International Journal of Pharmaceutical Development & Technology

e ISSN - 2248 - 910X

www.ijpdt.com

Print ISSN - 2248 - 9096

DEVELOPMENT OF MICROBALLOONS AND IMMEDIATE RELEASE GRANULES OF PANTOPRAZOLE SODIUM FOR GASTRO RETENTIVE DRUG DELIVERY

N. Bhanu Priya[1], S. Brito Raj[1]*, G. Sravani[1], P.Srikanth[1], S. Wasim Raja[2], Narayana Raju[1]

[1]Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, R.V.S. Nagar, Tirupati Road, Chittoor, Andhra Pradesh.
[2]Department of Pharmacy Practice, Sri Venkateswara College of Pharmacy,
R.V.S. Nagar, Tirupati Road, Chittoor, Andhra Pradesh, India.

ABSTRACT

The intention of the present research work was to develop once daily controlled release floating microballoons of pantoprazole using different polymers like HPMC, EC and gelatin for GRDDS along with the loading dose granules with superdisintegrants. The immediate release (IR) granules were prepared by wet granulation method by using Sodium starch glycolate, Cross povidone as superdisintegrants and evaluated for the flow property and release studies. The granules showed good flowability and *in vitro* release of pantoprazole IR granules was found to be 96-102%. The floating microballoons were prepared by emulsion solvent diffusion method. The prepared microballoons were characterized for scanning electron microscopy (SEM), drug content, entrapment efficiency, production yield, floating ability, buoyancy percentage, *in vitro* drug release and release kinetics studies. The prepared microballoons were spherical and showed good flow properties. DSC studies revealed that the drug is having a very good compatibility with the polymers. SEM revealed that the microballoons had smooth surface and hollow cavity in the middle. The entrapment efficiency of microballoons was found to be 72-95 % and the drug release from the microballoons in simulated gastric fluid (SGF) was found to be 54-68 % up to 12 h. The floating ability and buoyancy percentage of the microballoons were found to be 75-88 % and it remains buoyant up to 12 h. The release kinetics study revealed that the prepared microballoons were best fitted to the zero order kinetics and indicates that the drug release obeys diffusion – controlled mechanism. Thus it conclude that GRDDS of pantoprazole (an anti-ulcer drug) loaded microballoons along with IR granules loaded capsule was an ideal drug delivery system for ulcer protective activity as both controlled and immediate release drug delivery systems.

Keywords: Buoyancy percentage, Emulsion solvent diffusion method, Floating Microballoons, Gastro retentive drug delivery system, Pantoprazole.

INTRODUCTION

Microballoons is a multiple-unit floating system that can be distributed widely throughout the gastrointestinal tract, providing the possibility of achieving a longer-lasting and more reliable release of drugs. The particle size of the microballoons ranges of 1-300 µ.

Floating multiparticulate oral sustained release drug delivery system includes hollow microspheres (micro balloons), low density floating micro pellets, floating micro beads (acrylic resin based) etc.

It is a type of Pelletized Delivery System (PDS) which is a sustained release system using pellets or beads manufactured using marumerization / Pheronization / pelletization techniques or by layering powders or solutions on nonpareil seeds. Release modulating polymers are sprayed on the beads using various coating techniques. The coated beads are filled in to hard gelatin capsules. Drug release occurs by diffusion associated with bio erosion or by osmosis via the surface membrane. The release mechanism can be pH-activated or pH-independent. The beads can be formulated to produce first order or zero order release.

Pantoprazole is a proton pump inhibitor that has been widely used in the treatment of gastric, duodenal ulcer and also in gastro esophageal reflux disease (GERD), Zollinger-Ellison syndrome. This the most popular drug used in cure and maintenance therapy of peptic ulcer along with

Corresponding Author :- **S.Brito Raj** Email:- britosraj@yahoo.co.in

antibiotics. It suppresses the acid production by inhibiting the Na+ K+ ATPase [1-4]. The absorption of pantoprazole is rapid (C_{max} of 2.5µg/ml,T_{max}~2.5 h) after single or multiple oral 40 mg doses. Pantoprazole is well absorbed (~77% bioavailability). Administration of pantoprazole with food may delay its absorption but does not alter its bioavailability. The serum protein binding of pantoprazole is about 98%, primarily to albumin. At ambient temperature, the degradation half-life is approximately 2.8 h at P^H 5.0 and approximately 220 h at P^H 7.8.

The intention of the present research work was to develop once daily controlled release floating microballoons of pantoprazole using different polymers like HPMC, EC and gelatin for GRDDS along with the loading dose granules with superdisintegrants.

MATERIALS AND METHODS

Pantoprazole sodium was gift sample from Miton laboratories (Pondicherry).HPMC, Ethyl cellulose, and gelatin were from Med zone (Pondicherry). All the chemicals were of analytical grade and double distilled water used throughout the experiment.

Preparation of Microballoons

Microballoons were prepared by Emulsion solvent diffusion method as follows: Pantoprazole and polymer were transferred into a mixture of ethanol and dichloromethane at room temperature separately to get a suspension. The polymeric suspension of Pantoprazole was added into an aqueous solution of polyvinyl alcohol (0.5%w/v, 15 cps, and 200ml) that was thermally controlled at 40^0c. The representative formulations for preparation of Microballoons are given in table 1. The above resultant suspension was stirred with a propeller type agitator at 300 rpm. The finely dispersed droplets of the polymer solution of drug were solidified in the aqueous phase via diffusion of the solvent. The dichloromethane that evaporated from the solidified droplet was removed by a fabricated aspirator flask, leaving the cavity of the microballoons filled with water. After agitating the system for one hour, the microballoons were filtered, washed repeatedly with distilled water and dried in an oven at 40°C [5].

Formulation of Immediate release Pantoprazole sodium granules

The pantoprazole sodium immediate release granules were formulated using sodium starch glycolate, crosspovidone by wet granulation method. All the powders were passed through 60 mesh sieve. Required quantity of drugs, polymers and diluents were mixed thoroughly and a sufficient quantity of granulating agent starch mucilage was added slowly to get dough mass. The mass was sieved through 22/40 mesh and dried at 50° for 2h.The dried granules retained on 40 mesh were mixed with 2% talc and 1% magnesium stearate. The representative proportions for all the formulations were given in table 2.

