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Research Article

Formulation and In-vitro Evaluation of Floating Drug Delivery System for Piretanide

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ABSTRACT

Piretanide as a loop diuretic compound by using a then-new method for introducing cyclic amine residues in an aromatic nucleus in the presence of other aromatically bonded functional groups. The objective of the present work is preparing floating tablets in controlled fashion. The gas generating agent sodium bicarbonate was added in different concentrations with varying amount of retardation polymers. Different grades of HPMC polymers HPMC K4M, K15M & K100M were used as retarding polymers. The formulation blend was evaluated for various physicochemical properties and all the parameters were found to be within limits. The formulations F1-F12 were formulated and evaluated for various quality control parameters. All the formulations were passed the tests and the results were within limits. From the dissolution data it was evident that formulation F10 was found to be best with maximum % drug release of 96.10% and lag time of 10 hours.

Keywords: Piretanide, HPMCK4M, HPMCK15M, HPMCK100M & Floating tablets.

INTRODUCTION

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation, Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. The floating drug delivery system (FDDS) also called Hydro dynamically Balanced Drug Delivery System (HBS). FDDS is an oral dosage forms (capsule or tablet) designed to prolong the residence time of the dosage form within the GIT. It is a formulation of a drug with gel forming hydrocolloids meant to remain buoyant on stomach contents. Drug dissolution and release from dosage retained in the stomach fluids occur at the pH of the stomach under fairly controlled condition. Piretanide is a sulfamoylbenzoic acid belonging to the class of loop diuretics. Piretanide is structurally related to furosemide and bumetanide.

METHODOLOGY-PIRETANIDE

Analytical Method Development:

a) Determination of Absorption Maxima:

A solution containing the concentration 10 µg/ ml drug was prepared in 0.1N HCl UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400 nm.

b) Preparation Calibration Curve:

100 mg of Piretanide pure drug was dissolved in 100 ml of 0.1N HCl (stock solution) 10 ml of solution was taken and make up with 100 ml of 0.1N HCl (100 µg/ml). From this 10 ml was taken and make up with 100 ml of 0.1N HCl (10 µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 1,2,3,4 and 5µg/ml of Piretanide per ml of solution. The absorbance of the above dilutions was measured at 266 nm by using UV-Spectrophotometer taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis.

Drug – Excipient Compatibility Studies:

Fourier Transform Infrared (FTIR) Spectroscopy:

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100 mg potassium bromide IR powder and compacted under vacuum

at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

Preformulation Parameters:

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of Repose:

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula,

$\tan \theta = h / r$

Where,

$\tan\theta$ = Angle of repose

h = Height of the cone,

r = Radius of the cone base.

Bulk Density:

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read. The bulk density was calculated using the formula,

Bulk Density = M / V_o

Where,

M = weight of Sample

V_o = Apparent volume of Powder

Tapped Density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula,

Tap= M / V

Where,

Tap= Tapped Density

M = Weight of Sample

V= Tapped volume of Powder

Measures of Powder Compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas,

Carr's Index = [(tap - b) / tap] × 100

Where,

b = Bulk Density

Tap = Tapped Density

Formulation Development of Tablets:

All the formulations were prepared by direct compression. The compressions of different formulations are given in Table 6.1.3.The tablets were prepared as per the procedure given below and aim is to prolong the release of Piretanide. Total weight of the tablet was considered as 300 mg.

Optimization of Sodium Bicarbonate Concentration:

Sodium bicarbonate was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of sodium bicarbonate were employed, floating lag time and floating duration were observed. Based on that the concentration of sodium bicarbonate was finalized and preceded for further formulations.

Table 1. Optimization Sodium Bicarbonate Concentration

S.No	Excipient Name	EF1	EF2	EF3
1	Piretanide	20	20	20
2	Guar gum	50	50	50
4	$NaHCO_3$	25	50	75
5	Mg.Stearate	5	5	5
5	Talc	5	5	5
7	MCC pH 102	Q.S	Q.S	Q.S
	Total weight	250	250	250

All the quantities were in mg.
Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimised.

