and placed in a 50 ml 0.1 N Hydrochloric acid. Stirred at 50 rpm for 8 hrs. Then the solution was filtered with whattmann filter paper. Content of the filtrate assayed spectrophotometrically [20,21].

% Entrapment Efficiency = Actual drug loading (mg)/Theoretical drug loading (mg) × 100

1.3.3. Percent Buoyancy study

In 50 ml of 0.1 N Hydrochloric acid containing 0.2 % w/v tween 80, 50 mg of microspheres were put. A magnetic stirrer was used to stir the mixture at 100 RPM. The buoyant microsphere layer, as well as the particles in the sinking particulate layer, were pipetted and filtered after 8 hours. Desiccators were used to dry both types of particles.[20,21] Both microsphere fractions were weighed, and buoyancy was determined using the following formula:

% buoyancy = Qf (Qf + Qs) × 100

The weights of the floating and settled microspheres, respectively, are Qf and Qs.

1.3.4. Particle Size Analysis

Optical microscopy was used to determine the particle sizes of the microspheres. The stage micrometers were used to calibrate the eyepiece. The microspheres were mounted onto the slide and the sizes of hundred particles were counted in various areas focused [22,23].

1.3.5. Differential Scanning Calorimetry

Thermal analysis can be used to investigate any drug-polymer interaction. Using Mettler-Toledo DSC 821 equipment with an intracooler (Mettler- Toledo, Switzerland), thermograms of pure Azilsartan and microsphere batches were recorded. Aluminum pans were used to seal samples and heated at 10°C/min in a nitrogen environment with a flow rate of 10 ml/min between 30°C and 300°C[24].

1.3.6. X-ray Diffractometry (XRD)

X-ray diffraction patterns of pure drug, formulations were recorded using X-ray diffractometer (XRD-D2 Phaser, Bruker AXS analytical instrument Ltd, Germany) with a copper target, testing angle of $2\Theta = 10–90$ º, voltage 30 kV, current 10 mA [25,26].

2.4.6. Scanning electron microscopy (SEM)

Scanning electron microscopy was used to analyze the morphology and porous nature of micro-sponges. The SEM experiment was conducted with a JSM 6360 Jeol Ltd, Japan, running at 500-30kv [27,28].

1.4. In-vitro drug release study

The drug release from microspheres was monitored with a USP Paddle instrument at 37±0.5°C and 50 rpm with 900 ml of 0.1N Hydrochloric acid as the dissolution media. Every 1 hour, 5 ml of dissolving fluid was taken and diluted to 10 ml as needed. At λmax 230 nm, the sample was spectrophotometrically examined. An equal volume of new dissolution medium was replaced immediately after the test sample was discarded to maintain the sink condition [29].

Results and discussion

1.5. IR spectroscopy

The major peaks found in drug spectrums were likewise found in drugs with polymer spectrums, demonstrating that there was no incompatibility between the drug and the polymer, according to the IR spectrum figure and table (Table No. 3) (Figure no. 2, Figure no. 3, Figure no. 4).

Table No. 3: Interpretation of IR.

Wave No. (cm-1)	Functional Group	Azilsartan	Azilsartan + HPMC	Azilsartan + EC
2962- 2853	C – H Stretching	Present	Present	Present

