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## Gastro-Retentive Microballoons of Propafenone HCL: Formulation, Development and its In-Vitro Evaluation

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### ABSTRACT:

The present study is aimed to develop gastro-retentive microballoons of Propafenone HCl using emulsion solvent diffusion method using Eudragit S 100 as a polymer and polyvinyl alcohol (PVA) as an emulsifier. As microballoons are hollow from inside and drug is loaded at outer shell with polymer, the drug is slowly released from the outer shell when they come into contact with gastric fluid. Due to low density than the gastric fluid they showed excellent buoyancy for more than 12 hrs and released the drug for that much period of time. Different concentration of Eudragit S 100 and PVA were taken as an independent variables and 32 full factorial design was applied for the optimization. Microballoons were evaluated in terms of % Drug entrapment efficiency, %Yield, %Buoyancy and In Vitro %Drug release profile. Cumulative percentage drug release of optimized batch was also carried out using modified dissolution method and short term stability was also carried out for the same. Kinetic model fitting showed that the first order fits best for the release of the drug from microballoons and n value from the Korsmeyer and Peppas model showed that the mechanism of was found to be non fickian diffusion. Optimized batch was compared with marketed product and was showing satisfactory results.

**Key words:** Microballoon, Propafenone HCl, Emulsion solvent diffusion, Gastroretentive, Eudragit S 100, PVA.

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### INTRODUCTION:

Despite of most important route, there are some obstacles which are associated with oral controlled release formulations such as physiological variations in GI transit and gastric retention time (GRT). In addition to this, drug release after passing through the absorption site cannot be completely utilized because of the less GRT of the delivery system. So that it is not possible to deliver the drug for more than 12 hrs orally [1]. So that to overcome this problem gastric retention is essential. The prolongation of gastric retention time of the delivery systems can be achieved by different gastroretentive systems such as mucoadhesive systems, magnetic systems, high density system, raft forming systems, superporous hydrogels, low density systems such as floating hollow microspheres and floating ion exchange resins. Here in the bioadhesive system the dosage form sticks to the mucin-epithelial cell surface, which will provide longer transit time because of the adhesion of the device to the gastric wall. This type of adhesion may cause difficulties such as irritation to mucosa if an over dose of the drug occur. Other option is floating dosage forms which have a specific density lower than the gastric fluids and due to this they remain buoyant in the stomach fluid. Most of the floating systems are single unit dosage forms which are also known as hydrodynamically balanced systems. But the main

disadvantage of this system is high variability of the GI transit time, because of its all or nothing emptying process. So that a multiple unit floating system is utilized which can be dispersed widely throughout the GI tract and so it will provide a longer and more reliable release of drugs [2, 3].

An object of the present study was to prepare floating microballoons which are one of the multiparticulate delivery systems consisting of propafenone HCl as a drug and Eudragit S 100 as a low density polymer. Microballoons are capable of floating on gastric fluid due to their excellent buoyancy for more than 12 hrs and are able to release the drug for that much period of time. Microballoons can also offer benefits like limiting fluctuation within the therapeutic range, reducing side effects, decreasing dosing frequency, and improving patient compliance. Microballoons have a characteristic internal hollow structure and show an excellent in vitro floatability.

Propafenone HCl is a Class 1C antiarrhythmic drug which is having direct stabilizing action on myocardial membrane as well as a local anaesthetic effect. It is mainly used in the treatment of atrial and ventricular arrhythmias. The main mechanism of action of this drug is that it decreases the influx of sodium ion in cardiac muscle cells which will ultimately lead to decrease excitability of the cells. Propafenone HCl has a short half-life i.e. about 2-10 hrs and low bioavailability (approximately 10%). It is also having a narrow absorption window. Because of this the drug has to be taken frequently. The usual dose is 150 mg to taken three times a day or 300 mg twice a day. Moreover absorption site of Propafenone HCl is a GI tract. So gastric retention will improve its absorption. In the treatment of cardiac arrhythmias, angina and hypertension, a loading as well as maintenance dose is required. So Propafenone HCl has all the properties which are required for gastroretention and due to this reason it was selected as the candidate drug for the preparation of gastroretentive microballoons [4-6].

#### **MATERIALS AND METHOD:**

Propafenone HCl was procured as a gift sample from Cadila Healthcare Ltd., (Ahmedabad). Eudragit S 100 was procured from Evonik Industries. Ethanol was procured from Shree ChaltanVibhag and Dichloromethane (DCM) was procured from Finar Chemicals Ltd. (Ahmedabad).