Table 2 Formulation Composition for Floating Tablets

Formulation No.	Piretanide	Sodium CMC	Chitosan	Guar gum	$NaHCO_3$	Mag. Stearate	Talc	MCC pH 102
F1	20	25	-----	-----	50	5	5	QS
F2	20	50	-----	-----	50	5	5	QS
F3	20	75	-----	-----	50	5	5	QS
F4	20	-----	25	-----	50	5	5	QS
F5	20	-----	50	-----	50	5	5	QS
F6	20	-----	75	-----	50	5	5	QS
F7	20	-----	-----	25	50	5	5	QS
F8	20	-----	-----	50	50	5	5	QS
F9	20	-----	-----	75	50	5	5	QS

All the quantities were in mg, Total weight is 300 mg.

Table 3 Formulation Composition for Floating Tablets

Formulation No.	PIRETANIDE	HPMC K4M	HPMC K15M	HPMC K100M	$NaHCO_3$ + Citric acid	Mag. Stearate	Talc	MCC pH 102
F10	20	50	-----	-----	50	5	5	QS
F11	20	75	-----	-----	50	5	5	QS
F12	20	100	----	-----	50	5	5	QS
F13	20	-----	50	-----	50	5	5	QS
F14	20	-----	75	----	50	5	5	QS
F15	20	-----	100	-----	50	5	5	QS
F16	20	-----	-----	50	50	5	5	QS

F17	20	-----	-----	75	50	5	5	QS
F18	20	-----	-----	100	50	5	5	QS

All the quantities were in mg, total weight is 300 mg.

Evaluation of Post Compression Parameters for Prepared Tablets:

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

A) Weight Variation Test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined.The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Table 4:Pharmacopoeial Specifications for Tablet Weight Variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

B) Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

C) Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

D) Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as,

% Friability = [(W1-W2) / W] × 100

Where,

W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

E) Determination of Drug Content:

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Piretanide were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV – Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

In vitro Buoyancy Studies:

The in vitro buoyancy was determined by floating lag time, and total floating time. The tablets were placed in a 100 ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

In vitro Drug Release Studies:

Dissolution parameters:

Apparatus --USP-II, Paddle Method
Dissolution Medium -- 0.1 NHCl
Rpm --75
Sampling Intervals (hrs) – 0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature --37° c + 0.5° c

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure:

900 ml 0f 0.1 HCl was placed in vessel and the USP apparatus – II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37° c + 0.5° c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCl was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5 ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 266 nm using UV - spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

RESULTS AND DISCUSSION-PIRETANIDE

The present study was aimed to developing gastro retentive floating tablets of Piretanide using various polymers. All the formulations were evaluated for physicochemical properties and invitro drug release studies.

Analytical Method:

A graph of Piretanide was taken in Simulated Gastric fluid (pH 1.2) at 266 nm.

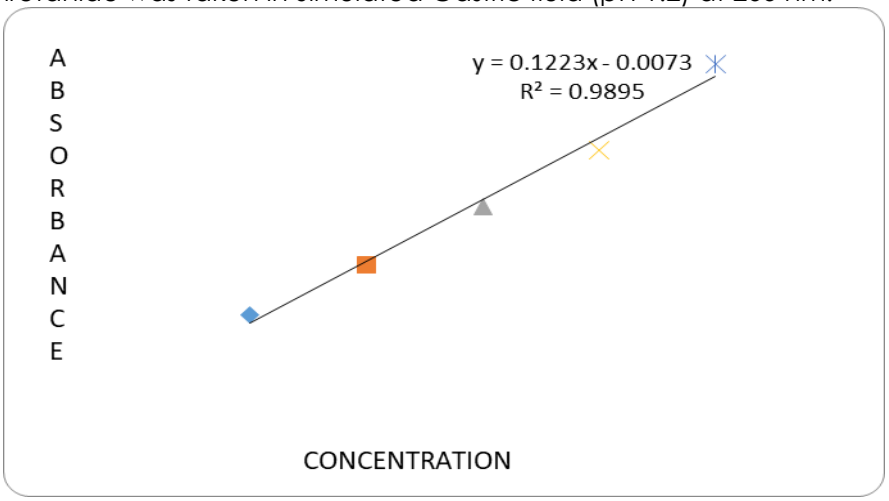

Fig.1:Standard Graph of Piretanide in 0.1N HCl

Table 5:Preformulation Parameters of Powder Blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
		0.49±0.07	0.57±0.01	16.21±0.06	0.86±0.06
F1	37.01±0.4				
		0.56±0.06	0.62±0.05	16.87±0.05	0.98±0.05
F2	35.8±0.4				