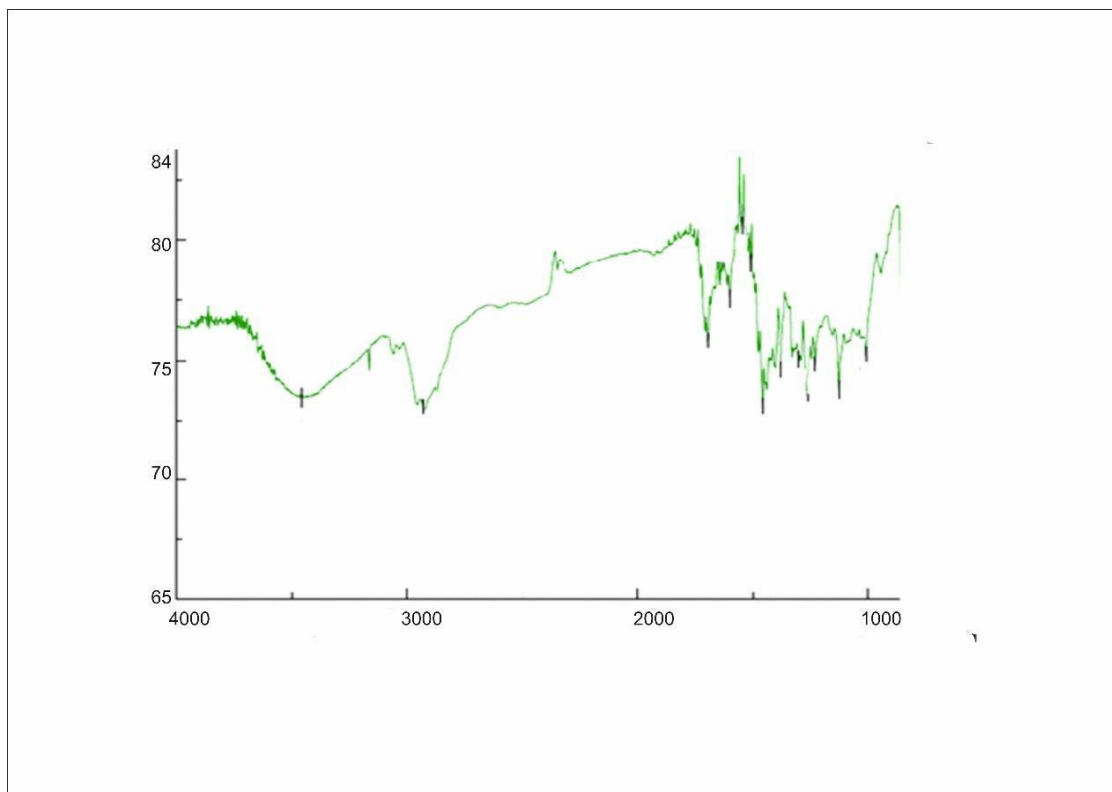| 1690 – 1660	Ketone (C= O)stretching	Present	Present	Present
1690- 1640	C = N stretching vibration	Present	Present	Present
1600- 1575	N – H bending	Present	Present	Present
1485 – 1445	C – H bending	Present	Present	Present
1340 – 1250	C – N stretching vibration	Present	Present	Present
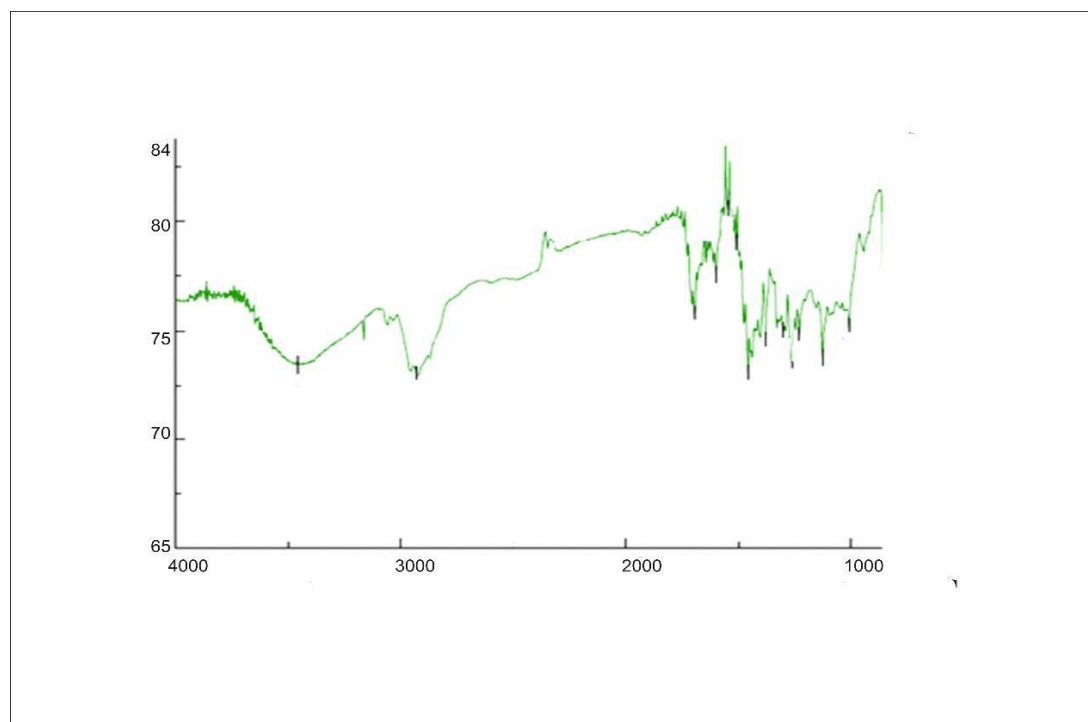
Figure No. 2: IR Spectrum of Azilsartan.

Figure No. 3: IR Spectrum of Azilsartan & HPMC.
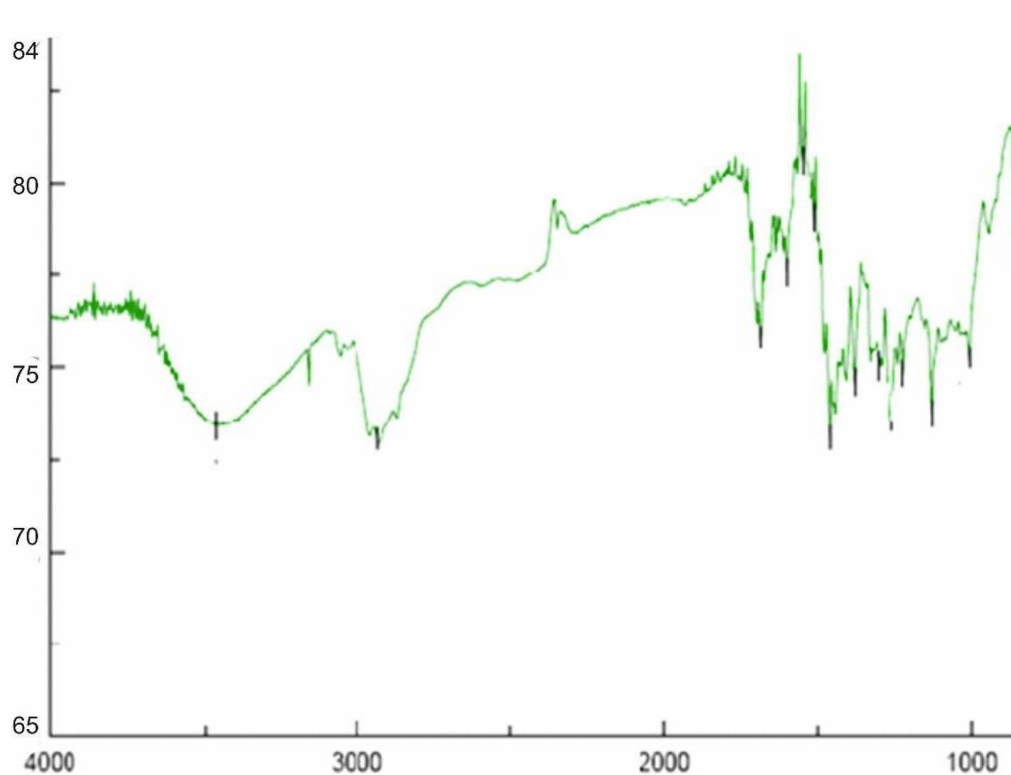

