FORMULATION AND IN VITRO EVALUATION OF GASTRO RETENTIVE FLOATING MICROBALLOONS OF PIRENTANIDE

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ABSTRACT
The present investigation deals with the development and evaluation of floating microballoons of Piretanide to extend the gastric residence time (GRT) and prolong the drug release. In the present work, floating microballoons of Piretanide were formulated using Eudragit RS 100, Eudragit S 100, and HPMC K4M and ethyl cellulose polymers by the solvent evaporation method. The prepared microballoons were evaluated for their physicochemical properties, *in-vitro* drug release, and *in-vitro* buoyancy. The *in-vitro* release studies demonstrated that microballoons of Piretanide prepared using Eudragit RS 100 along with Eudragit S 100 in 1:1 ratio (PRTF10) shown the maximum amount of drug release; hence it is considered as the optimized formulation. The *in-vitro* release kinetics revealed that the optimized formulation releases the drug in zero-order manner based on the regression values of kinetic models.
Key Words: Eudragit S 100, Eudragit RS 100, Ethyl Cellulose, Floating Microballons, Hydroxy Propyl Methyl Cellulose (HPMC), Piretanide.

I. INTRODUCTION:

Historically, oral drug administration has been the predominant route for drug delivery. During the past two decades, numerous oral delivery systems have been developed to act as drug reservoirs from which the active substance can be released over a defined period of time at a predetermined and controlled rate.

The existence of narrow absorption window in the upper GIT for several drugs these difficulties have prompted researchers to design a drug delivery system that can stay in the stomach for prolonged and predictable period. Attempts are being made to develop a drug delivery system that can provide therapeutically effective plasma drug concentration for a longer period, thereby reducing the dosing frequency and minimizing fluctuation in plasma drug concentration at a steady state by delivering the drug in a controlled and reproducible manner [1].

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. It improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment [2].

Microballoons (Hollow microsphere) are in the strict sense, empty particles of spherical shape without core. These Microballoons are characteristically free-flowing powders comprising of proteins or synthetic polymers, ideally having a size less than 200 micrometer [3]. The slow release of drug at desired rate and better-floating properties of floating Microballoons mainly depends on the type of polymer, plasticizer, the solvents employed for the preparation and the release of the drug can be modulated by optimizing polymer concentration and the polymer - plasticizer ratio [4].

Piretanide is absorbed mostly in the stomach and upper small intestine, possibly due to its weak acidic properties (pKa 3.93) and is characterized by a short half-life (1-2 h). The narrow absorption window of Piretanide leads to its low bioavailability (60-70%). The narrow absorption window of Piretanide in the upper part of the gastrointestinal tract provides a rationale for developing a gastro retentive dosage form [5].

II. MATERIALS AND METHODS:

2.1. Materials: Piretanide was purchased from Yarrow chem. Products, Mumbai, India. Vitamin E TPGS, Eudragit RS 100, Eudragit S 100, HPMC K_4M, Ethyl cellulose, Ethanol, Dichloromethane chemicals of Laboratory-grade from SD Fine chemicals Pvt. Ltd., were used.

2.2. Methods:

2.2.1. Drug Excipient Compatibility Study:

2.2.1.1. Differential Scanning Calorimetry: The physicochemical compatibilities of the drug and the excipients were tested by differential scanning calorimetric (DSC) analysis. DSC thermograms of the drug alone and optimized formulation were derived from DSC (Perkin-Elmer, 4000). The instrument was calibrated with an indium standard. The samples (2-4 mg) were heated (20-30°C) at a constant scanning speed (10°C / min) in sealed aluminum pans, using nitrogen purged gas [6].

2.2.1.2. FTIR Spectroscopy: Drug-polymer compatibility studies were carried out using the FTIR spectrophotometer by KBr pellet technique. Pure drug and optimized formulation were subjected to FTIR study. Compatibility studies were carried out to know the possible interactions between Piretanide and excipients used in the formulation [7].

2.2.2. Formulation Development: As the drug Piretanide poorly water-soluble, before formulating it as floating microballoons, it was converted to freely soluble solid dispersion using Vitamin E TPGS as a solubility enhancing carrier. The composition of solid dispersions prepared is given in below Table1. Solid dispersions were prepared by solvent evaporation method. Drug and carrier were dissolved in a suitable quantity of methanol, and solvent was slowly evaporated. The obtained solid residue was collected and evaluated [8].

