EFFERVESCENT GASTRORETENTIVE FLOATING TABLETS OF AMLODIPINE BESYLATE FORMULATION AND INVITRO EVALUATION.

Abboju. Prasad\textsuperscript{1}, K.Nirmala, K.Keerthi and D.Sathish\textsuperscript{2}

\textsuperscript{1}Surapharmalabs, Dilshknagar, Hyderabad-500060 (T.S.)
\textsuperscript{2}Vaagdevi Pharmacy College Bollikunta, Warangal- 506005 (T.S.)

ABSTRACT
In the present research work gastro retentive floating formulation of Amlodipine besylate by using various hydrophilic polymers were developed. 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 grades of HPMC and Guar gum as polymeric substances. The formulation blend was subjected to various preformualtion 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 HPMC K100 as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 100 mg(F5 Formulation, 99.33% Drug release). Where as in low concentrations the polymer was unable to produce the desired action. The formulations prepared with HPMC K15 were also retarded the drug release for more than 6 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 zero order mechanism of drug release.

KEYWORDS: Amlodipine besylate, HPMC polymers, Floating tablets.

INTRODUCTION
Hypertension (HTN) or high blood pressure, sometimes called arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated. Blood
pressure involves two measurements, systolic and diastolic, which depend on whether the heart muscle is contracting (systole) or relaxed between beats (diastole). Normal blood pressure at rest is within the range of 100-140mmHg systolic (top reading) and 60-90mmHg diastolic (bottom reading). High blood pressure is said to be present if it is persistently at or above 140/90 mmHg.

Hypertension is a major risk factor for stroke, myocardial infarction (heart attacks), heart failure, aneurysms of the arteries (e.g. aortic aneurysm), peripheral arterial disease and is a cause of chronic kidney disease. Even moderate elevation of arterial blood pressure is associated with a shortened life expectancy.

**Aim of the Work**

Aim of the study is to formulate and evaluate Amlodipine besylate floating tablets using different polymers HPMC K15M, HPMC K100 M, HPC and Guar gum.

**Objective of the Study**

Amlodipine besylate is a calcium channel blocker used in the treatment of Hypertension, Angina Pectoris, Cardiac Arrhythmias and cluster headaches. When it is given orally, 90% of the drug gets absorbed through it and reaches the maximum concentration within 2-3 hrs.

- Amlodipine besylate under goes hepatic metabolism, therefore it has high bioavailability (64-98%) and long half-life (3-4hrs) due to which the drug is administered in multiple doses. So to enhance the bioavailability and reduce the dosage regimen of Amlodipine besylate it is best formulated as Intra gastric floating tablets.
- One of the purposes of this formulation was to maintain in vitro buoyancy as well as in vivo duration of floating stable for at least 12 hours
- The present work is aimed at formulating sustained release effervescent floating tablet dosage forms of Amlodipine besyate (10mg) using various low-density polymers.
- To study the effect of various factors like.

**a) Effect of sodium bicarbonate**

Sodium bicarbonate was used as a gas generating agent. In this present study the sodium bicarbonate was used in the amounts of 15, 20, 25 and 30 mg. Depending upon the amount of NaHCO₃ the floating lag time was varied. For optimum floating lag time the quantity of NaHCO₃ inclusion also should be studied.
b) Drug polymer ratio or conc. of polymer

Drug polymer ratio will show definitely effect on the release of drug. In the present study 2 grades of HPMC polymers [K\textsubscript{15} M, K\textsubscript{100} M] and 1 grades of Guargum polymer and HPC 5%, 10% and 15% concentrations are used. The quantity used and the method of application was carefully regulated such that the tablets remain intact while swallowing & then release the medicaments.

c) Effect of polymer grade or viscosity

Most polymers based on their mechanism of action show retardant effect on drug release from tablets. This retardation of drug release is varied by the viscosity of polymer grades. In the present investigation the ability of 2 grades of HPMC polymer i.e., HPMC K\textsubscript{15} M, K\textsubscript{100} M and 1 grades of Guargum and one grade of HPC on duration of floating & release rate was carefully evaluated.

d) Nature of the polymer

Most of the polymers by virtue of their nature show drug retardation and drug release mechanisms. In the present investigation two polymers [HPMC & Guargum] are used in different concentrations. The mechanism and rate of drug release in the compressed tablets were evaluated.

A. Effervescent system
B. Non-effervescent system

A. Effervescent system

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds e.g., sodium bicarbonate, tartaric acid and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO\textsubscript{2} is liberated and get entrapped in swollen hydrocolloids.

B. Non-Effervescent System: The most commonly used excipients in noneffervescent FDDS are gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. One of the approaches used for the formulation of such floating dosage forms involves intimate mixing of drug with a gelforming hydrocolloid, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier. The air trapped by the
swollen polymer confers buoyancy to these dosage forms. In addition, the gel structure acts as a reservoir for sustained drug release since the drug is slowly released by a controlled diffusion through the gelatinous barrier.

**MATERIALS**

This study was carried out for the selection of suitable polymer and excipients for the proposed Formulations. Amlodipine as gift sample from Merck Specialities Pvt Ltd, Mumbai, India. Polymers, HPMC K15M, Guar gum, HPMC K100M, sodium bicarbonate, magnesium stearate, talc and lactose are gift Sample from Merck Specialities Pvt Ltd, Mumbai, India.