Figure no. 4: IR Spectrum of Azilsartan & Ethyl cellulose.

1.6. Evaluation of microspheres
1.6.1. Percent Practical Yield

All batches show more than 75% practical yield. The maximum yield was found to be 91% for Ethyl cellulose microspheres that were prepared by ionic gelation technique, 82 % for Hydroxypropyl methylcellulose microspheres. Ethyl cellulose with Hydroxypropyl methylcellulose microspheres gave 83% as the maximum yield. There is no satisfactory yield obtained by solvent evaporation technique for Hydroxypropyl methylcellulose microspheres. % Practical yield of all batches is shown in the following table (Table No. 4).

Table No. 4: Percentage practical yield

Sr. no.	Batch code	% yield
1	E1(s)	77.6
2	E2(s)	76.53
3	E3(s)	89.4
4	HE1(s)	83.33
5	HE2(s)	79.73
6	HE3(s)	81.86
7	H1(g)	82
8	H2(g)	70.22
9	H3(g)	78
10	HE1(g)	79.73
11	HE2(g)	82.40
12	HE3(g)	86
13	E1(g)	84.36
14	E2(g)	91.12
15	E3(g)	87.68
16	H(s)	NSY

1.6.2. Percent Entrapment efficiency

It has been found that as the polymer concentration rises, so does the percent entrapment. Formulation containing a higher concentration of EC prepared by solvent evaporation show better entrapment efficiency. Microspheres prepared by ionic gelation technique show less entrapment compared to those prepared by solvent evaporation technique (Table No. 5).

Table No. 7: Percentage entrapment efficiency

Sr. No.	Batch code	% Entrapment efficiency
1	ET1(s)	67.66%
2	ET2(s)	79%
3	ET3(s)	95 %
4	HET1(s)	59 %
5	HET2(s)	81 %
6	HET3(s)	41 %
7	HT1(g)	69%
8	HT2(g)	83 %
9	HT3(g)	82.66 %
10	HET1(g)	60 %
11	HET2(g)	58 %
12	HET3(g)	65 %
13	ET1(g)	44.43 %
14	ET2(g)	48.96%
15	ET3(g)	51 %

1.6.3. Particle size determination

The particle size of prepared microspheres was determined using optical microscopy, and a table was created to illustrate the average particle sizes of all batches of microspheres. The drug concentration and solvent volume were kept constant in all batches of microspheres. The particle sizes of floating microspheres were determined to be in the range of 65 to 90 μm when using the solvent evaporation technique, and 450 to 600 μm when using the ionic gelation technique (Table No. 6).

Table No. 6: Particle size in μm.

Sr. No.	Batch code	Particle size in μm.
1	ET1(s)	76.67
2	ET2(s)	81.97
3	ET3(s)	89.12
4	HET1(s)	70.35
5	HET2(s)	66.67
6	HET3(s)	73.53
7	ET1(g)	470
8	ET2(g)	540
9	ET2(g)	660
10	HT1(g)	619
11	HT2(g)	571
12	HT3(g)	520
13	HET1(g)	430
14	HET2(g)	613
15	HET3(g)	589

1.6.4. DSC Thermal analysis

DSC studies were used to observe drug-polymer compatibility and interactions; the following table shows the results (Figure No. 5, Figure No. 6, Figure No. 7) (Table No. 7).

Table No. 7: Various thermogram parameters

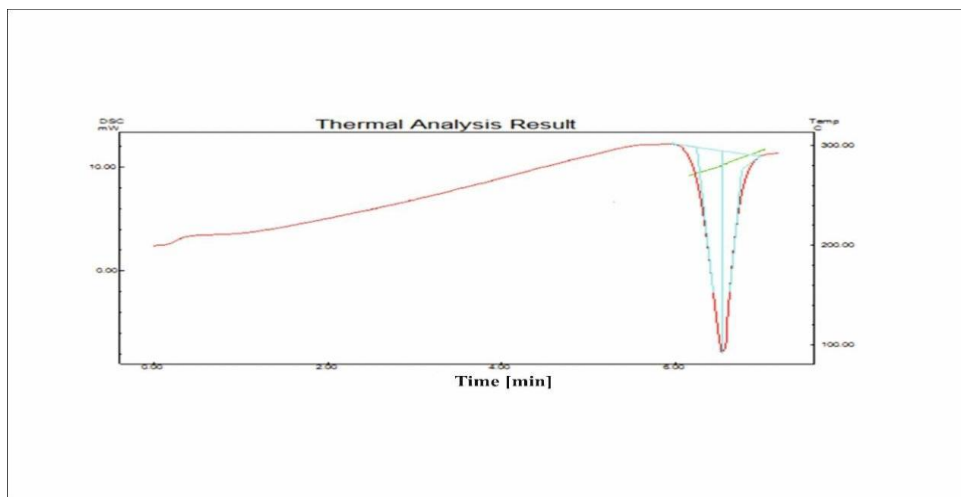| Sr. no.	DSC Thermogram	Onset temp(°C)	Peak temp(°C)	Endset temp(°C)
1	Azilsartan	263.04	280.40	287.70
2	Telmi + EC	264.20	272.06	280.99
3	Telmi +HPMC	264.20	272.06	280.99