Table 1: Compositions of solid dispersions of Piretanide

Sl. No.	Materials	PRT1	PRT2
1	Piretanide	10 mg	10 mg
2	Vitamin E TPGS	10 mg	20 mg
3	Methanol	10 mL	10 mL
Ratio of drug to polymer		1:1	1:2

2.2.3. Evaluation of Solid Dispersions:

2.2.3.1. Saturation Solubility:

Saturation solubility studies were conducted for prepared solid dispersions along with pure drug by adding an excess amount of drug in 2 mL of water and shaking it for 48-72 hours until equilibrium is attained [9]. Then the solution is centrifuged and the supernatant is analyzed for amount of drug dissolved by spectrophotometrically at 276 nm.

2.2.3.2. *In-vitro* Dissolution Study:

The drug release study was carried out using USP dissolution apparatus type XXIII basket type dissolution apparatus at 37 ± 0.5°C and at 50 rpm using 900 ml of 0.1N Hydrochloric acid (pH 1.2) as a dissolution medium[10].

2.2.3.3. Formulation of Floating Microballoons:

Solid dispersion prepared with 1:2 ratio of drug to Vitamin E TPGS (PRT2) has shown improved solubility and dissolution and hence was chosen for preparing floating microballoons. The floating microballoons were formulated by solvent evaporation method. The polymer is dissolved in an organic solvent and the solid dispersion (10 mg) equivalent to 30 mg of drug is either dissolved or dispersed in the polymer solution. The solution containing the drug is then emulsified into an aqueous phase containing suitable additive (surfactants /polymer) to form oil in water emulsion. After the formation of a stable emulsion, the organic solvent is evaporated either by increasing the temperature under pressure. Stirring was continued for 6 h under 3 blade propellers at 500 rpm, 40°C until the smell disappears [11].

The solvent removal leads to polymer precipitation at the oil/water interface of droplets, forming cavity and thus making them hollow to impart the floating properties. Then microballoons are collected and washed with excess

amount of distilled water to remove any remnants. Collected microballons were dried at room temperature and subjected for further evaluation [11].

Table 2: Composition of floating microballoons of Piretanide

Materials	PRT F1	PRT F2	PRT F3	PRT F4	PRT F5	PRT F6	PRTF 7	PRT F8	PRT F9	PRT F1 0	PRT F1 1	PRT F1 2	PRT F13	PRT F1 4	PRT F1 5
Piretanide Eqvt. to 0 mg	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
Eudragit RS 100	10	10	10	20	20	20	10	10	20	20	NA	NA	NA	NA	NA
Eudragit S 100	10	20	30	10	20	30	30	30	20	20	NA	NA	NA	NA	NA
HPMC K4M	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	10	10	10	20	20
Ethyl cellulose	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	10	20	30	10	20
Ethanol	15	15	15	15	15	15	20	10	20	10	15	15	15	15	15
Dichloromethane	15	15	15	15	15	15	10	20	10	20	15	15	15	15	15
Ratio of drug to polymer	1:01:01	1:01:02	:01:03	1:02:01	1:02:02	:02:03	:01:03	:01:03	1:02:02	1:02:02	1:01:01	1:01:02	1:01:03	:02:01	:02:02
Ratio of solvent	1:01	1:01	1:01	1:01	1:01	1:01	2:01	1:02	2:01	1:02	1:01	1:01	1:01	1:01	1:01

2.2.3.4. *In-vitro* Evaluation of Microballoons:

2.2.3.4.1. Micromeritic Properties: Microballoons are evaluated by their micromeritic properties such as particle shape and size, density, tapped density and flow properties, which are determined by car's index, Hausner's ratio and angle of repose [13].

2.2.3.4.2. Particle Size Measurement: Particle size of prepared microballoons was measured using an optical microscope, and the mean particle size was calculated by measuring 100 particles with the help of a calibrated ocular micrometer [14].

2.2.3.4.3. Scanning Electron Microscope (SEM): The surface morphology and surface characteristics of best formulation were carried out by scanning electron microscope. Microballoons were scanned and examined under Electron Microscope connected with a fine coat, Ion sputter. The sample was loaded on a copper sample holder and sputter-coated with carbon followed by gold [15].

2.2.3.4.4. Floating properties:

The prepared microballoons of all batches were evaluated for Percentage Yield, Entrapment Efficiency *In-vitro* Buoyancy *and In-vitro* Drug Release Study.

2.2.3.4.5. Drug Release Kinetic Studies: The mechanism of release was determined by fitting the release data to the various kinetic equations such as zero-order, first-order, higuchi and Korsmeyer-Peppas and finding the R^2 values of the release profile corresponding to each model using PCP Disso v 3 software [16].

2.2.3.4.6. Stability Studies: Microballoons were hermetically sealed in glass bottles and stored for 3 months at 4 ± 0.5°C, room temperature and 40 ± 1°C and 75% RH as per ICH guidelines [18,19] after every month, one bottle was used for evaluation. The microballoons were evaluated for physicochemical properties, drug content, percentage entrapment efficiency and percentage buoyancy and percentage of drug release [17].