Then polyvinyl alcohol (PVA) was procured from Laser Laboratories.

#### **METHOD OF PREPARATION:**

In the present work Microballoons were prepared by **emulsion solvent diffusion method**. In this drug here propafenone HCl (225mg) and polymer (Eudragit S 100) (in different ratio) were dissolved or dispersed into the mixture of ethanol and dichloromethane (in 1:1 ratio). Then this mixture was added drop wise into the solution of PVA in water (in different concentration). This was then stirred with magnetic stirrer at room temperature at 200 rpm for 1 hr. Then the formed microballoons (floating Microspheres) were washed with purified water and dried into the desiccator at room temperature. Then they were sieved and collected.

#### **EVALUATION PARAMETERS OF MICROBALLOONS: [7]**

##### **Micromeritic Properties:**

The prepared microballoons were characterized and evaluated by their micromeritic properties such as Particle size, True density, Bulk density, Tapped density, Carr's index (Compressibility), Hausner's ratio and Angle of repose.

##### **Particle size:**

The Particle size of microballoons was determined using an optical microscopic method. Hundred particles were measured in the optical microscope at a time. Then their mean particle size was calculated using calibrated ocular micrometer.

##### **True density:**

Microballoons were placed in metal mesh basket which is then immersed into the solution of tween 80 (0.02%) for three days. After three days, the submerged microballoons were used for the measurement of density. True density was determined by liquid displacement method with the help of relative density bottle.

##### **Bulk Density:**

The bulk density is the ratio of the mass of an untapped material and its volume which is including the interparticulate void volume. Hence it is depending on both the density of material and the arrangement of particles. The bulk density of a powder is determined by

measuring the volume of a known weight of sample into a graduated cylinder, or by measuring the mass of a known volume of material that has been passed through a volumeter into a cup or a measuring vessel.

$$\text{Bulk density} = \frac{\text{Weight of sample}}{\text{Volume of sample}}$$

It is expressed in gm/ml or gm/cm<sup>3</sup>.

#### **Tapped Density:**

It is an increased bulk density which is obtained by mechanically tapping a container containing sample. Here graduated measuring cylinder is used for tapping. After observing initial volume or weight the container is tapped and the readings are taken until further change in volume or weight is observed. It can be calculated by following equation:

$$\text{Tapped density} = \frac{\text{Weight of sample}}{\text{Tapped volume}}$$

#### **Carr's Index (Compressibility):**

The carr's index is mainly used for an indication of compressibility of sample. This will help into the indication of flowability of sample. It can be calculated by following equation:

$$\text{Carr's index(\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

The relationship between type of flow and carr's index is shown in table 1

#### **Angle of Repose:**

It is an indicative term for the flow property of sample. Here angle of repose was determined by fixed funnel method. In this method, funnel was adjusted in such a way that the stem of the funnel lies 2.5 cm above the horizontal surface. The sample was allowed to flow from the funnel until the height of pile touched the tip of funnel. Then the diameter of pile was determined. This can be calculated by following equation:

$$\tan \theta = h/r$$

$$\text{Therefore, } \theta = \tan^{-1} (h/r)$$

Where,  $\theta$  is angle of repose,  $h$  is height of the pile;  $r$  is the radius of the pile.

Angle of repose as an indication of flow property has been given in the table 2

#### **Hausner's ratio**

The Hausner's ratio is mainly used for an indication of the compressibility of a powder. It is calculated by the formula,

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

The Hausner's ratio is also used for the indication of the flowability of a powder. If a Hausner's ratio greater than 1.25 then it is considered to be an indication of poor flowability.

#### **Drug-Excipient Compatibility:**

Drug-Excipient compatibility study was done by FTIR spectra of pure drug and formulation. Differential Scanning Calorimetry (DSC) was also carried out for detection of interaction between drug and excipients.