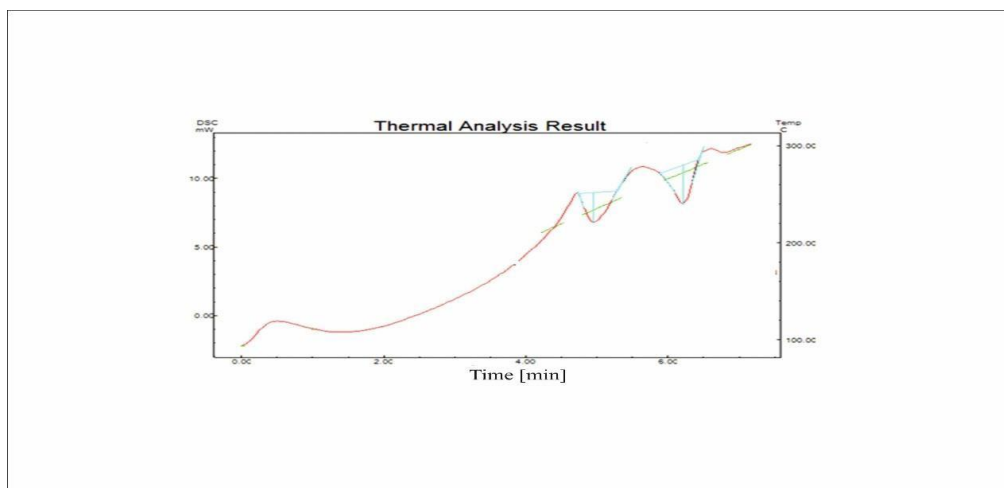**Figure No. 5:** DSC Thermogram of Azilsartan.

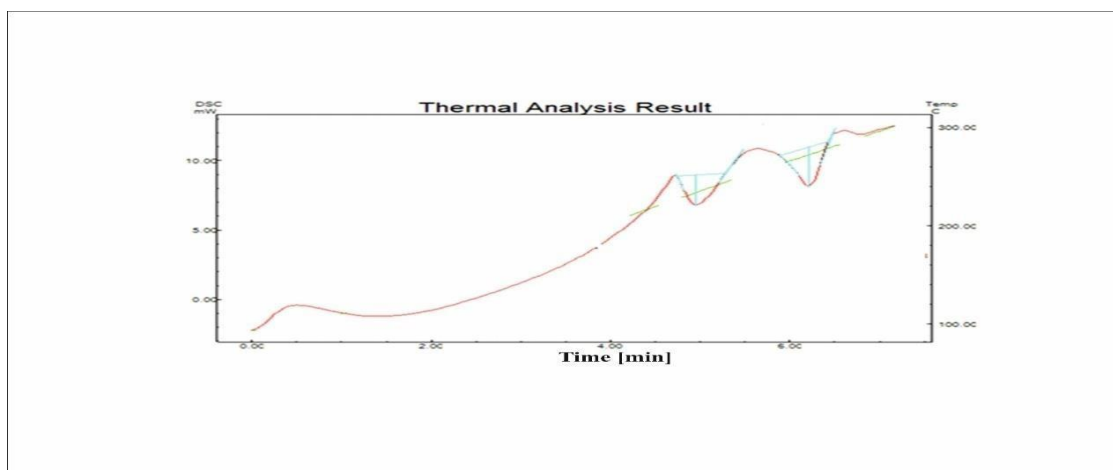**Figure No. 6:** DSC thermogram of Azilsartan and Ethylcellulose.

Figure No. 7: DSC Thermogram of Azilsartan and HPMC

When compared to the thermogram of pure drug, DSC thermogram revealed no significant differences in onset temperature, peak temperature, or endset temperature, as shown in Figures and Table. The drug and the polymers did not interact in any way.