III. RESULTS AND DISCUSSION:

3.1. Solubility studies

Table 3: Solubility studies of Piretanide

Solvent	Solubility (mg/mL)				
	1	2	3	Average	SD
Double distilled water	0.01	0.02	0.015	0.015	0.05
0.1N Hydrochloric acid	0.025	0.035	0.042	0.034	0.008
pH 6.8 Phosphate buffer	0.034	0.056	0.057	0.049	0.01
pH 7.4 Phosphate buffer	0.045	0.058	0.052	0.052	0.06

Solubility of pure drug was determined in different solvents and the values obtained are given in the **Table 3**. From the results obtained it was observed that the drug was very freely soluble in distilled water. Solubility was found to be comparatively lesser in 0.1N Hydrochloric acid and the solubility was increased with increase in pH.

3.2. Acid stability of Piretanide

Table 4: Acid stability of Piretanide in 0.1N Hydrochloric acid (n=3)

Time (h)	Absorbance	Concentration (µg/ml)
0	0.362	10.00±0.07
1	0.366	10.04±0.19
2	0.365	10.07±0.08
4	0.367	10.05±0.05
6	0.365	10.03±0.06
8	0.366	10.02±0.21
12	0.367	10.18±0.34
24	0.366	10.14±0.07

3.3. Drug Excipient Compatibility Study:

3.3.1. Differential Scanning Calorimetry:

DSC thermogram of the pure drug is shown in Figure 1 endothermic peak was observed at 194.1°C indicates the drug melting point for the pure drug.

The shift in the endothermic peak of the drug was very less (190.5 °C), which indicates that the drug and polymers used were compatible with one another in the DSC of optimized formulation Figure 2.

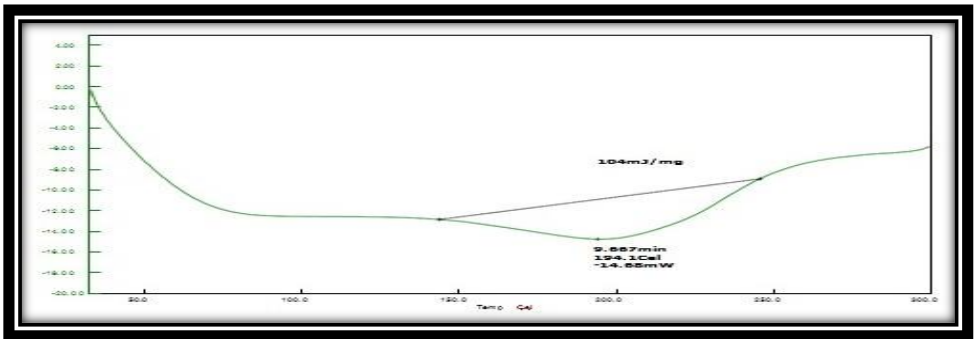

Figure 1: DSC thermogram of pure drug Piretanide

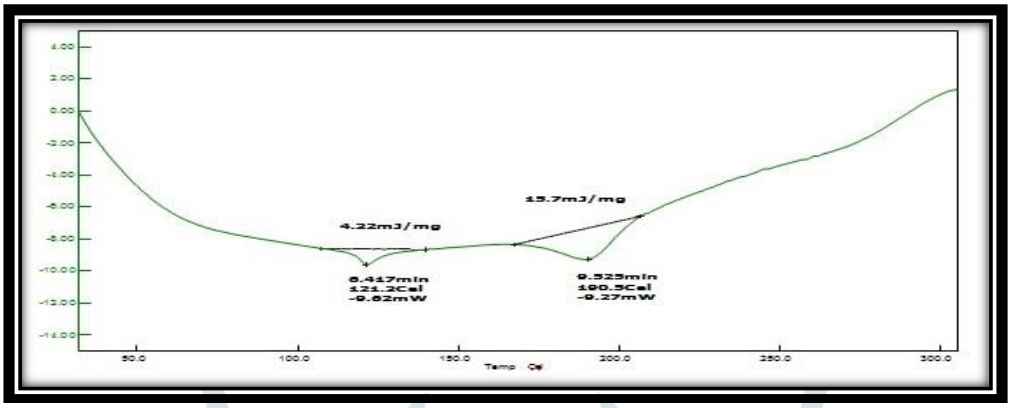

Figure 2: DSC thermogram of optimized formulation of Piretanide

DSC thermogram of pure drug is shown in **(Figure 1)** Endothermic peak was observed at 194.1°C corresponding to the melting point of pure drug (206 ^{0}C). The shift in the endothermic peak of drug was very less in optimized formulation which indicates that the drug and polymers used were compatible with one another.