F3	22.74±0.6	0.52±0.03	0.68±0.07	17.11±0.01	0.64±0.03
F4	25.33±0.5	0.54±0.04	0.64±0.08	17.67±0.08	1.12±0.04
F5	37.24±0.3	0.53±0.06	0.67±0.03	16.92±0.04	1.2±0.08
F6	26.12±0.2	0.56±0.05	0.66±0.06	17.65±0.09	1.06±0.09
F7	38.08±0.4	0.58±0.06	0.69±0.04	16.43±0.05	0.76±0.03
F8	25.12±0.5	0.48±0.05	0.57±0.02	17.97±0.02	1.15±0.09
F9	25.45±0.6	0.54±0.08	0.62±0.03	17.54±0.09	1.17±0.02

Tablet powder blend was subjected to various preformulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.49 ± 0.07 to 0.58 ± 0.06 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.57 to 0.69 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 16 to 18 which show that the powder has good flow properties. All the formulations has shown the hausners ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Table 6:Pre-Formulation Parameters of Blend

Formulation Code	Angle of Repose	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Hausner's Ratio
F10	36.01±0.5	0.55±0.2	0.645±0.3	14.72±0.1	0.85±0.3
F11	34.8±0.2	0.57±0.5	0.66±0.2	13.63±0.3	0.86±0.1
F12	32.74±0.1	0.53±0.2	0.606±0.5	14.19±0.2	0.858±0.3
F13	35.33±0.3	0.531±0.1	0.613±0.2	13.37±0.5	0.866±0.2
F14	36.24±0.3	0.549±0.1	0.641±0.1	14.35±0.2	0.856±0.5
F15	36.12±0.1	0.564±0.3	0.666±0.2	15.31±0.5	0.846±0.2
F16	37.08±0.7	0.581±0.2	0.671±0.5	13.41±0.2	0.865±0.1

F17	35.12±0.2	0.567±0.5	0.654±0.2	13.12±0.1	0.845±0.7
F18	35.45±0.5	0.571±0.2	0.689±0.1	13.28±0.7	0.855±0.3

Piretanide blend was subjected to various preformulation parameters. The apparent bulk density and tapped bulk density values ranged from 0.55 to 0.581 and 0.606 to 0.671 respectively. According to Tables 7.1.3 the results of angle of repose and compressibility index (%) ranged from 32.74±0.12 to 37.08±0.76 and 13.37±0.50 to 14.72±0.10 respectively. The results of angle of repose (<35) and compressibility index (<23) indicates fair to passable flow properties of the powder mixture. These results show that the powder mixture has good flow properties. The formulation blend was directly compressed to tablets and in-vitro drug release studies were performed.