1.6.5. X-ray diffraction spectroscopy

XRD study informs that the pure drug shows the highest peak intensities at 22.24, 22.26, 22.30; which indicates the drug is crystalline. The formulation shows a less intensive peak than the pure drug. The RDC value was determined to be 0.49, indicating that the drug has amorphized or reduced its crystallinity. It has long been known that converting a crystalline state to a partially amorphous state produces a high-energy state with a high disorder, which improves solubility and dissolution rate (Figure No. 8, Figure No. 9).
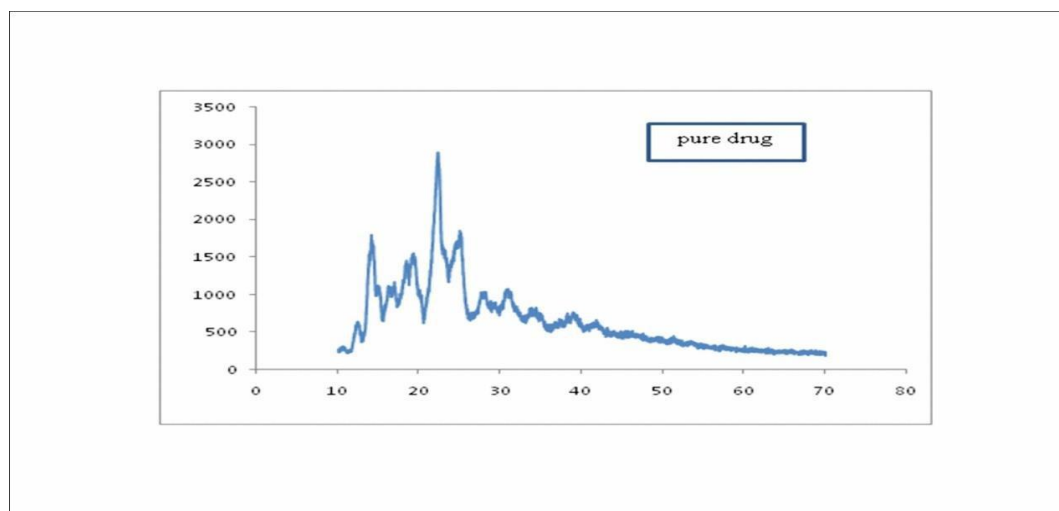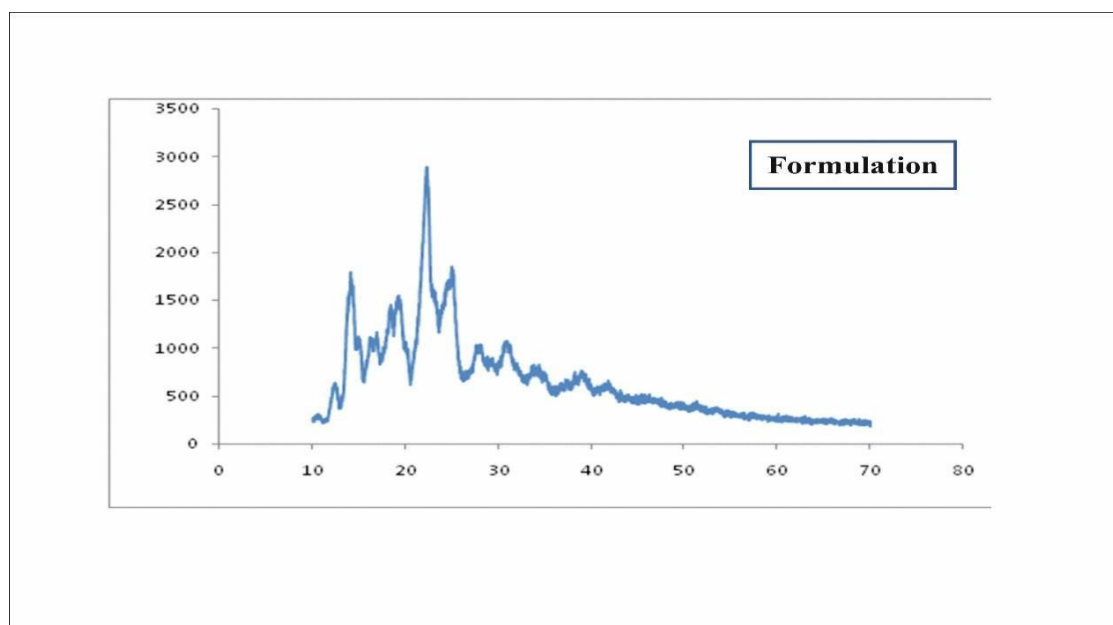

Figure No. 8: XRD of Azilsartan.

Figure No. 9: XRD of formulation.

1.6.6. Scanning Electron Microscopy

To study the surface morphology and structural properties of microspheres scanning electron microscopy was used. The microspheres were spherical with a rough, hollow surface and were mildly aggregated, as evidenced in SEM figure (Figure No. 10):