EVALUATIONS

Differential Scanning Calorimetry

Calorimetric analysis of drug, polymer and drug loaded Microballoons were performed using model DSC-&, Perkin Elmer, equipped with a measuring cell DSC 20. About 2 mg sample was placed in pierced aluminum pans and sealed. All samples were heated at a scanning rate of 10 ºC/min over a temperature range of 25-300 ºC in atmosphere of nitrogen. The instrument was calibrated with an indium standard [6].

Flow properties of IR granules and Microballoons

The flow properties of microparticles were characterized in terms of angle of repose, Carr's index and Hausner's ratio.

Bulk Density

Apparent bulk density was determined by placing pre-sieved drug excipients blend into a graduated cylinder. Measure the weight of the powder. 10g of pre-weighed microparticles were transferred into a graduated measuring cylinder. The Thermonik bulk density apparatus was used to measure bulk density. The volume of the powder is measured. Bulk density of the powder can be determined by the formula given below.

Db = Weight of Powder / Volume occupied by the Powder [7].

Tapped Density

Tapped density was determined by USP method II. Formulation blend was filled in 100 ml graduated cylinder of tapped density tester which was operated for 100 number of tappings, thus tapped density was calculated by following formula [8].

$$Dt = M/Vb$$

Where, M = Weight of powder taken; Vb = tapped volume.

Compressibility Index and Hausner's Ratio

This was measured for the property of a powder to be compressed, as such they are measured for relative importance of inter particulate interactions. Compressibility index was calculated by following equation,

Compressibility index = [(Dt –Db)] / Dt x 100

Where, Dt = tapped density; Db = bulk density;

Hausner's ratio was calculated by following equation,

Hausner's ratio= Dt/ Do

Where, Dt = tapped density; Do = bulk density [9,10].

Angle of repose

A funnel is fixed at a particular height 'h' cm on a burette stand. A white paper is placed below the funnel on the tablet. The given powdered drug whose angle is to be determined is passed slowly through the funnel, until it forms a pile, care is taken to see that the drug particles slip and roll over each other through the sides of the funnel. Further addition of drug is stopped as soon as the drug pile

touches the tip of the funnel. Circumference of the pile of drug is drawn with a pencil and measure the height of the pile without disturbing the pile. The radius of the pile is noted down as 'r' cm. and is calculated by following formula.

$$\text{Tan } \theta = h/r$$

$$\theta = \text{Tan}^{-1} h/r$$

Where, h = height of the pile: r = radius of the pile

Physico chemical properties of Microballoons

Particle Size Determination

The particle size was measured using an optical microscope. The microspheres were dispersed in water, the size of the microspheres were determined by using calibrated eye piece micrometer. The particle size distribution was plotted and the average size was determined [11].

Surface morphology /Scanning Electron Microscopy (SEM)

The external morphology of the microspheres was studied by scanning electron microscopy. The sample of the SEM analysis was prepared by sprinkling the microballoons onto one side of the double adhesive stub. The stubs were then coated with gold using polaran SC 500 sputter coater, to neutralize the electrons and to obtain a clear morphology of the microballoons. The SEM was performed on microballoons after and before dispersing it in 0.1N HCl [12].

Drug entrapment efficiency or incorporation efficiency

To determine the drug entrapment efficiency or incorporation efficiency the microspheres were crushed in glass mortar and powered, then suspended in 10 ml of methanol, after 24 hrs the solution was filtered and filtrate was analysed for drug content [13]. The drug incorporation efficiency was calculated by the following formula:

$$\text{Incorporation efficiency} = \frac{b}{a} \times 100$$

b = calculated amount of drug present in the formulation,
a = theoretical amount of drug present in the formulation

Drug content

Four portions each containing 200 mg were randomly picked from the prepared samples and were crushed with help of mortar and pestle. Then it was stirred continuously for 3h with simulated gastric fluid (pH 1.2). After 3 h, the samples were filtered suitably diluted and estimated spectrophotometrically at 289nm. The estimation was done in 5 replicates to determine the uniformity of drug in microballoons [14].

Production yield

The production yield of the microballoons can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microballoons obtained [15].

$$\text{Production Yield (Y)} = \frac{\text{Practical mass of Microballoons}}{\text{Theoretical Mass (Polymer + drug)}} \times 100$$

Invitro buoyancy

Fifty milligrams of the floating microballoons were placed in simulated gastric fluid (pH 1.2, 100 ml) containing 0.02 w/v% Tween 20. The mixture was stirred at 100 rpm in a magnetic stirrer. After 8 h, the layer of buoyant microballoons was pipetted and separated by filtration. Particles in the sinking particulate layer were separated by filtration. Particles of both types were dried in a desiccator until constant weight. Both the fractions of microballoons were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

$$\text{Buoyancy (\%)} = Wf / (Wf + Ws) \times 100$$

Where Wf and Ws are the weights of the floating and settled microballoons, respectively. All the determinations were made in triplicate [16].

Invitro floating ability

Fifty mg of floating Microballoons were placed in 50 ml beakers and 20 ml of 0.1 M HCl containing 0.02% Tween 20 was added. The beakers were shaken horizontally in a water bath at 37 ± 0.1^{O}C. Floated particles were collected after 10 h and dried in a desiccator to constant weight. The percentage of floating Microballoons was calculated as

% Floating ability = Weight of floating Microballoons/Initial weight of Microballoons X 100

***Invitro* drug release of IR Pantoprazole granules**

The Invitro release studies of pantoprazole from IR granules was carried out in simulated gastric fluid (pH 1.2) using USP XXII apparatus at 100 rpm maintained at a temperature of 37+1ºC for a period of 1h. At periodic time intervals 5ml of sample was withdrawn suitably diluted and the extent drug released was determined spectrophotometrically at 289 nm [17].

***Invitro* drug release of Gastroretentive Pantoprazole Microballoons**

The Invitro release studies of pantoprazole from optimized Microballoons of Gelatin was carried out in simulated gastric fluid (pH 1.2) using USP XXII apparatus at 100 rpm maintained at a temperature of 37+1ºC for a period of 12h. At periodic time intervals 5ml of sample was withdrawn suitably diluted and the extent drug released was determined spectrophotometrically at 289 nm.