Compatability Studies by FTIR

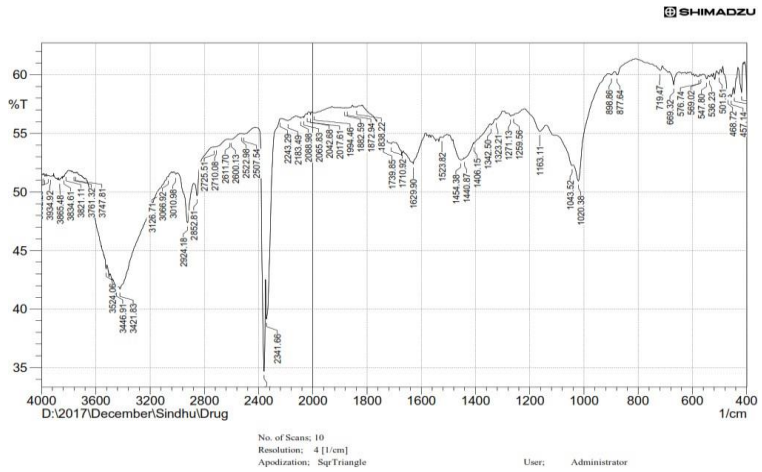

Fig.2:FTIR Spectrum of Pure Drug

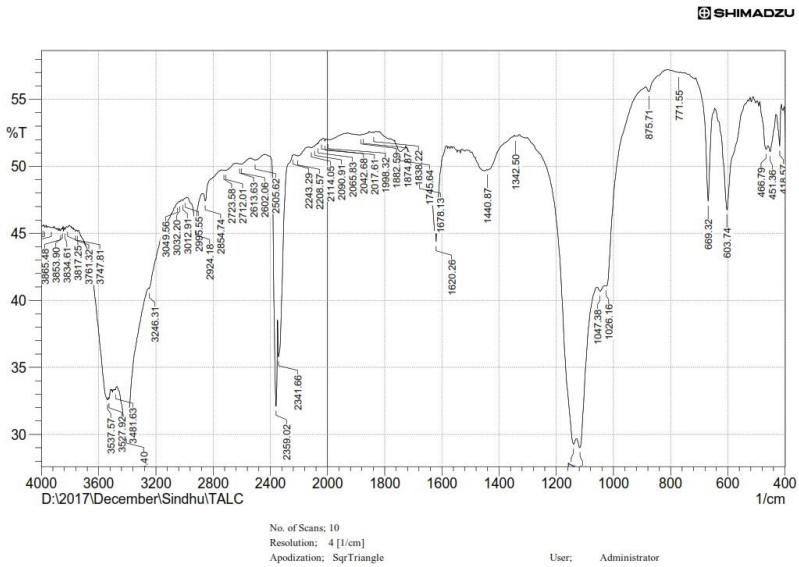

Fig.3:FTIR Spectrum of Pure Drug and Chitosan

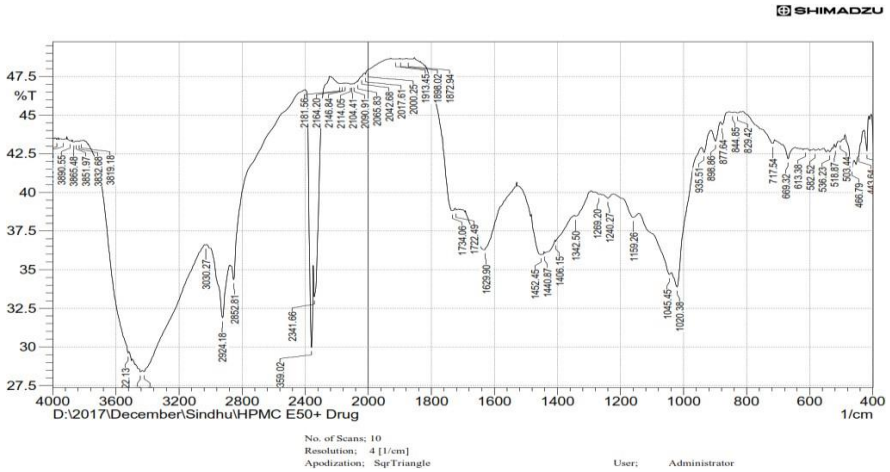

Fig.4:FTIR Spectrum of Pure Drug and HPMC K4M

By the observation of the FTIR spectrums we noticed that there is a minimal change in the peaks of the pure drug in the combined forms but which are acceptable and therefore concluded that there is no incompatability between the formulations.

DSC Studies:

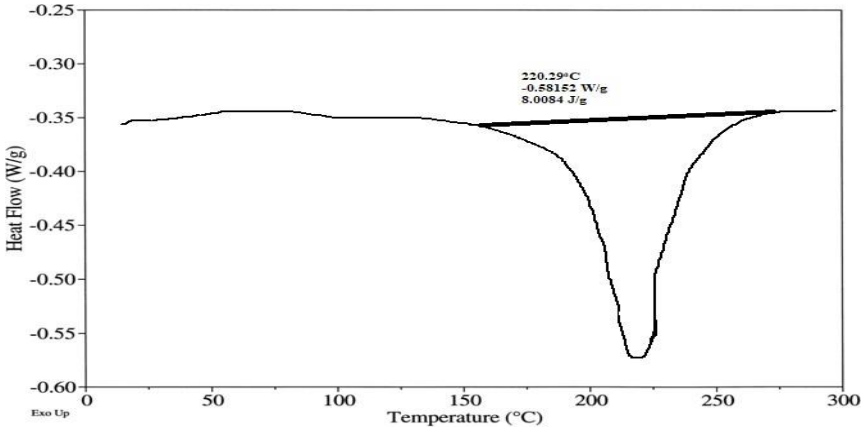

Fig.5:DSC Spectrum of Pure Drug Piretanide

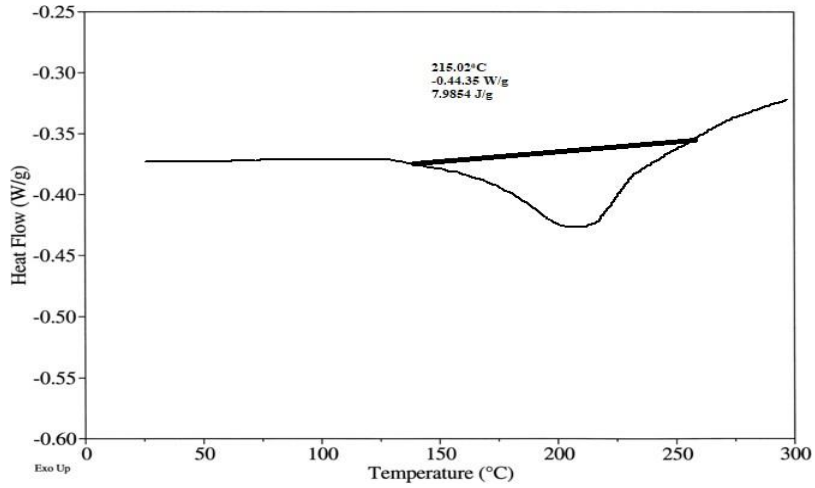

Fig.6:DSC Spectrum of Chitosan

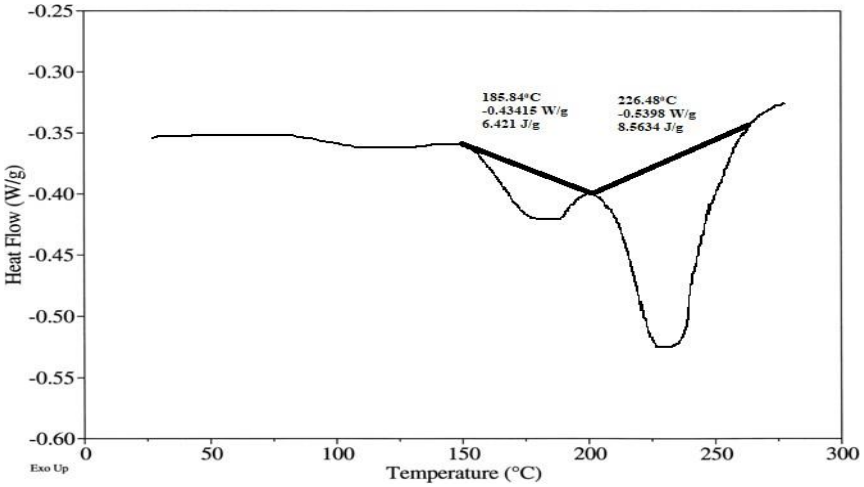

Fig.7:DSC Spectrum of Piretanide and Chitosan

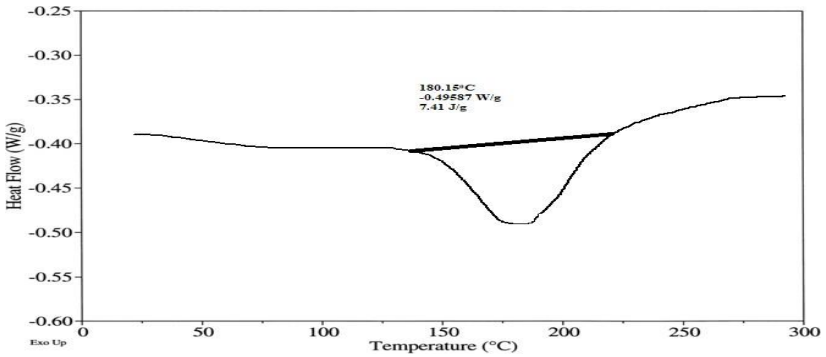

Fig.8:DSC Spectrum of HPMC K4M

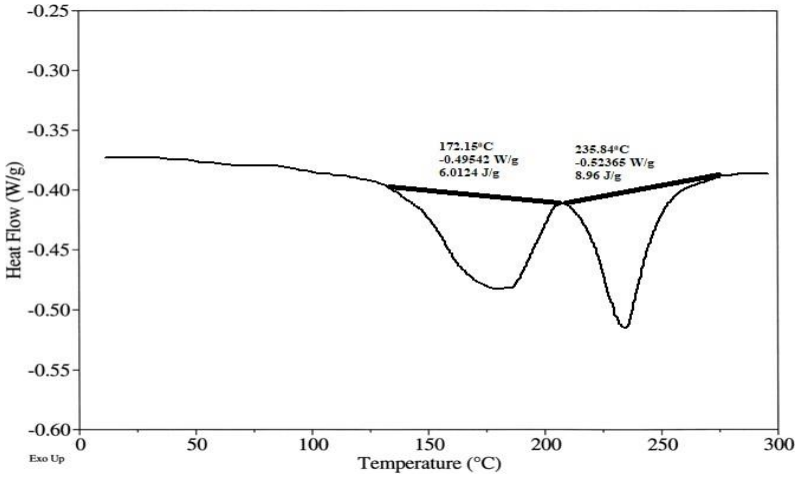

Fig.9:DSC Spectrum of Piretanide and HPMC K4M

Optimization of Sodium Bicarbonate Concentration:

Three formulations were prepared with varying concentrations of sodium bicarbonate. The formulation containing sodium bicarbonate in 50 mg concentration showed less floating lag time of 4 min and the tablet was in floating condition for more than 12 hours.

Quality Control Parameters for Tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the tablets.

Table 7:In Vitro Quality Control Parameters for Tablets

Formulation code	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (min)
F1	300.5±0.7	4.5±0.8	0.52±0.8	4.8±0.8	99.76±0.7	4.0±0.4
F2	300.4±0.4	4.2±0.7	0.54±0.8	4.9±0.5	99.45±0.4	4.2±0.7
F3	300.6±0.5	4.4±0.4	0.51±0.7	4.9±0.4	99.34±0.7	4.5±0.8
F4	300.6±0.8	4.5±0.5	0.55±0.4	4.9±0.7	99.87±0.8	4.1±0.8
F5	300.4±0.5	4.4±0.4	0.56±0.7	4.7±0.4	99.14±0.7	4.0±0.7