Pores were seen on the microscopic surface, indicating that the drug was leached during dissolution without gelation of the polymer matrix.
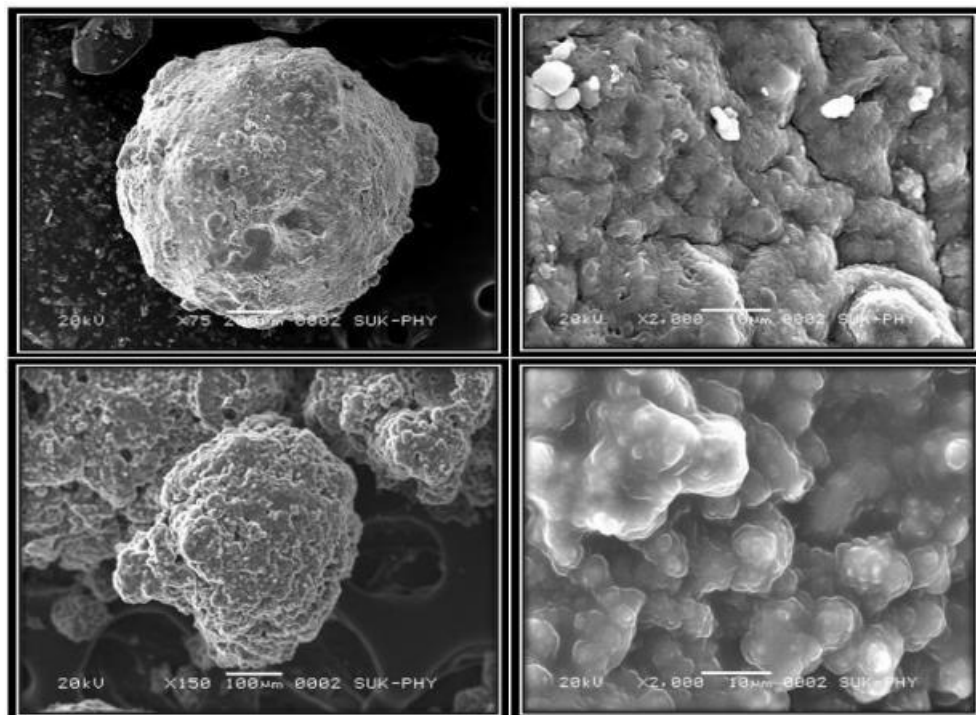

Figure No. 10: Scanning electron micrograph of HE(s) and HE(g) microspheres.

1.6.7. In-Vitro Buoyancy study

For more than 8 hours, all of the formulations floated on the surface of the dissolution media. The microspheres with lower densities had greater buoyancy and had to be kept for longer than 8 hours, which helped to improve drug bioavailability. The percentage buoyancy of the microspheres was shown in the table and diagram for floating microspheres shown in fig. The microspheres prepared by solvent evaporation technique; containing Ethyl cellulose and Hydroxypropyl methylcellulose show the highest percentage of buoyancy compared with that prepared by ionic gelation technique (Table No. 8), (Figure No. 11).

Table No 8: In vitro percentage buoyancy.

Sr. No.	Batch code	% Buoyancy
1	ET1(s)	77
2	ET2(s)	82
3	ET3(s)	84
4	HET1(s)	81
5	HET2(s)	78
6	HET3(s)	84
7	ET1(g)	63
8	ET2(g)	66
9	ET3(g)	72
10	HT1(g)	67
11	HT2(g)	69
12	HT3(g)	71
13	HET1(g)	64
14	HET2(g)	67
15	HET3(g)	72
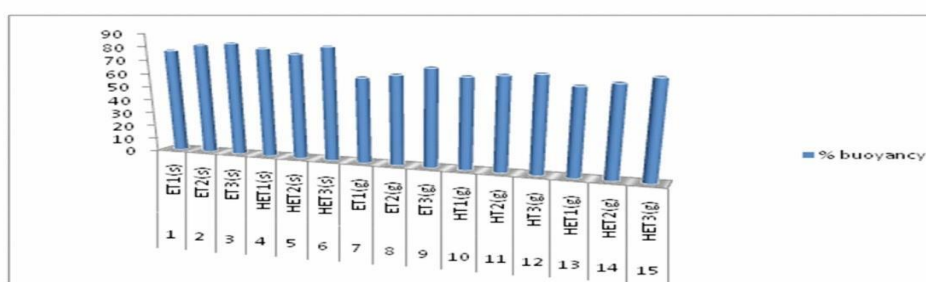
Figure No. 11: % Buoyancy of microspheres.

1.6.8. In-vitro dissolution studies

The in vitro dissolution studies were carried out in 0.1 N Hydrochloric acid for up to 8 hrs. The percentage of drug released up to 8 hours was found to be 81.18%, 69.65%, 67.09% for ET1(s) %, ET2(s) %, ET3(s) %

respectively. Similarly; the % drug release at 8 hours for HET1(s), HET2(s), HET3 (s) was found to be 88.48%, 93.47%, 89.69 % respectively. The dissolution of microspheres prepared by ionic gelation technique at 8 hours was found to be as; for HT1 (g), HT2 (g), HT3 (g) 84.46%, 80.05%, 79.31% respectively. The formulations ET1 (g), ET2 (g), ET3 (g) show 60.59%, 57.09%, 54.48% and that of HET1(g), HET2(g), HET3(g) 43.37%, 47.27% and 40.53% respectively. It was also observed that increasing the polymer concentration decreases the released rate of the drug (Table No. 9, Table No. 10, Table No. 11, Table No. 12, Table No. 13), (Figure No. 12, Figure No. 13, Figure No. 14, Figure No. 15, Figure No. 16).

Table No. 9: Dissolution profile of EC microspheres prepared by solvent evaporation technique.

Time in hours	E1(s)	E2(s)	E3(s)
1	20.38±1.1	21.53±0.21	39.49±0.25
2	26.92±0.61	45.90±0.42	41.03±0.24
3	30.28±0.25	49.23±0.25	44.65±0.66
4	32.83±.01	53.31±0.24	46.12±0.74
5	50.80±1.18	56.70±0.28	53.89±0.60
6	55.86±0.16	60.65±0.38	58.49±0.52
7	65.73±0.43	65.35±0.08	63.85±0.60
8	81.18±0.53	69.65±0.14	67.09±0.32

Table No. 10: Dissolution profile of EC+HPMC microspheres prepared by solvent evaporation technique.