#### **% Yield:**

% Yield of floating microballoons was calculated by dividing actual weight of product to the total amount of all non-volatile components that are used for preparation of microballoons. It can be calculated by following formula:

$$\% \text{ Yield} = \frac{\text{Actual weight of product} \times 100}{\text{Total weight of drug and Excipients}}$$

#### **% Drug Entrapment Efficiency (DEE):**

The drug entrapment efficiency was determined by crushing the microballoons and then extracting them with aliquots of 0.1N HCl repeatedly. Then this extract was transferred to a 100 ml volumetric flask. Then the volume was made up with the help of 0.1N HCl. The solution was then filtered and the absorbance is measured by UV- Spectrophotometer against appropriate blank. Then entrapped amount of drug can be calculated by following equation:

$$\% \text{DEE} = \frac{\text{Amount of drug actually present} \times 100}{\text{Theoretical drug load expected}}$$

#### **In vitro Buoyancy:**

% Buoyancy of microballoons was done by using an USP dissolution test apparatus II. In this microballoons (50mg) were taken into the 0.1 N HCl as a medium. Then the medium was agitated with a paddle which is rotating at 100 rpm and maintained at 37°C by heater. After 12 hours, both the floating and the settled microballoons were collected separately. Then the microballoons were dried and weighed. The % buoyancy was calculated by the following equation:

$$\% \text{ Buoyancy of microspheres} = \frac{W_f \times 100}{W_f + W_s}$$

Where  $W_f$  and  $W_s$  are the weight of the floating and settled microspheres respectively.

#### **In-Vitro drug release of microballoons:**

*In vitro* dissolution studies were done using USP paddle type apparatus (Type - II Apparatus). Microballoons equivalent to the drug dose were filled in hard gelatine capsules size "0". The capsules were placed in the vessel containing 900 ml of 0.1 N HCl. The temperature and stirring rate were  $37 \pm 0.5$  °C and 100 rpm respectively. 5 ml Sample was withdrawn at regular time intervals and replaced with freshly prepared medium. The collected sample was filtered using whatman filter paper and after suitable dilution was analysed spectrophotometrically at 250 nm using Shimadzu-1700 UV-Visible spectrophotometer.

#### **Modified Dissolution Method**

In this method glass beaker (100ml capacity) was modified at the base by adding S-shaped glass tube so that the glass beaker can hold 70 ml of dissolution medium. The medium was stirred on the magnetic stirrer. A burette was mounted above the beaker to deliver the dissolution medium at a flow rate of 2 ml/min.

#### **Morphological Study using SEM**

The external and internal morphology of the microballoons were determined by scanning electron microscopy (SEM). SEM mainly uses the focused beam of high electrons to generate variety of signals at the surface of sample and due to electron-sample interactions the information about external morphology can be determined. Essential components of SEM are electron source, electron lenses, sample stage, detectors, and display.

#### **Gas Chromatography**

Gas chromatography of dosage form was done for the detection of volatile substances into the final product. In GC the mobile phase is a carrier gas usually helium or nitrogen and the stationary phase is a microscopic layer of liquid or solid inside the column.

#### **Kinetic Analysis of Drug Release Data:**

In order to investigate the mechanism of release, the data were analyzed with the following mathematical models [8]: Zero order kinetic (1), First order kinetic (2), Higuchi Model (3).

$$Q_t = Q_0 + K_0 t \dots\dots\dots (1)$$

$$\log Q_t = \log Q_0 + K_1 t / 2.303 \dots\dots\dots (2)$$

$$Q_t = K_H \cdot t^{1/2} \dots\dots\dots (3)$$

The following plots were made:  $Q_t$  vs.  $t$  (zero order kinetic model),  $\log (Q_0 - Q_t)$  vs.  $t$  (first order kinetic model) and  $Q_t$  vs.  $t^{1/2}$  (Higuchi model), where  $Q_t$  is the percentage of drug released at time  $t$ ,  $Q_0$  is the initial amount of drug present in the formulation and  $K_0$ ,  $K_1$  and  $K_H$  are the constants of the equations[9]. Further, to confirm the mechanism of drug release, the Krosmeier and Peppas Release Model was also applied because from  $n$  value release mechanism can be determined. (4)

$$M_t / M_\infty = K \cdot t^n \dots\dots\dots (4)$$

Where  $M_t / M_\infty$  are the fraction of the drug release at time  $t$ ,  $K$  is the rate constant and " $n$ " is the release exponent. The value of " $n$ " is used to characterize different release mechanisms and is calculated from the slope of the plot of log of fraction of drug released ( $M_t / M_\infty$ ) vs. log of time.

#### **RESULTS AND DISCUSSION:**

The microballoons were prepared by emulsion solvent diffusion method. In this method, a solution of polymer and propafenone HCl in ethanol and dichloromethane was poured into an agitated aqueous solution of PVA in purified water.