***Invitro* drug release kinetics**

The release data obtained was fitted into various mathematical models using PCP disso-V2.08 software. The

parameters 'n' and time component 'k', the release rate constant and 'R', the regression coefficient were determined by korsmeyer-Peppas equation to understand the release mechanism [18].

To examine the release mechanism of drug from microballoons, the release data was fitted into the Peppa's equation.

$$M_t / M_\infty = Kt^n$$

Where, M_t / M_∞ is the fractional release of drug, 't' denotes the release time, 'K' represents a constant incorporating structural and geometrical characteristics of the device, 'n' is the diffusional exponent and characterize the type of release mechanism during the release process.

If n < 0.5, the polymer relaxation does not affect the molecular transport, hence diffusion is Fickian.

If 0.5<n<1.0, the solid transport will be non – Fickian and will be relaxation controlled.

Zero order:

$$\%R = kt$$

This model represents an ideal release in order to achieve prolonged pharmacological action. This is applicable to dosage forms like transdermal systems, coated forms, osmotic systems; as well matrix tablets containing low soluble drugs.

Peppas Korsmeyer Equation:

$$\%R = kt^n$$

$$\text{Log } \% R = \log k + n \log t$$

This model is widely used when release mechanism is well known or when more than one type of release phenomenon could be involved. The 'n' values could be used to characterize different mechanisms.

RESULTS AND DISCUSSION

Pantoprazole sodium immediate release (IR) granules

Micromeritic properties of granules

Among the five formulations of IR granules, F1 showed good flow properties as shown in table 4.

1. Bulk density was found within the range of 0.51±0.01 to 0.55±0.05, tapped density is within range of 0.60±0.02 to 0.65±0.05, it shows good packing efficiency of granules.
2. Hausner's ratio is within the range of 1.1±0.06 to 1.18±0.03, which indicate good flow character, when compared to limits (USP Limits 1.12-1.18).
3. Compressibility Index (%) is within range of 11.35±0.95 to 14.12±1.88, which showed good compressibility of the powder when compared to limits (USP Limits 10-15).
4. Angle of repose was found within range of 22º75'±0.85' to 26°57'±2º48', which indicates that powder exhibit good flow properties, when compared to limits (USP Limits 25° to 30°).

Invitro drug release

The *invitro* drug release profiles of all IR formulations containing SSG, CP superdisintegrants have been shown in figure 3 & table 5. The release of IR pantoprazole mainly depends upon the concentration and type of superdisintegrants. Pantoprazole release from all the formulations was found to be fast and immediate within 60 min, but F1 possess maximum release of 100.74± 1.24 in 30 minutes itself. So, F1 is selected as the best formulation among the Pantoprazole IR granules. The release rate of the drug from the IR granules was found to be maximum with less concentration of SSG.

Flow properties of Pantoprazole Microballoons

All the formulated Microballoons showed good flow properties.

1. For bulk density was found within the range of 0.21±0.01 to 0.29±0.01, tapped density is within range of 0.23±0.01 to 0.41±0.05, it shows good packing efficiency of granules.
2. Hausner's ratio is within the range of 1.19±0.01 to 1.23±0.01, which indicate good flow character, when compared to USP Limits 1.12-1.18.
3. Compressibility Index (%) is within range of 15.9±0.55 to 19.23±0.11, which showed good compressibility of the powder. when compared to USP Limits-10-15.
4. Angle of repose was found within range of 22º34'±0º01'to 22º98'±0º02', which indicates that powder exhibit good flow properties, when compared to USP Limits-25° to 30°.

The flow properties of all the formulations were given in table 6.

Physical properties of Pantoprazole Microballoons

Particle size

The particle size and surface morphology was determined with the help of optical microscope and Scanning Electron microscope. Spherical shaped microballoons were observed with optical microscope. Among the five formulations of Microballoons, F3 possess small particle size (57.75 ± 3.5 µm) and also uniform particle size distribution, with increase in the concentration of surfactant. The use of oil soluble surfactant (2% Span 80) permits the remarkable reduction in size of Gelatin Microballoons as the result of decreasing the interfacial tension and preventing the droplets coalescence and particle size between 57.75µm to 93.75µm. The particle size ranges of all the formulations were shown in figure 8 and table 7.

Surface morphology

SEM study showed that the Microballoons prepared by using gelatin polymer were predominantly spherical in shape with a rough surface. The porous nature and characteristic internal structure of the Microballoons, a hollow cavity inside enclosed with the rigid shell constructed with drug and polymer was clearly evident. The porous nature and cavity formed 6in the Microballoons would dictate the floating behavior of Microballoons of pantoprazole as shown in figure 7.

Drug Entrapment Efficiency

On increasing the concentration of gelatin, the amount of drug entrapment increased as it was observed

maximum 95.31% in F3 and less 72.52% in F5 where the polymer to polymer ratio is 0.5:0.5 for HPMC and gelatin respectively. This shows that increased concentration of controlling agent leads to greater degree of cross linking of polymer chains.The rank order of entrapment efficiency F3> F2> F1>F4> F5 as given in figure 8 and table 8.

Drug content

The drug content in the micro beads was found to be in the range of 85.09 ±1.87 to 96.56 ±1.32 mg. The formulation F3 shows maximum drug content and the values are given in figure 8 and table 7.

Production yield

The percentage yield of all the formulated batches of Microballoons was more than 60 %. Among the prepared batches, batch F3 showed highest percentage yield of 87.50%. The results of production yield for all the batches were shown in figure 8 and table 7.

Buoyancy and floating ability

The formulated floating Microballoons show average Percentage Buoyancy more than 75%. Among the formulated batches, batch F3 shows highest percentage buoyancy effect (88.43%). The comparative buoyancy effect of all the formulations was illustrated in figure 8 and table 7.The floating microballoons can be seen in figure 9.

***Invitro* drug release**

These studies show the effect of environment of the body on the drug release pattern from the prepared Microballoons. The Invitro release was observed in simulated gastric fluid for 12 hrs. It was found that the release rate from all the formulations was found to be different for the different polymer proportions used. The percentage drug release was found to be 54.67%, 59.98%, 68.24%, 59.42% & 66.21 for formulation F1, F2, F3, F4 and F5 respectively. The F3 with polymer gelatin, showed maximum controlled release pattern i.e., 68.24± 3.79 in 12^{th} hr, as shown figure 11 & table 9. So F3 was selected as the best Gastro retentive formulation.