Time in Hours	HE1(s)	HE2(s)	HE3(s)
1	27.63±0.07	16.70±0.26	20.16±0.50
2	53.11±0.09	23.89±0.16	39.17±0.14
3	56.34±0.38	42.10±0.15	46.39±0.09
4	59.70±0.11	50.56±0.69	54.89±0.26
5	63.09±0.28	61.58±0.04	66.75±0.0140
6	68.51±0.12	67.15±0.12	74.09±0.02
7	77.99±0.12	89.30±0.25	80.67±0.113
8	88.48±0.52	93.47±0.226	89.69±0.09

**Table No. 11:** Dissolution profile of HPMC microspheres prepared by ionic gelation technique.

Time in hours	HT1	HT2	HT3
1	29.06±0.34	15.69±0.42	21.49±0.73
2	38.34±0.42	26.61±0.44	25.03±0.33
3	42.57±0.37	33.77±0.57	36±0.47
4	54.71±0.63	42.98±0.66	54.76±0.64
5	64.13±0.46	52.53±0.38	61.32±0.32
6	70±0.53	61.74±0.75	64.27±0.44
7	79.54±0.67	72.65±0.54	68.90±0.53
8	84.46±0.53	80.05±0.33	79.31±0.76

Table No. 12: Dissolution Profile of EC microspheres prepared by ionic gelation technique.

Time in hours	ET1(g)	ET2(g)	ET3(g)
1	12.32±0.13	20.76±0.62	20.19±0.32
2	28.27±0.28	34.35±0.48	27.47±0.56
3	34.65±0.43	38.77±0.53	35.48±0.16
4	40.44±056	39.61±0.71	41.02±0.54
5	50.11±0.32	46.39±0.26	46.20±0.32
6	52.94±0.19	54.16±0.65	52.87±0.66
7	57.26±0.32	56.97±0.43	54.48±0.44
8	60.59±0.46	57.02±0.24	54.48±0.37

Table No. 13: Dissolution profile of EC+HPMC microspheres prepared by ionic gelation technique.

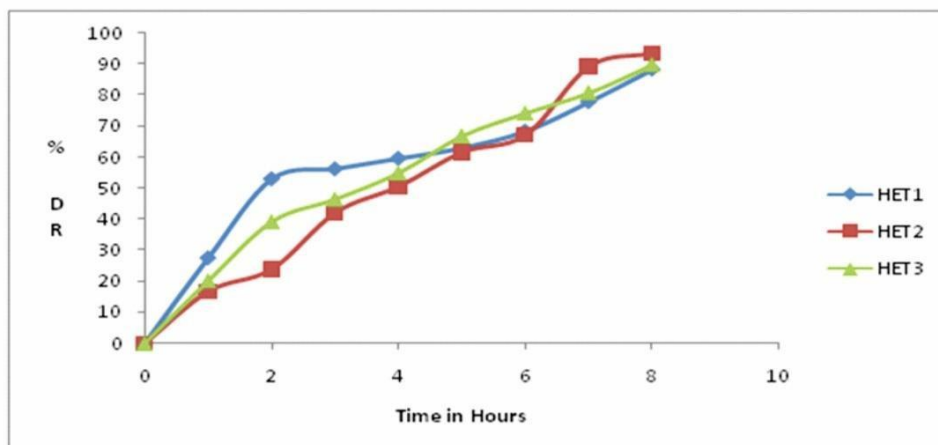| Time in hours	HET1(g)	HET2(g)	HET3(g)
1	15.77±0.24	13.03±0.73	11.49±0.28
2	19.94±0.52	18.15±0.51	16.34±0.37
3	23.50±0.32	21.99±0.47	22.12±0.46
4	27.68±0.63	26.71±0.39	29.86±0.75
5	30.85±0.45	36.63±0.56	30.58±0.55
6	36.51±0.44	38.87±0.66	32.97±0.58
7	39.04±0.56	41.59±0.53	34.68±0.65
8	43.37±0.65	47.27±0.37	40.53±0.47
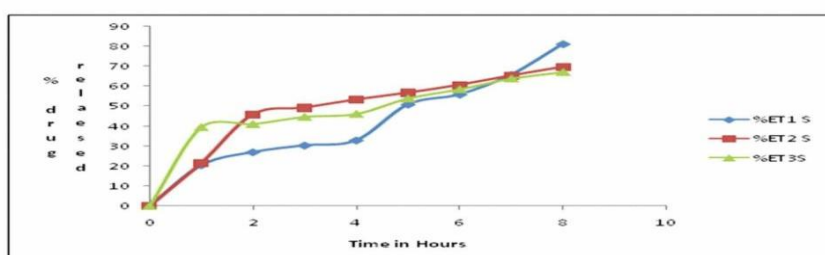
Figure No. 12: % DR of E1(s) – E3(s)

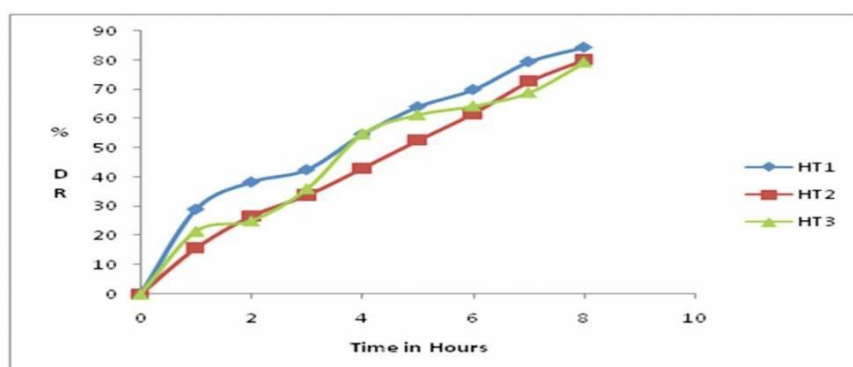**Figure No. 13:** % Drug release of HE1(s) – HE3(s)