As a part of preliminary study three batches were prepared at a different stirring speed while keeping all other parameters constant. Based on preliminary trials (data not shown), 200 rpm speed was selected as an optimized speed. From the other preliminary trials (data

not shown) it was found that Eudragit S 100 was giving more % Yield, %DEE, %Buoyancy and %drug release as compared to Eudragit L 100. So Eudragit S 100 was selected as the final polymer based on preliminary evaluation. Different batches were prepared with different concentration of Eudragit S 100 in order to determine optimum concentration range. The results showed that, as the concentration of Eudragit S 100 increases, the particle size of microballoons also increases. Drug to polymer ratio of 1:1, 1:3, and 1:5 were selected for full factorial design. For the selection of concentration ranges of PVA different batches were prepared at different concentration of PVA which were showing that %DEE (% Drug entrapment efficiency) and buoyancy were decrease as on increasing PVA concentration due to emulsifying ability which would lead to increase the extraction of drug into processing medium. Buoyancy would decrease due to tightening of polymeric network. Three levels of PVA: 0.75%, 1% and 1.25% were selected on the bases of evaluation parameters.  $3^2$  full factorial design was applied with Drug: Polymer ratio (1:1, 1:3, 1:5) and PVA concentration (0.75%, 1% and 1.25%) as independent variables. Dependent variables were %Yield, %Drug Entrapment Efficiency, %Buoyancy and %Drug release at 12 hr. Formulation of  $3^2$  full factorial design has been given in the table 3.

Drug-Excipient compatibility was done by FTIR [10] spectroscopy [Figure 1, 2, & 3] and DSC to establish any possible interaction of Propafenone HCl with polymer. The results indicated that the characteristic absorption peak for pure drug was also appeared in the mixture of drug and excipient indicating that there was no interaction between drug and excipient.

Propafenone HCl gave sharp endothermic peak at 174.5 °C in DSC study. The peak of drug in physical mixture with polymer observed at 173.49 °C indicating that the drug and polymer were compatible with each other [Figure 4 & 5].

#### Optimization of Process Variables:

##### Effect of Polymer:

Concentration of polymer was found to be the most vital factor on preparation of microballoons. As the concentration of Eudragit S 100 increases particle size, % yield, % drug entrapment efficiency and % buoyancy also increases but % drug release decreases. This effect may

be attributed to the formation of tight matrix with Eudragit S 100 which will reduce drug release.

##### Effect of emulsifying agent:

As the concentration of emulsifying agent (PVA) increases the drug entrapment efficiency and buoyancy were found to decrease. Increase in emulsifier concentration resulted in increase in miscibility of ethanol with dichloromethane, which may increase the extraction of drug into the processing medium. The decrease in buoyancy with increase in emulsifier concentration is due to tightening of polymeric network leading to microballoon shrinkage and increase in density.

##### Micromeritic Properties:

The bulk density values of formulation M1 to M9 were found in the range of  $0.3153 \pm 0.0004 \text{ gm/cm}^3$  to  $0.1056 \pm 0.005 \text{ gm/cm}^3$ . The tapped density values were ranged from  $0.352 \pm 0.002 \text{ gm/cm}^3$  to  $0.1239 \pm 0.003 \text{ gm/cm}^3$ . True density was found to be in range of  $0.88 \pm 0.02 \text{ gm/cm}^3$  to  $0.74 \pm 0.008 \text{ gm/cm}^3$ . Microballoons showed excellent floating ability due to low density. Flow properties were found to be good as expressed in terms of angle of repose and carr's index. Good flow property ensures uniform filling in capsules during capsule filling operation. (Shown in the table 4)

##### Particle Size:

It was found that mean particle size was increased as the concentration of Eudragit S 100 increased. This is due to the fact that the viscosity of the medium increases at a higher polymer concentration resulting in enhanced interfacial tension. Shearing efficiency is also diminished at higher viscosities. This results in the formation of larger particles. The mean particle size was found in the range of  $425.82 \pm 2.66 \mu\text{m}$  to  $123.52 \pm 1.34 \mu\text{m}$ . (Shown in the table 4)