F6	300.7±0.4	4.2±0.7	0.45±0.8	4.5±0.5	98.56±0.4	4.4±0.7
F7	300.3±0.7	4.1±0.4	0.51±0.5	4.4±0.8	98.42±0.7	4.5±0.4
F8	300.2±0.3	4.3±0.7	0.49±0.4	4.7±0.7	99.65±0.4	4.6±0.5
F9	300.3±0.8	4.5±0.8	0.55±0.7	4.6±0.4	99.12±0.5	4.7±0.8
F10	301.4±0.4	4.2±0.8	0.56±0.5	4.9±0.8	99.56±0.4	4.1±0.3
F11	302.4±0.5	4.3±0.4	0.52±0.8	4.9±0.4	99.55±0.8	4.2±0.4
F12	301.5±0.3	4.5±0.8	0.50±0.4	4.9±0.8	99.54±0.3	4.1±0.8
F13	302.3±0.8	4.2±0.4	0.50±0.3	4.9±0.4	99.85±0.8	4.1±0.3
F14	301.4±	4.3±0.3	0.51±0.4	4.8±0.8	99.54±0.4	4.2±0.8
F15	303.8±0.3	4.3±0.4	0.54±0.8	4.8±0.3	98.55±0.8	4.1±0.4
F16	301.2±0.4	4.2±0.8	0.53±0.3	4.9±0.8	98.45±0.4	4.2±0.5
F17	300.2±0.8	4.2±0.4	0.57±0.8	4.8±0.4	99.55±0.3	4.1±0.5
F18	300.5±0.3	4.3±0.8	0.59±0.4	4.9±0.3	99.15±0.5	4.2±0.3

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

In-Vitro Drug Release Studies:

Table 8:Dissolution Data of Piretanide Tablets Prepared with SODIUM CMC in Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3+SD)		
	F1	F2	F3
0.5	21.73±0.5	18.52±0.4	19.53±0.7
1	59.23±0.4	37.47±0.6	28.97±0.4
2	84.9±0.6	59.93±0.5	35.89±0.6
3	94.873±0.4	65.85±0.6	45.7±0.7
4	94.873±0.5	77.54±0.4	54.38±0.5
5		89.55±0.7	61.2±0.4
6		96.6±0.5	67.06±0.6
7			72.52±0.7
8			77.88±0.4