3.3.2. FTIR

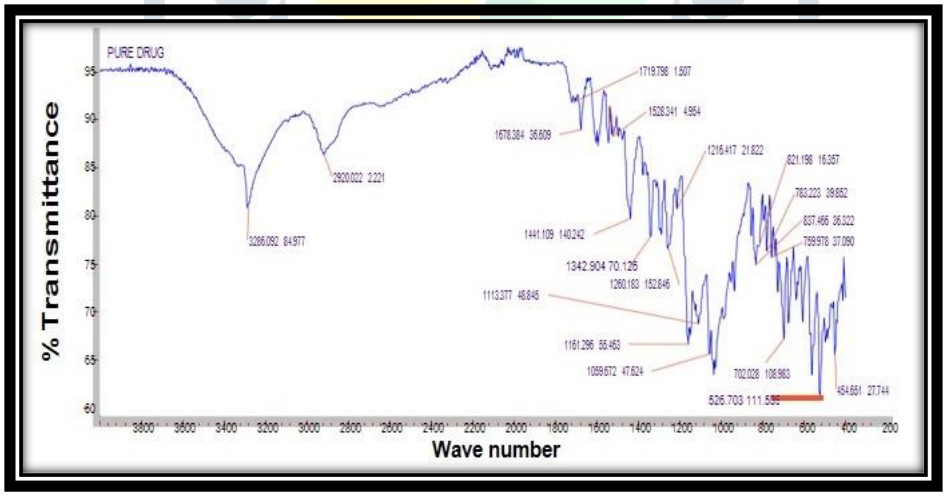

Figure 3: FTIR of pure drug Piretanide

Table 5: FTIR data of pure drug Piretanide

Sl. No	Frequency(cm^{-1})	Functional group
1	3286.09	OH
2	1678.38	C=O
3	1440.2	-NH
4	1047.62	C-O

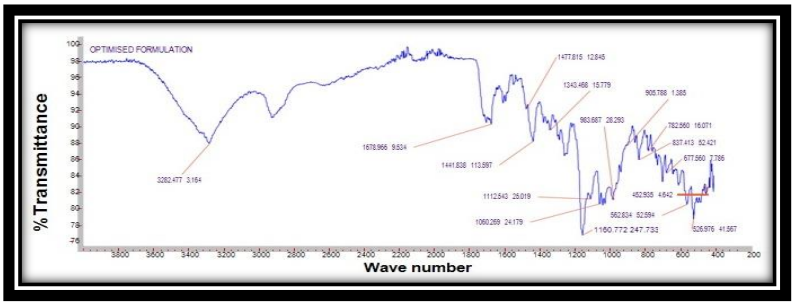

Figure 4: FTIR of optimized formulation of Piretanide

Table 6: FTIR data of optimized formulation of Piretanide

Sl. No	Frequency(cm^{-1})	Functional group
1	3262.47	OH
2	1678.96	C=O
3	1441.83	-NH
4	1160.77	C-O

The drug-excipient compatibility study was done by Fourier transform infrared (FT- IR) spectroscopy study. The prominent peaks of Piretanide pure drug were shown at 3286.09cm^{-1} (due to –O-H), 1678.38cm^{-1} (due to C=O), 1440cm^{-1} (due to –N-H) and1047.62 cm^{-1}(due to –C-O) **(Figure 3 & Table 5)**. These prominent peaks of drug were also observed in the IR spectrum of optimized formulation **(Figure 4 & Table 6)** which indicates that the drug was not interacted with the polymers used in the study which confirms the stability of the drug.

3.4. Evaluation of physicochemical parameters floating microballoons

Table 7: evaluation of physicochemical parameters of floating microballoons of Piretanide

Formulations	Mean particle size (µm)**	Bulk density*	Tapped density*	Carr's index*	Angle of repose*	Drug content
PRTF1	135.24±1.34	0.7±0.19	0.65±0.05	7.14±0.18	14.6±0.49	98.78±0.19
PRTF2	143.34±3.45	0.72±0.97	0.64±0.18	11.11±0.26	16.6±0.28	99.02±0.02
PRTF3	156.32±1.56	0.78±0.65	0.69±0.92	11.54±0.19	16.5±0.29	96.68±0.19
PRTF4	144.24±3.25	0.82±0.06	0.72±0.22	12.20±0.92	15.6±0.34	07.89±0.11
PRTF5	156.54±2.35	0.78±0.88	0.66±0.18	15.38±0.94	15.8±0.18	98.02±0.76
PRTF6	131.23±3.26	0.77±0.54	0.66±0.19	14.29±0.22	15.9±0.28	98.54±0.54
PRTF7	145.39±2.34	0.77±0.43	0.64±0.28	16.88±0.91	16.3±0.91	98.72±0.63
PRTF8	135.26±2.54	0.72±0.32	0.65±0.17	9.72±0.84	15.5±0.18	98.29±0.82