##### %Yield and % Drug Entrapment Efficiency:

%Yield of all formulation batches M1 to M9 were found in the range of  $92.14 \pm 0.36$  to  $78.86 \pm 1.85 \%$ . All the formulations showed satisfactory yield. % yield was found to be directly proportional to the concentration of the polymer as well as PVA. All the formulations showed satisfactory entrapment efficiency ranging in  $75.32 \pm 1.24$  to  $81.87 \pm 1.20$ . The results showed that as the concentration of Eudragit S 100 increases the

entrapment efficiency also increases but it decreases with increasing concentration of PVA due to extraction of drug in presence of high emulsifying agent. (See table 5 & Figure 6, 7)

#### **%Buoyancy:**

Density values of all formulations were less than that of gastric fluid ( $1.004\text{gm/cm}^3$ ) indicating that they exhibit good buoyancy. It was found in the range of  $80.08 \pm 0.63$  to  $91.34 \pm 0.48$ . Buoyancy decreases as the concentration of PVA increases due to tightening of polymeric network. (See table 5 & Figure 8)

#### **In Vitro drug release study:**

The required quantities of microballons (Corresponds to 225 mg of propafenon HCl) were filled in hard gelatine capsule size "0". *In Vitro* drug release study was carried out in 0.1 N HCl for 12 hrs. The drug release data are shown in figure 9. From the result, it was found that higher ratio of polymer blends lead to lower drug release. This is due to increase in density of the polymer matrix at higher concentrations resulting in an increased diffusional path-length. Batch M4 to M6 showed high cumulative drug release ( $97 \pm 0.10$ ,  $96.28 \pm 0.15$ ,  $95.36 \pm 0.05$ ) but M6 gave best results in terms of yield, drug entrapment efficiency and buoyancy so it was found to be the best formulation.

#### **Kinetic Analysis of release data:**

The result shows that **first order** model was best fit for the release of propafenone HCl from microballoons because it showed minimum MSE and AIC value and maximum MSC value. In Korsmeyer and Peppas model,  $n$  was found to be 0.60 which indicated non fickian diffusion was the proposed mechanism of drug release. (Data shown in the table 6)

#### **Scanning Electron Microscopy:**

SEM for optimized batch M6 suggested that microballoons were found to be spherical in shape with smooth surface with a hollow space inside. (See figure 10)

#### **Gas Chromatography:**

From the gas chromatography of standard (ethanol and DCM solution) and sample (Batch M6) it was found that in the final product the negligible amount of ethanol and

DCM were present. GC of sample they were showing very small peak (where DCM level was found to be approximately 15 ppm and Ethanol was approximately 80 ppm). So it can be said that the final product was free from ethanol and DCM. (See figure 11 & 12)

#### **Modified Dissolution Technique: (Modified rosette rise dissolution apparatus)**

The results showed that drug released at the slower rate for the first 1 to 5 hrs. After 6 hrs, release rate was higher. After 12 hrs drug release was found to be 96.37%. (See figure 13 & 14)

#### **CONCLUSION:**

From all the above studies it can be concluded that microballoons for gastric retention by emulsion solvent diffusion method using eudragit s 100 were successfully prepared. These prepared microballoons were showing sustained release action by remaining into the stomach for more than 12 hrs due to their excellent buoyancy. From SEM it was found that prepared microballoons were spherical in shape and hollow from inside. Optimized batch was found to be satisfactory in terms of % Yield, % DEE, % Buoyancy and dissolution profile. Kinetic study was showing that the drug release was by diffusion mechanism. Stability study for one month showed that there was no significant difference in responses as well as on physical appearance. Furthermore the drug release profile of optimized and marketed was found to be similar. Thus it can be concluded that microballoons were potential candidates for multiple unit delivery devices and were able to release drug in a controlled manner.

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Carr's index	Type of Flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Extremely poor

**Table 1: Relationship between type of flow and carr's index**

Angle of Repose(°)	Flowability
< 25	Excellent
25-30	Good
30-40	Passable
> 40	Very Poor

**Table 2: Angle of repose as an indication of flow property**

Formulation Ingredient	M1	M2	M3	M4	M5	M6	M7	M8	M9
<b>Drug:</b>	1:1	1:3	1:5	1:4	1:5	1:6	1:1	1:3	1:5
<b>Eudragit S 100</b>				1	3	5			
<b>Ethanol(ml)</b>	8	8	8	8	8	8	8	8	8
<b>Dichloromethane (DCM)(ml)</b>	8	8	8	8	8	8	8	8	8
<b>PVA in purified water (%)</b>	0.7	0.7	0.7	1	1	1	1.2	1.2	1.2
	5	5	5				5	5	5