9			86.6±0.6
10			89.09±0.4
11			94.52±0.6

Table 9:Dissolution Data of Piretanide Tablets Prepared With Chitosan in Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3+SD)		
	F4	F5	F6
0.5	18.45±0.7	18.42±0.3	19.62±0.1
1	36.26±0.2	27.73±0.7	27.86±0.3
2	52.16±0.1	35.63±0.2	36.35±0.7
3	70.01±0.3	42.04±0.7	41.45±0.2
4	87.26±0.7	57.25±0.2	47.80±0.1
5	93.10±0.2	64.33±0.7	55.25±0.3
6		75.41±0.2	60.24±0.7
7		83.84±0.7	66.73±0.2
8		92.80±0.2	71.34±0.7
9			78.52±0.2
10			80.17±0.7
11			88.75±0.2
12			96.33±0.7

Table 10:Dissolution Data of Piretanide Tablets Prepared With Guar Gum In Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3+SD)		
	F7	F8	F9
0.5	18.81±0.2	19.89±0.3	14.21±0.6
1	29.02±0.6	28.04±0.2	18.87±0.3
2	35.70±0.3	35.43±0.6	27.19±0.2
3	43.32±0.3	41.65±0.2	35.66±0.6
4	49.25±0.2	47.18±0.6	43.32±0.3
5	55.28±0.6	53.81±0.2	51.06±0.3
6	60.92±0.8	58.89±0.6	57.13±0.2
7	66.08±0.8	64.53±0.2	63.63±0.6
8	70.44±0.2	69.43±0.6	69.71±0.6
9	77.22±0.6	72.83±0.2	73.34±0.3
10	80.90±0.8	79.98±0.6	79.27±0.2
11	87.83±0.6	83.52±0.2	82.86±0.6
12	91.90±0.2	88.65±0.6	85.97±0.8

From the dissolution data it was evident that the formulations prepared with Sodium CMC as polymer were unable to retard the drug release up to desired time period i.e., 12 hours.

Whereas the formulations prepared with Chitosan retarded the drug release in the concentration of 75 mg showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.33 % in 12 hours (Formulation F6) with good floating lag time and floating buoyancy time.

The formulations prepared with Guar gum showed more retardation even after 12 hours they were not shown total drug release. Hence they were not considered.

Table 11 In-vitro Drug Release Profile

TIME(hrs)	%Drug release of F10	%Drug release of F11	%Drug release of F12	%Drug release of F13	%Drug release of F14	%Drug release of F15	%Drug release of F16	%Drug release of F17	%Drug release of F18
0	0	0	0	0	0	0	0	0	0
1	18.8±0.1	28.94±0.3	16.1±0.9	14.47±0.7	29.42±0.5	26.56±0.2	16.14±0.1	11.12±0.3	11.52±0.9
2	24.87±0.3	37.88±0.1	29.74±0.3	24.89±0.5	32.05±0.7	34.92±0.1	27.35±0.3	33.45±0.1	29.36±0.3
3	36.12±0.5	48.2±0.7	30.56±0.1	32.11±0.3	44.1±0.1	44.52±0.3	30.73±0.5	45.62±0.3	35.2±0.1
4	45.25±0.7	55.45±0.5	48.29±0.2	41.82±0.1	51.25±0.3	54.85±0.9	45.24±0.3	58.73±0.1	49.65±0.2
5	51.24±0.5	69.52±0.7	57.1±0.10.5	56.01±0.3	63.33±0.1	67.21±0.3	51.27±0.1	62.64±0.2	61.1±0.5
6	57.35±0.2	71.53±0.1	68.25±0.3	67.35±0.5	69.24±0.3	70.05±0.1	57.83±0.3	70.43±0.5	68.99±0.7
7	62.17±0.1	77.56±0.3	79.32±0.5	76.25±0.3	70.01±0.1	74.16±0.2	62.19±0.1	76.21±0.3	72.58±0.9
8	65.65±0.3	81.45±0.1	86.25±0.3	80.24±0.1	76.45±0.7	79.61±0.5	67.02±0.7	81.26±0.1	79.56±0.3
9	66.98±0.9	82.35±0.3	87.65±0.1	81.25±0.2	78.54±0.5	80.35±0.7	68.25±0.5	83.64±0.3	80.36±0.1
10	68.89±0.3	84.65±0.1	90.23±0.3	83.54±0.1	81.26±0.7	81.87±0.5	70.34±0.3	87.94±0.1	81.12±0.9
11	71.26±0.1	86.27±0.7	92.23±0.5	85.16±0.3	84.29±0.1	82.83±0.3	72.01±0.1	89.75±0.7	82.95±0.5
12	76.25±0.2	89.75±0.5	95.69±0.7	90.98±0.9	91.25±0.3	89.21±0.1	79.58±0.9	92.89±0.5	86.25±0.7