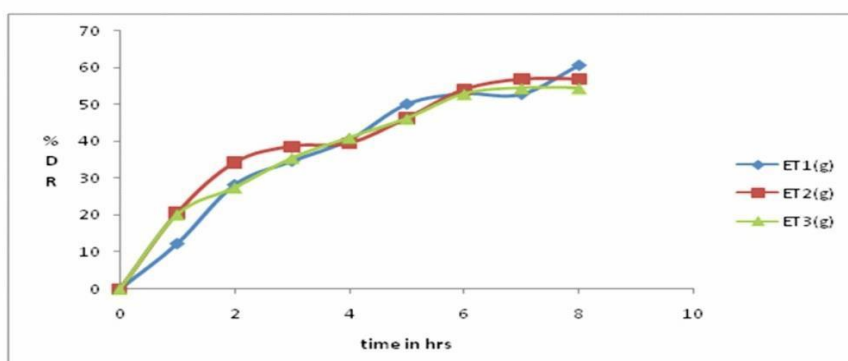**Figure No. 14:** % Drug release of H1(g) – H3(g) by Ionic gelation technique.

Figure No. 15: % DR of EC microspheres prepared by Ionic gelation technique.
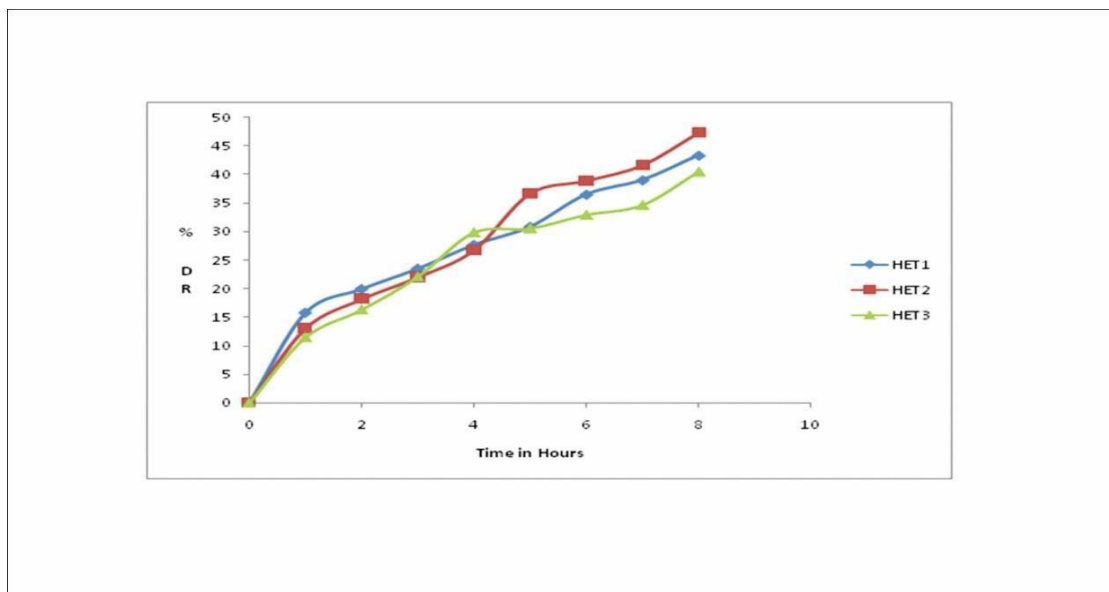
Figure No. 16: % DR of EC +HPMC microspheres prepared by Ionic gelation technique.

2. Conclusion

The current study was a significant attempt to formulate Azilsartan floating microspheres for oral administration to enhance oral bioavailability and provide prolonged release. Azilsartan is a poorly soluble drug that is having solubility only in stomach pH that is at pH 1.2. Hence, it is a good candidate for a floating drug delivery system. The melting point and FTIR spectroscopy were used to identify the drug. The appearance, solubility study, and other physicochemical properties were examined. The drug's analytical profile was evaluated to determine the absorption maximum, developing a standard curve, and determining the percentage purity of the drug. DSC and XRD studies were used to determine the drug and polymer mixture's compatibility. There was no interaction between the drug and the polymer, according to the findings. To produce floating microspheres, researchers used solvent evaporation and the ionic gelation method with ethyl cellulose and Hydroxypropyl methylcellulose. All formulations were examined for percent yield, entrapment efficiency, particle size, scanning electron microscopy, in vitro buoyancy, and in vitro drug release profile. The formulation HEs (2) was shown to be the superior formulation based on a percentage of buoyancy, total buoyancy time, and in vitro drug released properties. It had a 78% percentage buoyancy and an 81% Entrapment Efficiency. After 8 hours, the % drug release was found to be 93%. The in vitro drug release was carried out for up to 8 hours. It was found that raising the polymer content reduced the rate of drug release.

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