Invitro release kinetics

By applying the time vs cumulative % drug release in release kinetics datas, formulation F3 shows a best fit for Peppas model and its *n* value is 0.7915 0.5<n<1.0, so the solid transport will be Non – Fickian and will be relaxation controlled release mechanism and it is based on Zero order release kinetics with R^2 value 0.999 which represents an ideal release in order to achieve prolonged pharmacological action. The results are shown in table 10, figure 12&13.

Table 1. Release Kinetics

Release Exponent 'n'	Drug Transport Mechanism	Rate as a function of time
0.5	Fickian Diffusion (Higuchi Matrix)	$t^{n-0.5}$
0.5<n<1.0	Non-Fickian Diffusion	t^{n-1}
1.0	Case – II Transport (Zero Order Release)	Zero Order Release
Higher Release (n>1)	Super Case – II Transport	t^{n-1}

Table 2. Formulation of pantoprazole microballoons

Microballoons ingredients(mg)	F1	F2	F3	F4	F5
Internal Phase					
Pantoprazole sodium	**1**	**1**	**1**	**1**	**1**
HPMC	**1**	**-**	**-**	**-**	**0.5**
EC	**-**	**1**	**-**	**0.5**	**-**
Gelatin	**-**	**-**	**1**	**0.5**	**0.5**
External Phase					
PVA	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**

Table 3. Formulation of Pantoprazole Sodium IR granules

IR ingredients (mg)	F1	F2	F3	F4	F5
Pantoprazole sodium	**5**	**5**	**5**	**5**	**5**
Lactose	**25**	**25**	**25**	**25**	**25**
Starch	**17**	**15**	**17**	**15**	**15**
Sodium Starch Glycolate(SSG)	**2**	**4**	**-**	**-**	**2**
Cross Povidone (CP)	**-**	**-**	**2**	**4**	**2**
Magnesium Stearate	**1**	**1**	**1**	**1**	**1**

Table 4. Preformulation studies of IR pantoprazole granules

Batch code	Parameters				
	Angle of repose(θ)	Bulk Density(g/ml)	Tapped density(g/ml)	Carr's Index (%)	Hausner's ratio
F1	22.75±0.85	0.55±0.03	0.45±0.05	11.35±0.95	1.12±0.01
F2	24.18±1.05	0.55±0.05	0.55±0.05	14.12±1.88	1.16±0.03
F3	23.60±0.02	0.53±0.01	0.45±0.05	13.81±0.77	1.16±0.01
F4	25.53±0.01	0.51±0.01	0.44±0.02	13.25±0.75	1.1±0.06
F5	26.57±2.48	0.55±0.05	0.64±0.05	15.36±2.03	1.18±0.03

Table 5. *Invitro* release study for IR Pantoprazole sodium granules F1-F5 in SGF

Time (min)	F1	F2	F3	F4	F5
0	10.37	0.35	1.99	2.82	8.37
5	53.22	17.87	19.62	28.82	31.14
10	76.03	36.22	40.77	53.97	59.07
15	87.91	46.61	53.22	79.41	70.25
20	98.80	54.13	69.34	96.12	88.37
30	100.74	79.26	86.27	98.44	94.80
45	101.56	85.72	94.98	100.11	98.44
60	102.25	93.25	98.21	101.23	99.68

EVALUATION PARAMETERS OF MICROBALLOONS

Table 6. Flow characteristics of Microballoons

Batch code	Parameters				
	Angle of repose(θ)	Bulk Density(g/ml)	Tapped density(g/ml)	Carr's index(%)	Hausner's ratio
F1	22.98±0.02	0.21±0.01	0.26±0.01	19.23±0.11	1.23±0.01
F2	22.34±0.01	0.29±0.01	0.35±0.01	16.34±0.02	1.20±0.02
F3	21.80±1.73	0.2±0.01	0.23±0.01	15.9±0.55	1.19±0.01
F4	21.91±0.73	0.34±0.01	0.41±0.05	16.76±1.50	1.20±0.01
F5	21.99±0.01	0.21±0.02	0.25±0.01	18.14±0.90	1.22±0.01

Table 7. Evaluation of Pantoprazole Microballoons F1-F5

Formulations code	Particle size(µm)	Production yield	Drug content (%w/v)	% drug entrapment efficiency	%Moisture loss	%buoyancy	Floating ability
F1	67.16± 3.0	77.55	86.15±1.42	78.16 ±1.12	4.57±0.02	75.89±2.3	77.80±4.2
F2	74.25 ±7.0	75.28	95.87 ±1.28	88.11 ±1.38	4.63±0.29	75.2±4.6	75.7±2.7
F3	57.75± 3.5	87.50	96.56 ±1.32	95.31 ±1.59	1.69±0.12	88.43±3.2	87.58±2.4
F4	87.65± 4.5	72.32	89.66 ±1.59	75.27 ±1.62	3.97±0.11	80.7±4.8	80.8±3.3
F5	93.75± 8.5	65.82	85.09 ±1.87	72.52 ±2.18	2.92±0.08	83.4±2.1	81.22±4.5

Table 8. Standard Graph for Pantoprazole sodium

Concentration µg/ml	Absorbance at 289 nm
5	0.185
10	0.411
15	0.630
20	0.814
25	1.065
30	1.296

Table 9. *Invitro* release profile for pantoprazole sodium Microballoons in SGF

Time (hr)	F1	F2	F3	F4	F5
1	4.94	5.26	6.93	4.38	5.68
2	10.30	15.47	18.84	10.54	12.51
3	12.57	18.29	20.17	15.54	19.25
4	16.40	18.42	20.90	15.76	20.63
5	16.73	20.28	23.96	18.46	21.67
6	19.64	21.97	24.79	20.68	22.16
7	20.47	24.21	27.58	21.75	26.10
8	22.89	24.89	35.69	23.90	29.64
10	42.35	45.65	62.58	55.71	60.64
12	54.67	59.98	68.24	59.42	66.21