*All values represent Mean ± SD; n=3 ** All values represent Mean ± SD; n=100

Table 8: Observations of *in vitro* evaluation parameters of floating microballoons of Piretanide

Formulations	Mean particle size (µm)**	Bulk density*	Tapped density*	Carr's index*	Angle of repose*	Drug content
PRTF9	125.35±2.38	0.77±0.76	0.66±0.21	14.29±0.72	16.2±0.38	99.04±0.07
PRTF10	127.35±3.24	0.78±0.82	0.69±0.28	11.54±0.92	14.2±0.32	99.38±0.06
PRTF11	121.35±3.36	0.81±0.95	0.71±0.84	12.35±0.99	15.5±0.48	98.06±0.17
PRTF12	128.35±3.36	0.76±0.33	0.68±0.93	10.53±0.17	16.3±0.11	99.08±0.04
PRTF13	145.32±3.69	0.78±0.28	0.68±0.84	1282±0.25	15.8±0.17	97.67±0.11
PRTF14	161.23±3.38	0.75±0.18	0.65±0.83	13.33±0.39	16.1±0.81	98.03±0.18
PRTF15	125.64±3.39	0.82±0.19	0.71±0.89	13.41±0.43	16.5±0.11	94.58±0.17

*All values represent Mean ± SD; n=3 ** All values represent Mean ± SD; n=100

The measured tapped density bulk density, Carr's index and angle of repose and drug content were within the limits which indicates good flow properties of microballoons. (Table 7 & Table 8). The particle size was measured using calibrated optical microscope and the average particle size of floating microballoons was found to be in the range of 120-160μm (Table 7 & Table 8).

3.4.1. Floating properties of prepared microballoons of Piretanide

Table 9: Floating properties of prepared microballoons of Piretanide

Formulation Code	% Yield	% Entrapment Efficiency	% Buoyancy
PRTF1	85.4	85.4	81.5
PRTF2	84.3	94.5	86.5
PRTF3	86.2	96.5	86.9
PRTF4	77.8	96.5	91.2
PRTF5	82.5	92.5	82.2
PRTF6	94.3	95.8	88.9
PRTF7	82.5	91.5	87.5
PRTF8	93.6	91.2	85.6
PRTF9	82.7	91.5	82.5
PRTF10	84.5	94.6	91.2
PRTF11	72.6	71.2	67.5
PRTF12	67.5	66.5	67.8
PRTF13	68.9	64.5	66.9
PRTF14	66.5	66.3	65.2
PRTF15	62.5	63.5	65.3

The floating microballoons were prepared and percentage yield was calculated for all the formulations. The results of % yield are shown in the Table 9. The percentage yield was in the range of 60-90 % for all the formulations. It was found to be less than 70% yield with ethyl cellulose and HPMC K4M and for optimized formulation the yield was 84.5 %.

The entrapment efficiency of floating microballoons of Piretanide was calculated and the results are depicted in the Table 9. The entrapment efficiency was in the range of 60-90 % for all the formulations and was found to be 94.6% for optimized formulation. The entrapment efficiency was low with formulations prepared with ethyl cellulose and HPMC K4M. There was no effect of solvent ratio was observed in the percentage entrapment efficiency.

The percentage buoyancy was calculated for all the formulations and it was found that all the formulations were able to float on the dissolution medium (0.1N hydrochloric acid) over a period of 12h. Even after 12h of agitation of the dissolution medium, the microballoons continued to float without any apparent gelation. The high buoyancy of the microballoons is mainly due to the presence of pores and cavities which were formed during solvent evaporation. The percentage buoyancy was slightly less with formulations prepared with ethyl cellulose and HPMC K4M and decreased as the concentration of the polymers increased. This is because of high viscosity of the polymer solution which in turn is the reason for the less formation of pores and cavities in microballoons during solvent evaporation. The results of *in vitro* buoyancy studies are shown in **Table 9**. The percentage buoyancy was in the range of 60-90 % for all the formulations and was found to be 91.2% for optimized formulation.