## TABLES AND FIGURES:

**Table 3 Formulation of full factorial design batches**

**Table 4: Evaluation of micromeritic properties of microballoons**

Batch Code	Mean Particle size(μm) Mean±SD	Bulk Density (gm/cm <sup>3</sup> ) Mean±SD	Tapped Density (gm/cm <sup>3</sup> ) Mean±SD	True Density (gm/cm <sup>3</sup> ) Mean±SD	Carr's Index Mean±SD D	Angle of Repose Mean±SD D	Hausner's Ratio Mean±SD D
<b>M1</b>	123.52 ±1.34	0.1162 ±0.003	0.1351 ±0.004	0.83 ±0.0169	13.98 ±0.65	31.69 ±1.041	1.1623 ±0.008
<b>M2</b>	333.89 ±2.64	0.1056 ±0.005	0.1301 ±0.006	0.78 ±0.0163	18.85 ±2.76	27.76 ±1.61	1.2335 ±0.041
<b>M3</b>	393.31 ±1.54	0.095 ±0.003	0.1239 ±0.003	0.74 ±0.008	23.22 ±1.61	21.91 ±1.53	1.3029 ±0.027
<b>M4</b>	132.96 ±2.27	0.2254 ±0.003	0.2665 ±0.0018	0.86 ±0.01	15.40 ±0.85	28.19 ±1.001	1.1822 ±0.011
<b>M5</b>	358.36 ±2.25	0.1623 ±0.009	0.1865 ±0.011	0.80 ±0.012	12.96 ±1.034	23.34 ±1.82	1.149 ±0.016
<b>M6</b>	413.82 ±2.37	0.1175 ±0.003	0.1391 ±0.004	0.71 ±0.012	16.93 ±2.54	17.67 ±0.80	1.183 ±0.011
<b>M7</b>	183.48 ±0.99	0.3153 ±0.0004	0.352 ±0.002	0.88 ±0.02	10.41 ±0.57	26.31 ±0.89	1.1162 ±0.007
<b>M8</b>	373.9 ±1.19	0.2693 ±0.005	0.3083 ±0.005	0.86 ±0.008	12.63 ±0.94	24.51 ±0.69	1.1448 ±0.012
<b>M9</b>	425.82 ±2.66	0.2376 ±0.003	0.2870 ±0.006	0.79 ±0.026	17.12 ±3.06	15.28 ±1.34	1.2048 ±0.045