Table 10. *Invitro* release kinetics

F3 Pantoprazole Sodium+ Gelatin(1:1)	2 hrs	0.898	0.902	0.962	0.571
	4 hrs	0.961	0.940	1	2.14
	8 hrs	0.999	0.996	1	0.986
	12 hrs	0.999	0.994	0.9653	0.7915

Figure 1. Diagram of stomach

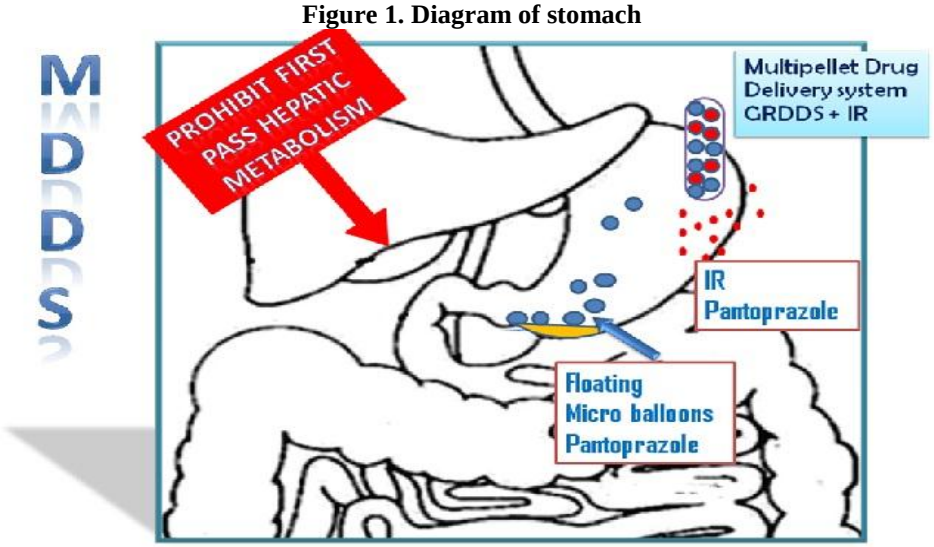


Figure 2. Capsulated Microballoons and IR Granules

Figure 3. Cumulative drug release profile for F1-F5 IR granules

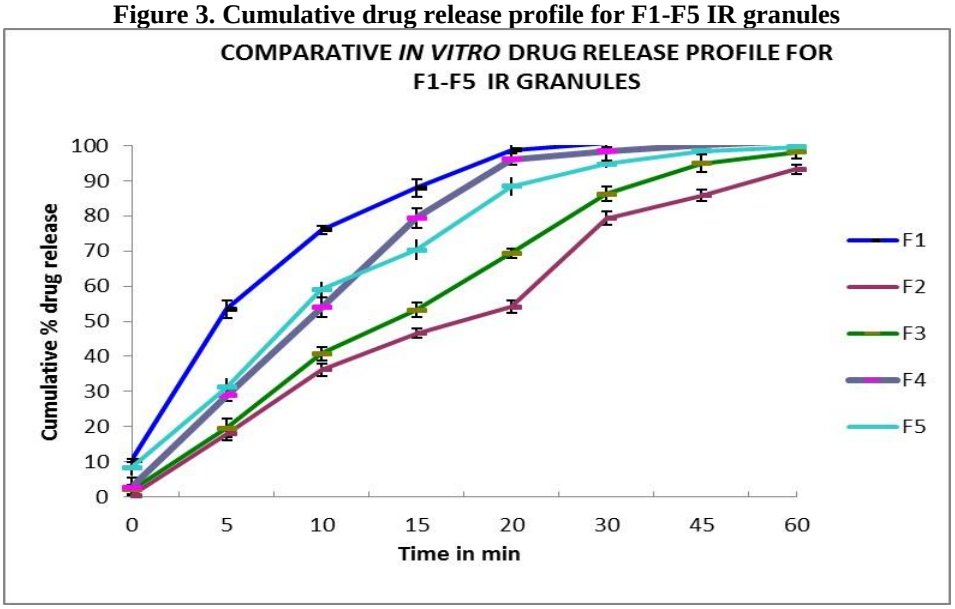


Figure 4. DSC- Pantoprazole + HPMC