From the dissolution values it was evident that the formulations F12 & F18 were retarded the drug release up to 12 hours, they shown drug release of 95.69 and 86.25 % respectively. Formulations F10 – F12 contains HPMC K4M alone. As the concentration of HPMC K4M increases retardation nature was increased. F13 formulation containing 50 mg of HPMC K15M was show almost negligible amount of drug release in first 3 hours from the 5 th hour onwards it shown drug release as the time proceeds slowly the polymer was undergone erosion and allowed the drug to come out from the dosage form. The formulation was retarded drug release up to 12 hours and it showed maximum drug release in 12 hours. Similarly the formulation F9 containing Guargum in the concentration of 75 mg also showed similar drug release pattern.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer Peppas release model.

Table 12:Release kinetics Data for optimised Formulation (F6)

CUMULATIVE (%) RELEASE Q	TIME (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASERATE (CUMULATIVE % RELEASE / t)	1/CUM % RELEASE	PEPPASlog Q/100	% Drug Remaining
0	0			2.000				100
19.62	0.5	1.293	0.301	1.905	39.240	0.0510	-0.707	80.38
27.86	1	1.445	0.000	1.858	27.860	0.0359	-0.555	72.14
36.35	2	1.561	0.301	1.804	18.175	0.0275	-0.439	63.65
41.45	3	1.618	0.477	1.768	13.817	0.0241	-0.382	58.55
47.8	4	1.679	0.602	1.718	11.950	0.0209	-0.321	52.2
55.25	5	1.742	0.699	1.651	11.050	0.0181	-0.258	44.75
60.24	6	1.780	0.778	1.599	10.040	0.0166	-0.220	39.76
66.73	7	1.824	0.845	1.522	9.533	0.0150	-0.176	33.27
71.34	8	1.853	0.903	1.457	8.918	0.0140	-0.147	28.66
78.52	9	1.895	0.954	1.332	8.724	0.0127	-0.105	21.48
80.17	10	1.904	1.000	1.297	8.017	0.0125	-0.096	19.83
88.75	11	1.948	1.041	1.051	8.068	0.0113	-0.052	11.25
96.33	12	1.984	1.079	0.565	8.028	0.0104	-0.016	3.67

Table 13:Release kinetics Data for Optimised Formulation (F12)

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0	0	0	2.000
16.1	1	0	1.207	0	1.924
29.74	2	1.000	1.473	0.000	1.847
30.56	3	1.414	1.485	0.301	1.842
48.29	4	1.732	1.684	0.477	1.714
57.1	5	2.000	1.757	0.602	1.632
68.25	6	2.236	1.834	0.699	1.502

79.32	7	2.449	1.899	0.778	1.316
86.25	8	2.646	1.936	0.845	1.138
87.65	9	2.828	1.943	0.903	1.092
90.23	10	3.000	1.955	0.954	0.990
92.23	11	3.162	1.965	1.000	0.890
98.69	12	3.317	1.994	1.041	0.117

CONCLUSION

In the present research work gastro retentive floating matrix formulation of Piretanide by using various hydrophilic polymerslike,Chitosan,Guargum,HPMCK4M,HPM CK100M,HPMC15M,Talc Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various natural polymers. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations prepared by using Sodium CMC were unable to produce desired drug release they were unable to retard drug release up to 12 hours. The formulations prepared with Chitosan retarded the drug release up to 12 hours in the concentration of 75 mg (F6). The formulations prepared with Guar gum were also retarded the drug release for more than 12 hours. Hence they were not considered. The optimized formulation dissolution data was subjected to release kinetics from the release kinetics data it was evident that the formulation followed Higuchi mechanism of drug release.

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