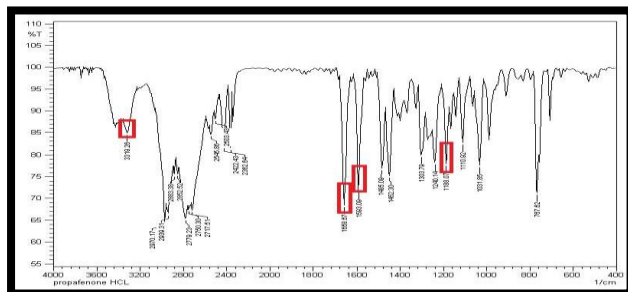
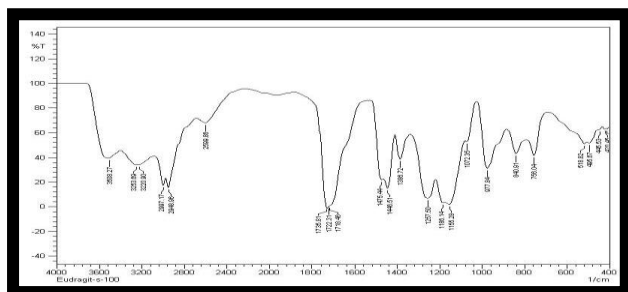
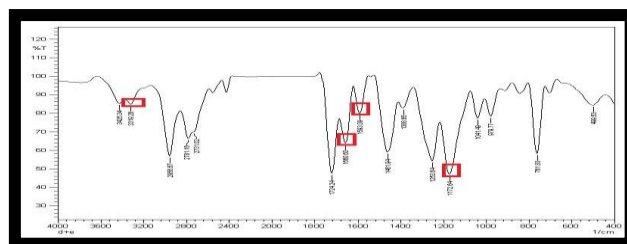
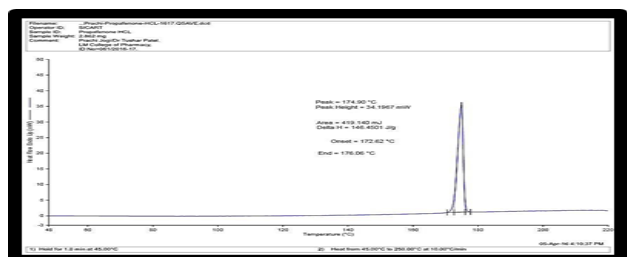
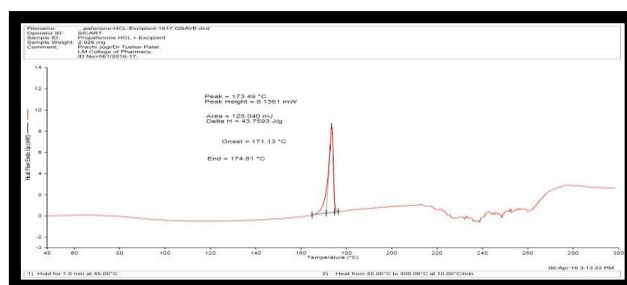
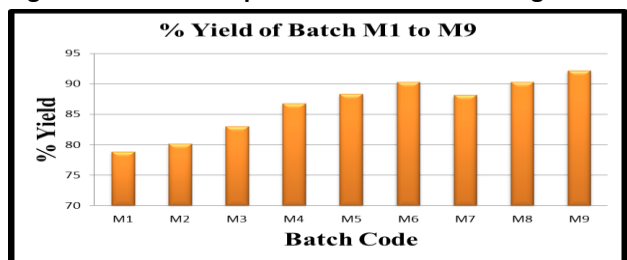
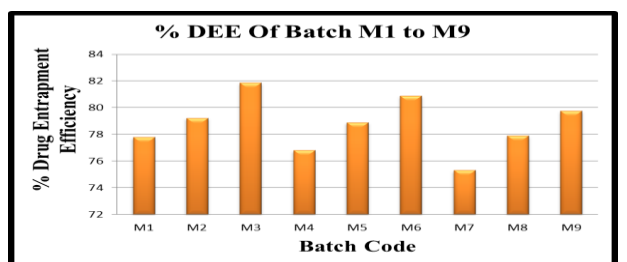