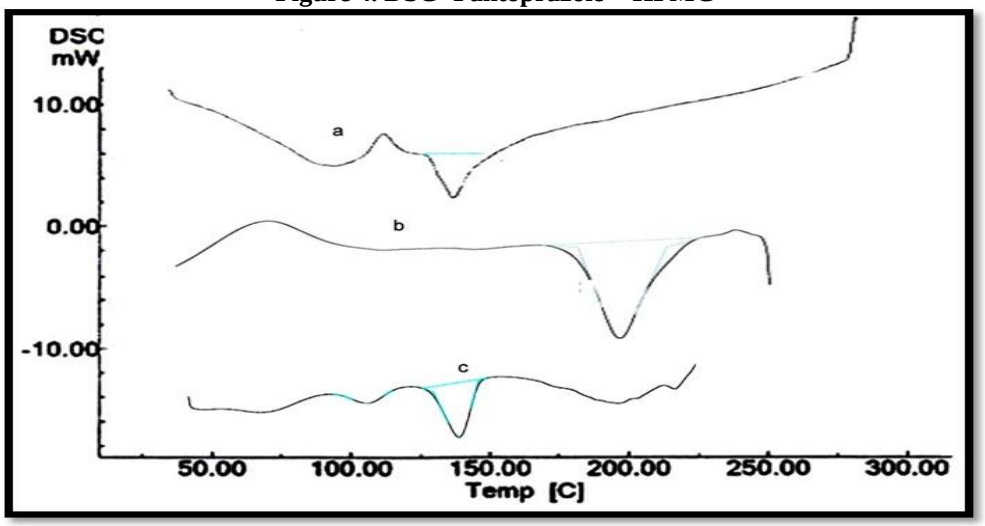


Figure 5. DSC- Pantoprazole + EC

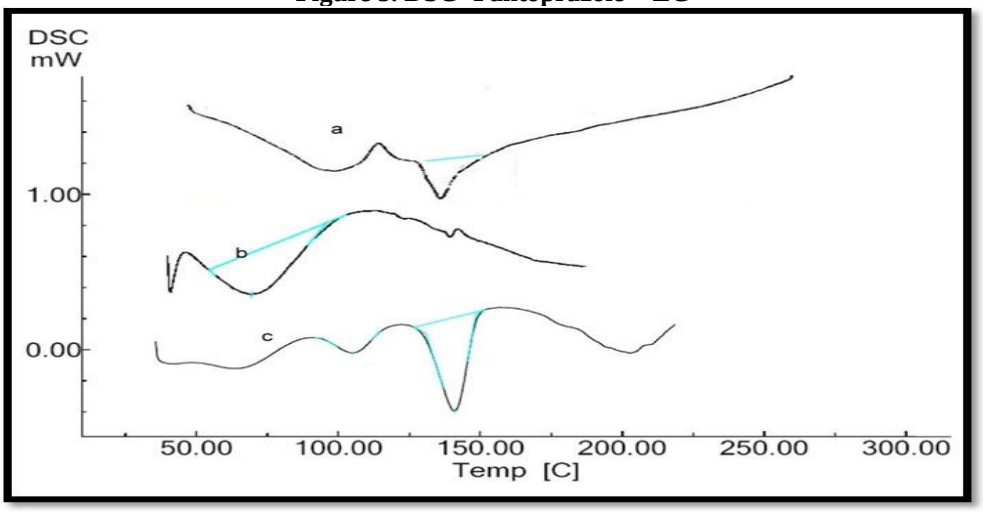


Figure 6. DSC- Pantoprazole + Gelatin

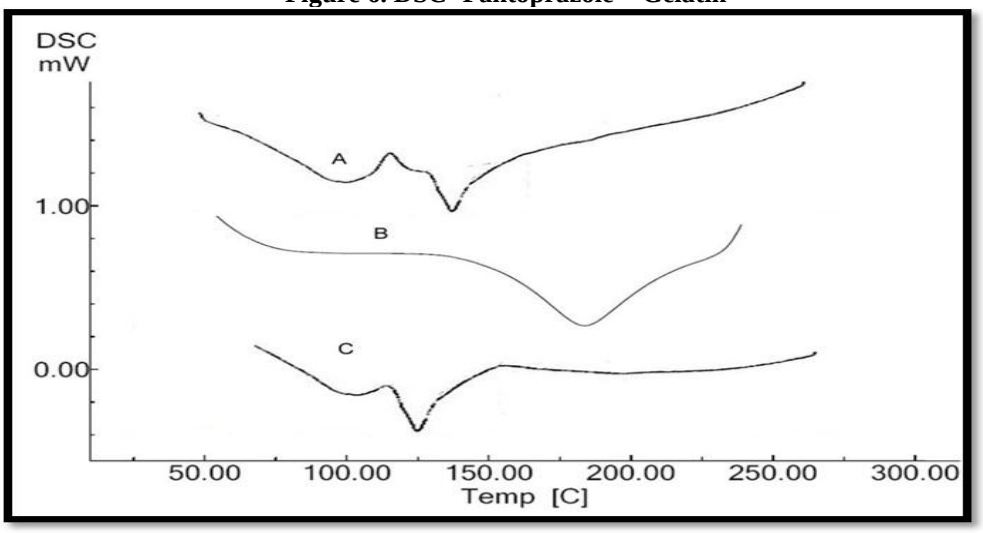


Figure 7. SEM Photography of pantoprazole loaded microballoons

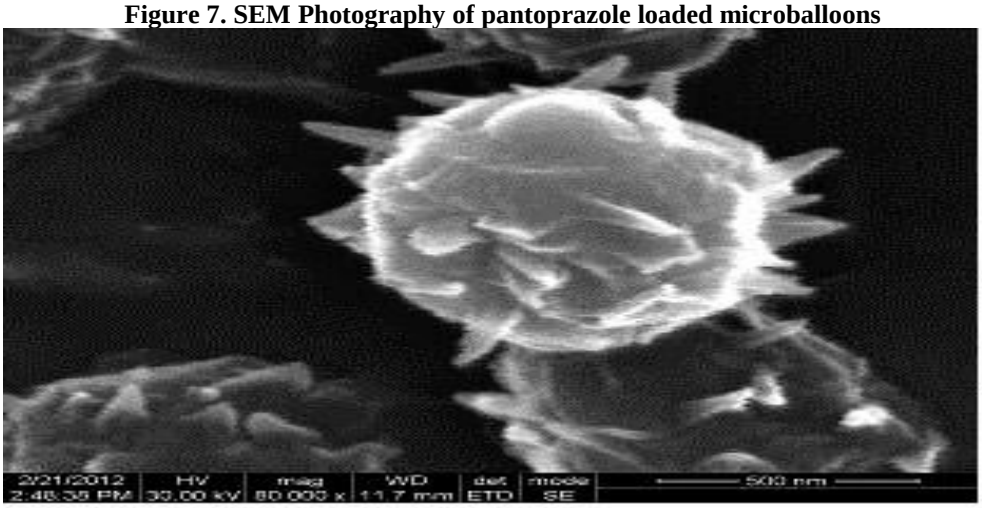


Figure 8. Particle size, Production yield, Drug content, Drug entrapment efficiency, Buoyancy effect of Microballoons