3.4.2. SEM studies of optimized floating microballoons of Piretanide

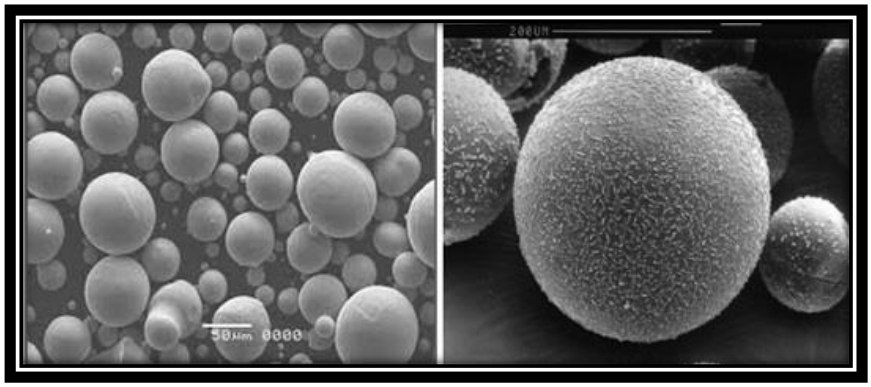

Figure 5: SEM image of Piretanide loaded optimized microballoons

The surface morphology of optimized formulation (PRTF10) was shown in the Figure 5. From the SEM micrographs it is apparent that the Piretanide loaded microballoons were predominately spherical in appearance. The surface was observed to be smooth, dense and less porous, whereas the internal core was highly porous and irregular with numerous depressions that are expression of evaporation of water, ethanol and dichloromethane. The less porous outer surface and highly porous internal surface supported controlled release of drug from the microballoons and good buoyancy.

Figure 6: Comparative physico-chemical properties of microballoons

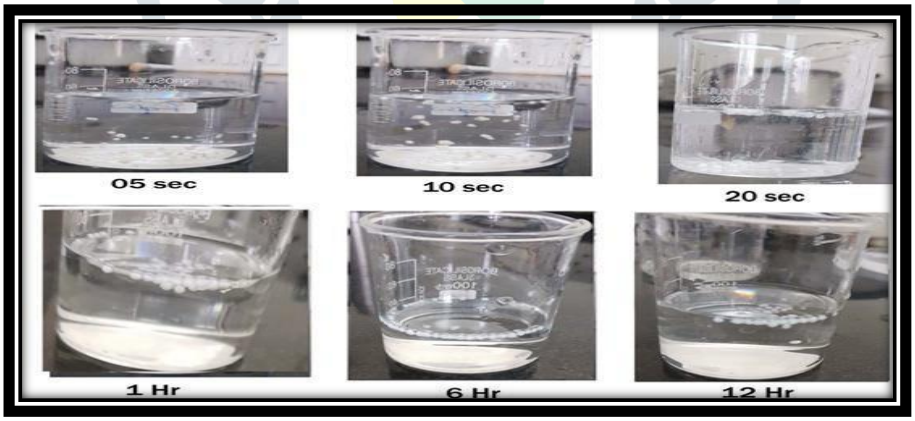

Figure 7: *In vitro* buoyancy of Piretanide microballons in 0.1N Hydrochloric acid

***In vitro* Percentage drug release data of Piretanide microballoons**

Table 10: Percentage drug release data of Piretanide microballoons of PRTF1-PRTF8

Time (Hr)	Percentage drug release							
	PRTF1	PRTF2	PRTF3	PRTF4	PRTF5	PRTF6	PRTF7	PRTF8
0	0	0	0	0	0	0	0	0
0.5	25.6±0.02	20.6±0.02	15.6±0.12	20.4±0.93	6.5±0.32	7.2±0.98	17.8±0.32	16.5±0.54
1	44.2±0.23	34.5±0.32	25.9±0.24	37.2±0.26	11.2±0.42	10.2±0.45	26.5±0.18	25.6±0.18
2	64.5±0.42	51.3±0.47	44.2±0.43	57.6±0.47	21.2±0.09	13.5±0.57	43.5±0.38	44.5±0.17
3	87.5±0.21	63.8±0.98	58.6±0.66	65.5±0.32	26.5±0.58	21.3±0.17	58.7±0.97	61.2±0.23
4	98.5±0.22	75.4±0.26	66.9±0.85	75.6±0.82	35.4±0.41	31.2±0.83	66.9±0.11	71.2±0.24
6	100.1±0.31	82.5±0.32	74.5±0.41	87.9±0.17	53.2±0.95	46.5±0.37	73.5±0.81	73.5±0.38
8	-	100.2±0.04	86.4±0.33	99.7±0.02	65.4±0.73	58.4±0.88	85.6±0.92	87.6±0.52
10	-	-	100.1±0.58	100.1±0.04	83.5±0.29	68.5±0.21	98.6±0.37	100.2±0.54
12	-	-	-	-	100.2±0.11	75.4±0.65	100.2±0.45	-

Table 11: Percentage drug release data of Piretanide microballoons of PRTF9-PRTF15