**Table 5: Evaluation Parameters of microballoons**

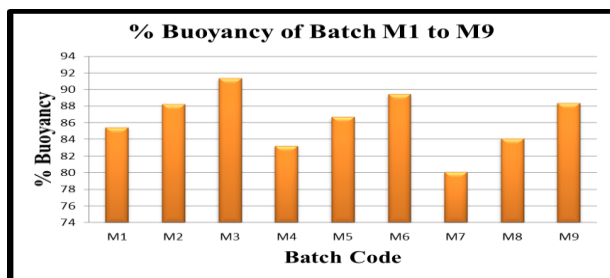
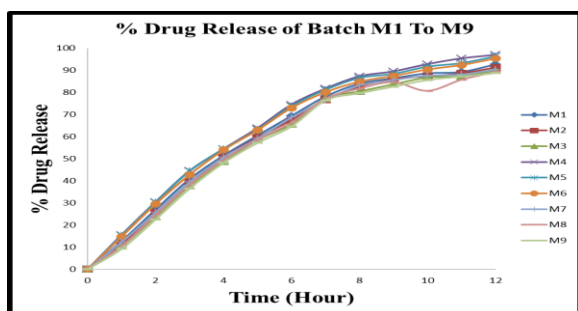
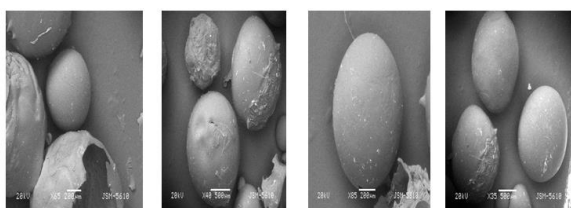
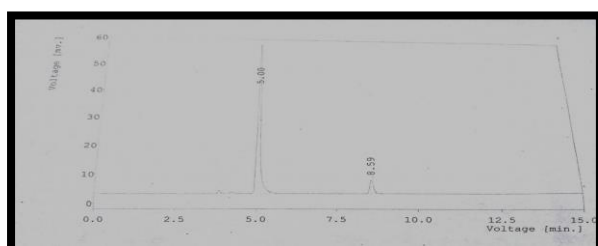
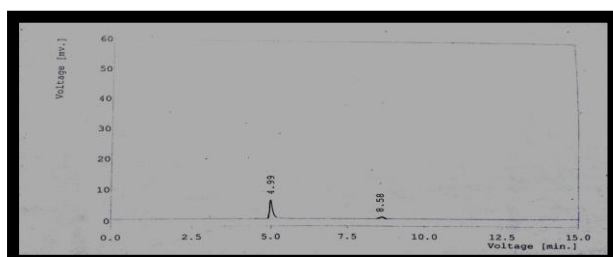
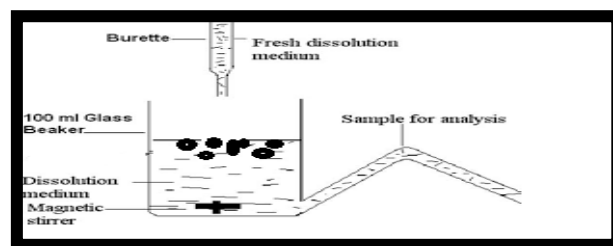
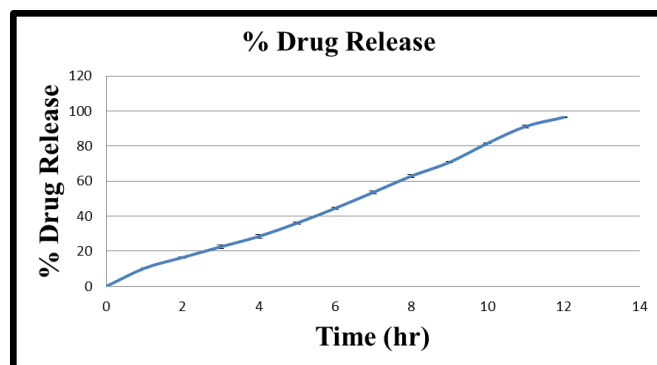
Batch Code	% Yield	% Drug Entrapment Efficiency	% Buoyancy
M1	78.86 ±1.85	77.78 ±1.33	85.44 ±0.86
M2	80.12 ±0.81	79.23 ±2.92	88.21 ±0.34
M3	82.98 ±0.87	81.87 ±1.20	91.34 ±0.48
M4	86.79 ±2.24	76.81 ±0.77	83.23 ±0.80
M5	88.32 ±0.55	78.9 ±1.74	86.68 ±1.17
M6	90.27 ±1.12	80.88 ±0.04	89.43 ±0.03
M7	88.16 ±0.04	75.32 ±1.24	80.08 ±0.63
M8	90.32 ±0.88	77.89 ±1.18	84.11 ±1.18
M9	92.14 ±0.36	79.76 ±1.01	88.34 ±0.53

**Table 6: Results of Kinetic Drug Release Profile of Batch M6**

KINETIC MODEL	K0	R2	MSE	AIC	MSC	n
Zero order	9.633	0.8451	155.20	99.88	1.32	
First order	<b>0.210</b>	<b>0.9898</b>	<b>10.19</b>	<b>64.48</b>	<b>4.04</b>	
Higuchi	28.14	0.9653	34.77	80.44	2.81	
Korsmeyer	22.91	0.9776	24.43	76.72	3.10	0.60
Peppas						

**Figure 1 FT-IR Spectra of PropafenoneHCl****Figure 2 FTIR Spectra of Eudragit S 100****Figure 3 FT-IR Spectrum of mixture of PropafenoneHCl and Eudragit S 100****Figure 4: DSC of Propafenone HCl****Figure 5: DSC of Propafenone HCl with Eudragit S 100****Figure 6: Column graph showing %yield of Batch M1 to M9**



**Figure 7: Column graph showing %DEE of Batch M1 to M9****Figure 8: Column graph showing % Buoyancy of Batch M1 to M9****Figure 9: Comparative % Drug Release of Batch M1- M9****Figure 10: SEM of microballoons of optimized batch****Figure 11: Gas chromatography of Solution of Ethanol and Dichloromethane Mixture (Standard)****Figure 12: Gas Chromatography of optimized batch M6****Figure 13: modified dissolution Apparatus****Figure 14: %Drug Release using modified dissolution method**