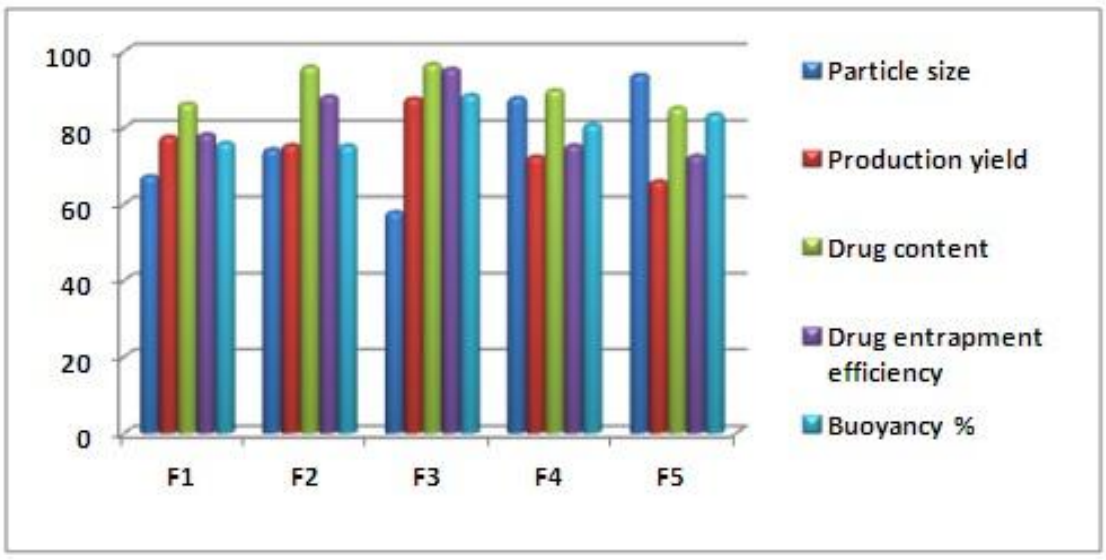


Figure 9. Floating view of Pantoprazole loaded Microballoons in SGF

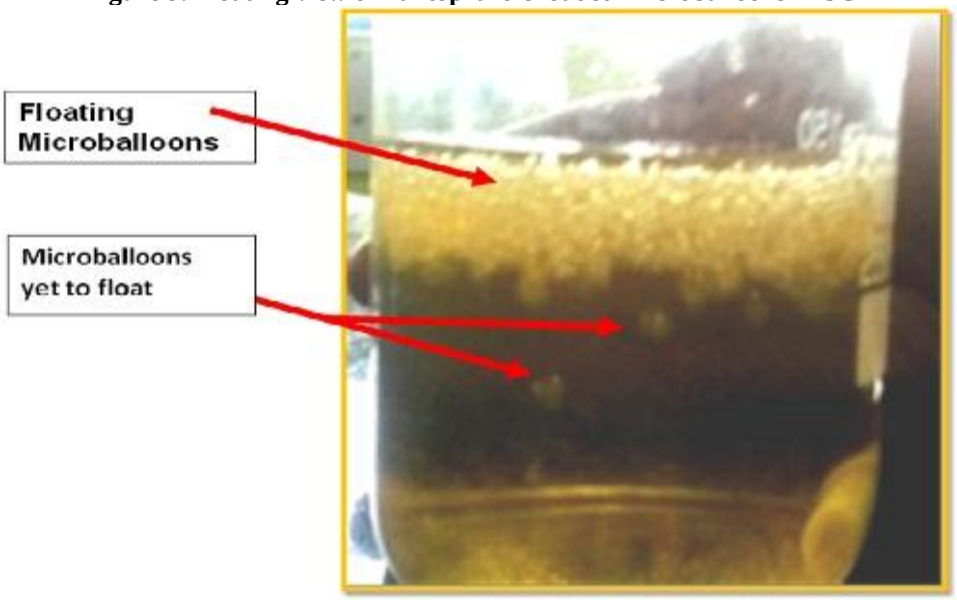


Figure 10. Standard graph for Pantoprazole sodium

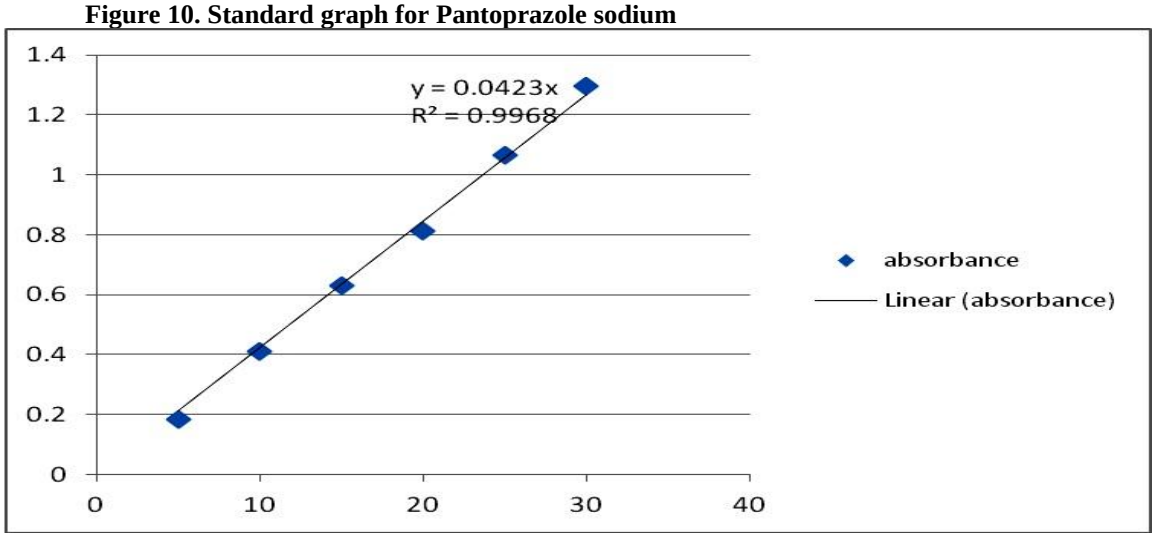


Figure 11. Comparative Invitro drug release - F1-F5 Microballoons

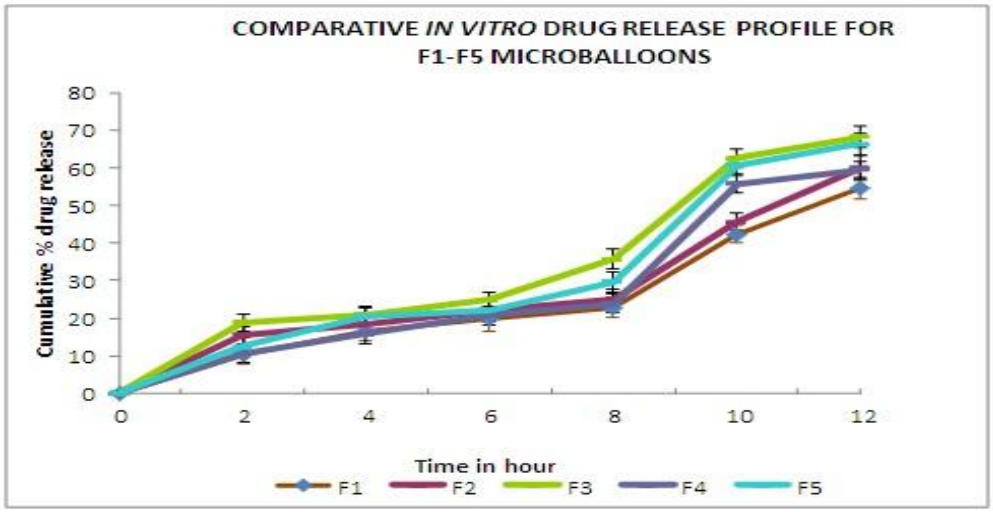


Figure 12. Zero order Invitro release kinetics

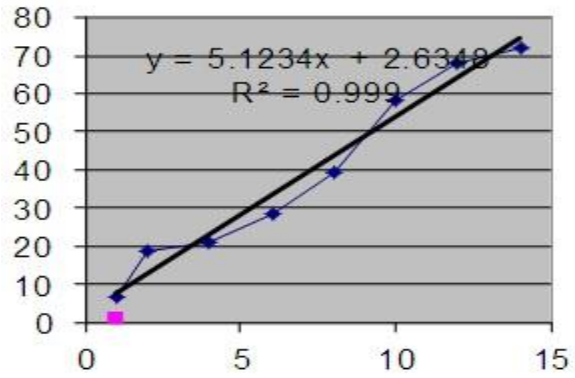
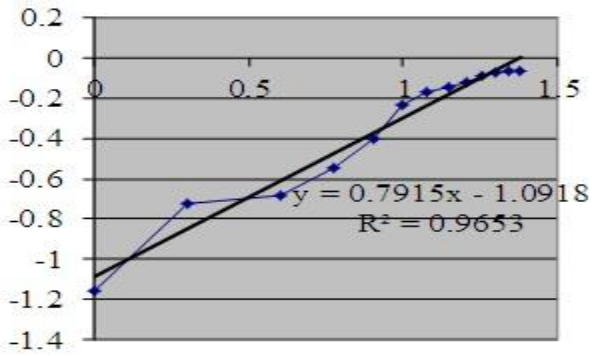


Figure 13. Peppas curve



CONCLUSION

Once daily dosage form of Floating Microballoons of Pantoprazole sodium along with immediate release granules were formulated and evaluated.

Thus the Pantoprazole Floating Microballoons (F3) has achieved the objective of controlled drug delivery with prolonged release, decreased dose and frequency of administration, cost effective and hence it will improve patient compliance.So the Optimized Formulation of Pantoprazole Microballoons (F3) and IR pantoprazole granules (F1) were an ideal dosage form for Chronic Peptic ulcer condition.

ACKNOWLEDGEMENT

We would like to express our sincere thanks to our Chairman Dr. Ravuri Venkataswamy and Vice Chairman Mr. R.V. Srinivas, for providing adequate facility to carry out our project successfully and also extend our sincere thanks to our beloved Principal Dr. K. Bhaskar Reddy for immense support in making this project a successful one.

REFERENCES

1. Paul W. Pantoprazole: A New Proton Pump Inhibitor. *Clinical Therapeutics*, 22, 2000, 1268-1293.
2. John H. The Proton-Pump Inhibitors: Similarities and Differences. *Clinical Therapeutics*, 22(3), 2000, 266-280.
3. Katz P. Pharmacologic Basis of Pantoprazole Dosing Current therapeutic research. *Clinical Therapeutics*, 61(6), 2000, 8.
4. Geraldine M, Ferron J. Pharmacokinetics of Pantoprazole in Patients with Moderate and Severe Hepatic Dysfunction. *Clinical therapeutics*, 23, 2000, 1180-1192.
5. Nagita A, Manago M. *Ther. Drug. Mon*, 16, 1994, 444-449.