Time (Hr)	Percentage drug release						
	PRTF9	PRTF10	PRTF11	PRTF12	PRTF13	PRTF14	PRTF15
0	0	0	0	0	0	0	0
0.5	7.6±0.11	5.5±0.94	6.4±0.65	5.6±0.34	5.6±0.10	7.5±0.54	10.2±0.89
1	11.2±0.09	10.2±0.03	10.2±0.88	10.2±0.98	8.5±0.16	13.6±0.36	16.5±0.78
2	16.8±0.29	21.2±0.46	16.4±0.74	14.5±0.28	13.5±0.21	18.9±0.46	22.5±0.38
3	25.6±0.28	26.5±0.87	21.2±0.44	18.5±0.88	15.6±0.27	25.9±0.03	23.6±0.27
4	37.8±0.32	36.9±0.45	27.5±0.57	23.6±0.67	18.9±0.37	32.5±0.19	29.5±0.51
6	55.6±0.46	61.2±0.04	42.3±0.32	38.9±0.03	28.6±0.55	46.5±0.28	43.5±0.46
8	66.5±0.76	68.5±0.26	48.9±0.56	43.5±0.05	38.9±0.46	53.6±0.97	52.6±0.47
10	85.9±0.74	88.9±0.18	68.5±0.33	58.6±0.24	48.9±0.73	75.4±0.56	63.9±0.65
12	100.1±0.85	100.3±0.67	75.4±0.63	68.9±0.46	59.6±0.89	83.6±0.58	73.5±0.99

The cumulative percentage drug release was decreased with increase in the polymer concentration. Based on the results of *in vitro* drug release studies it was found that PRTF10 has shown sustained drug release for 12h with zero order drug release. The results of the *in vitro* drug release studies were shown in the Table 10 & Table 11.

Table 12: Release kinetic parameters of Piretanide microballoons

Formulation	Release Kinetics Parameters				
	Zero order	First order	Higuchi model	Korse-meyer peppas	Hixon Crowell
PRTF1	0.073	0.991	0.795	0.823	0.947
PRTF2	0.551	0.989	0.962	0.960	0.979
PRTF3	0.723	0.989	0.985	0.977	0.978
PRTF4	0.476	0.992	0.947	0.952	0.979
PRTF5	0.995	0.946	0.886	0.998	0.971
PRTF6	0.981	0.984	0.901	0.990	0.993
PRTF7	0.711	0.987	0.987	0.981	0.972
PRTF8	0.690	0.986	0.976	0.965	0.973
PRTF9	0.995	0.943	0.881	0.996	0.970
PRTF10	0.999	0.947	0.887	0.983	0.973
PRTF11	0.987	0.974	0.892	0.991	0.985
PRTF12	0.987	0.978	0.890	0.991	0.986
PRTF13	0.989	0.977	0.880	0.989	0.984
PRTF14	0.979	0.969	0.908	0.989	0.981
PRTF15	0.941	0.974	0.947	0.985	0.972

The *in vitro* drug release kinetics based on the regression values reveals that the optimized formulation (PRTF10)

releases the drug in zero order manners. **(Table 12).**

Table 13: Stability data of optimized microballoons formulation of Piretanide

Optimized formulation PRTF10	Bulk density	Tapped density	Carr's index	Angle of repose	Mean particle size (µm)	Percentage buoyancy	Drug content
1st Month	0.77±0.81	0.68±0.27	11.52±0.91	13.9±0.31	126.31±3.02	81.2±0.87	99.35±0.01
2nd Month	0.76±0.79	0.67±0.26	11.06±0.87	13.8±0.29	125.29±2.09	81.1±2.1	99.21±0.09
3rd Month	0.75±0.76	0.66±0.24	11.05±0.85	13.5±0.24	124.25±1.89	80.09±1.9	99.05±0.11

Table 14: Percentage drug release of optimized microballoons Piretanide (PRTF10)

PRTF10 (Hrs)	1st Month	2nd Month	3rd Month
0	0	0	0
0.5	5.4±0.04	4.9±0.01	4.7±0.19
1	10.1±0.11	9.1±0.9	9.1±0.8
2	21.1±0.31	20.9±0.18	19.9±0.28
3	26.1±0.71	25.9±0.65	25.1±0.61
4	35.1±0.31	34.8±0.28	34.1±0.25
6	60.1±0.01	59.1±0.21	58.1±0.19
8	67.1±0.21	66.11±0.19	65.8±0.15
10	87.1±0.11	86.9±0.10	85.8±0.12
12	100.1±0.61	100±0.58	100±0.53