6. Parmar Kunal Vinodbhai, Gohel MC, Parikh RK, Shital Bariya and Rajeshvari Suthar N. Sustained Release Floating Microspheres Of Acyclovir: Formulation, Optimization, Characterization And In Vitro Evaluation. *International Journal of Drug Development and Research*, 3(1), 2011, 242-251.
7. Arora S, Ali J, Ahuja A, Khar RK and Baboota S. Floating Drug Delivery Systems: A Review. *AAPS PharmSciTech*, 06(03), 2005, E372-E390.
8. Talukder R, Fassihi R. Gastroretentive drug delivery system: A mini review. *Drug Dev.Ind.Pharm*, 30, 2004, 1019-1028.
9. Gaba Punam.Floating microspheres : A Review. *Pharmainfo.net*, 6(5), 2008.
10. Tanwar YS, Floating microspheres: Development, Characterization and applications. Pharmainfo.net, 4(3), 2006.
11. Orlu M, Cevher E and Araman A. Design and evaluation of colon specific drug delivery system containing flubiprofen microsponges. *Int. J. Pharm*, 318, 2006, 103-17.
12. Ramachandran S, Shaheedha SM, Thirumurugan G and Dhanaraju MD. Floating Controlled Drug Delivery System of Famotidine Loaded Hollow Microspheres (Microballoons) in the Stomach. *Current Drug Delivery*, 7, 2010, 93-97.
13. Rajeshwar KK, Arya, Vijay juyal and Ripudaman singh. Development and evaluation of gastro resistant microspheres of pantoprazole. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2(3), 2010, 103-107.
14. Koresmeyer RW, Gurny R, Doelkar E, Buri P and Peppas NA. Mechanisms of solute release from porous hydrophilic polymer. *Int. J. Pharm*, 15, 1983, 23-25.
15. Kilicarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. *Int. J. Pharm*, 252, 2003, 99–109.
16. Kawashima Y. Physicochemical properties to determine the buoyancy of hollow microspheres (microballoons) prepared by the emulsion solvent diffusion method. *Eur. J. Pharm. Bio pharm*, 55, 2003, 297-304.
17. Choi BY, Park HJ, Hwang SJ and Park JB. Preparation of alginate beads for floating drug delivery system: effects of CO_2 gas forming agents. *Int. J. Pharm*, 239, 2002, 81-91.
18. Costa Paulo, Souse Lobo JM. Modeling and compression dissolution profiles. *Eur. J. Pharm. Sci*, 13, 2001, 123-33.