IV. CONCLUSION:

Gastro-retentive drug delivery system for Piretanide was successfully prepared and evaluated by the solvent evaporation technique using Eudragit RS 100, Eudragit S 100, HPMC K4M, ethyl cellulose polymers. From the drug-excipient compatibility studies, it was observed that, there was no interaction between drug and excipients used in the formulations. Prepared floating microballoons showed significant floating ability, good buoyancy, and sustained drug release. *In vitro* drug release of microballoons was influenced by polymers concentration. From the percentage loading efficiency and *in-vitro* drug release studies, it was observed that PRTF10 formulation exhibits greater drug loading efficiency and sustained release behavior. On fixing the *in-vitro* drug release data of optimized formulation to various kinetic models, it was found that it exhibits the zero-order kinetics. $BaSO_4$ loaded optimized formulation PRTF10 selected for radiological study reveals that gastric retention time of floating microballoon in unfed state was 4.5 h, and in the fed state it was 5.5 h. Microballoons prepared in this study provide a promising gastro retentive drug delivery system to deliver Piretanide with sustained-release in order to improve oral drug bioavailability.

V. REFERENCES:

[1] Gupta G, Singh A. Short review on stomach specific drug delivery system. Int. J Pharm Tech Resea. 2012; 4(4): 1527-45.[2] Vyas SP, Khar RK. Targeted and controlled drug delivery novel carrier system. 4th ed. CBS Publishers and Distributors: New Delhi 2002: 417-54.

[3] Gattani YS, Kawtikwar PS, Sakarkar DM. Formulation and evaluation of gastro retentive multiparticulate drug delivery system of aceclofenac. Int J Chem Tech Res. 2009; 1: 1-10.

[4] Lenkalapally Matsyagiri, Dr. Bontha Vijaya Kumar. Formulation and evaluation of gastro retentive floating microballoons of Ursodeoxycholic acid. Int J Res Analy Rev. 2019; 6(2):396-411.

[5] Pusp RN, Myung KC, Hoo KC. Preparation of floating microspheres for fish farming. Int J Pharma. 2007; 341: 85-90.

[6] Jain SK, Awasthi AM, Jain NK and Agrawal GP. J Cont Rele. 2007; 107(2): 300-09.
[7] Awasthi R, Kulkarni GT. Development and characterization of amoxicillin loaded floating micro-balloons for the treatment of *Helicobacter pylori* induced gastric ulcer. Asi J Pharma Sci. 2013; 8: 174-80.
[8] Saniya Jawed, Amit Sorathiya, Srivastava AK. Floating controlled drug delivery system of Verapamil loaded Microballoons, The Pharma Inno J. 2017; 6(2): 85-88.
[9] Peeyush Bhardwaj, Himanshu chaurasia, Deepti Chaurasia, et al. Formulation and *in- vitro* evaluation of floating microballoons of Indomethacin. Acta Polo Pharmaceu and Drug Resea. 2010, 67(3): 291-298.
[10] Mali AD, Bathe RS, An updated review on microballoons for better approach in gastro retention. Asia J Res Pharm Sci. 2015; 5(3): 188-92.
[11] Singh BN, Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery *via* gastric retention. J Con Relea. 2000; 63: 235-59.
[12] Lenkalapally Matsyagiri, Vangala Kiran Kumar, Takkadapalliwar Santoshi, Bandapalli Saritha, Pasham Pranathi. Spectrophotometric Method for the Estimation of Abacavir Sulphate in Bulk and Pharmaceutical Dosage Forms in Different Solvents, VRI Phytomedicine. 2013; 1(3): 64-68.
[13] Lenkalapally Matsyagiri1, Dr. Bontha Vijaya Kumar. Formulation and evaluation of gastro retentive floating microballoons of Alendronate sodium. J Emer Techn and Inno Rese. 2019; 6(2):622-636.
[14] Singhal P, Kumar K and Shubhini A. Saraf formulation and evaluation of sustained release microballoons of Piretanide. Int J Pharma Sci Rev and Rese. 2011; 6(1): 75-82.
[15] Gangadharappa H, Srirupa B, Anil G, Gupta V, Kumar P. Development *in-vitro* and *in- vivo* evaluation of novel floating hollow microspheres of Rosiglitazone maleate. Der Pharmacia Let. 2011; 3(4): 299-16.
[16] Mandal UK, Chatterjee B. Faria gias senjoti gastro-retentive drug delivery systems and their *in-vivo* success: a recent update. Asia J Pharma Sci. 2016; 11: 575-84.
[17] Bagre A, Awasthi S and Kori ML. Clarithromycin loaded floating Eudragit microsphere for anti h. Pylori Therapy *in-vitro* and *in-vivo* Assessment. J Chem Pharma Rese. 2017; 9(4): 270-76.