**METHODS**

**Formulation Development**

**Formulation of effervescent matrix floating tablet of Amlodipine.**

a) Preparation calibration curve

100mg of Amlodipine besylate pure drug was dissolved in 100ml of 0.1N HCl (stock solution) 10ml of solution was taken and make up with 100ml of 0.1N HCl (100μg/ml). From this 10ml was taken and make up with 100 ml of 0.1N HCl (10μg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions containing 5, 10, 15, 20 and 25 μg/ml of Amlodipine besylate per ml of solution. The absorbance of the above dilutions was measured at 238 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.

6.2. 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 100mg 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.

6.3. 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:

\[ \tan \theta = \frac{h}{r} \]

where

- \( h \) = Height of the cone,
- \( r \) = Radius of the cone base.

<table>
<thead>
<tr>
<th>Angle of Repose (( \theta ))</th>
<th>Nature of Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>Excellent</td>
</tr>
<tr>
<td>25-30</td>
<td>Good</td>
</tr>
<tr>
<td>30-40</td>
<td>Passable</td>
</tr>
<tr>
<td>&gt;40</td>
<td>Very poor</td>
</tr>
</tbody>
</table>

**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, \( V_o \), was read.

The bulk density was calculated using the formula:

\[ \text{Bulk Density} = \frac{M}{V_o} \]

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:

\[
\text{Tap} = \frac{M}{V}
\]

Where, Tap= Tapped Density

\[M = \text{Weight of sample}\]

\[V = \text{Tapped volume of powder}\]

**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. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. 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:

\[
\text{Carr’s Index} = \left(\frac{\text{tap} - b}{\text{tap}}\right) \times 100
\]

Where, \(b = \text{Bulk Density}\)

\(\text{Tap} = \text{Tapped Density}\)

**Table 6.2: Carr’s index value (as per USP)**

<table>
<thead>
<tr>
<th>Carr’s index</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 – 15</td>
<td>Excellent</td>
</tr>
<tr>
<td>12 – 16</td>
<td>Good</td>
</tr>
<tr>
<td>18 – 21</td>
<td>Fair to Passable</td>
</tr>
<tr>
<td>2 – 35</td>
<td>Poor</td>
</tr>
<tr>
<td>33 – 38</td>
<td>Very Poor</td>
</tr>
<tr>
<td>&gt;40</td>
<td>Very Very Poor</td>
</tr>
</tbody>
</table>

**6.3. Formulation development of Tablets:** All the formulations were prepared by direct compression. The compression of different formulations are given in Table 6.3. The tablets were prepared as per the procedure given below and aim is to prolong the release of Amlodipine besylate. Total weight of the tablet was considered as 250mg.
Procedure

- Amlodipine besylate and all other ingredients were individually passed through sieve no ≠ 60.
- All the ingredients were mixed thoroughly by triturating up to 15 min.
- The powder mixture was lubricated with talc.
- The tablets were prepared by using direct compression method.

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 6.3: Optimization sodium bicarbonate concentration

<table>
<thead>
<tr>
<th>S.No</th>
<th>Excipient Name</th>
<th>EF1</th>
<th>EF2</th>
<th>EF3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amlodipine besylate</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>HPMC K 100M</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>NaHCO₃</td>
<td>25</td>
<td>50</td>
<td>75</td>
</tr>
<tr>
<td>5</td>
<td>Mg.Stearate</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>5</td>
<td>Talc</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>7</td>
<td>MCC pH 102</td>
<td>110</td>
<td>95</td>
<td>60</td>
</tr>
</tbody>
</table>

All the quantities were in mg.

Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimised.

Table 6.4: Formulation composition for floating tablets

<table>
<thead>
<tr>
<th>Formula tion No.</th>
<th>Amlodipine besylate</th>
<th>HPMC K15</th>
<th>HPMC K100</th>
<th>Guar Gum</th>
<th>HPC</th>
<th>NaHCO₃</th>
<th>Mag. Stearate</th>
<th>Talc</th>
<th>MCC pH 102</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>10</td>
<td>50</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>135</td>
</tr>
<tr>
<td>F2</td>
<td>10</td>
<td>100</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>85</td>
</tr>
<tr>
<td>F3</td>
<td>10</td>
<td>150</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>35</td>
</tr>
<tr>
<td>F4</td>
<td>10</td>
<td>-----</td>
<td>50</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>135</td>
</tr>
<tr>
<td>F5</td>
<td>10</td>
<td>-----</td>
<td>100</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>85</td>
</tr>
<tr>
<td>F6</td>
<td>10</td>
<td>-----</td>
<td>150</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>35</td>
</tr>
<tr>
<td>F7</td>
<td>10</td>
<td>-----</td>
<td>-----</td>
<td>50</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>135</td>
</tr>
<tr>
<td>F8</td>
<td>10</td>
<td>-----</td>
<td>-----</td>
<td>100</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>85</td>
</tr>
<tr>
<td>F9</td>
<td>10</td>
<td>-----\</td>
<td>-----</td>
<td>150</td>
<td>-----</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>35</td>
</tr>
<tr>
<td>F10</td>
<td>10</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>100</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>135</td>
</tr>
<tr>
<td>F11</td>
<td>10</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>100</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>85</td>
</tr>
<tr>
<td>F12</td>
<td>10</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>150</td>
<td>50</td>
<td>2.5</td>
<td>2.5</td>
<td>35</td>
</tr>
</tbody>
</table>

All the quantities were in mg
6.4. Evaluation of post compression parameters for prepared Tablets: All the evaluation parameters of tablets were studied for their weight variation, hardness, thickness, friability and drug content.

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 determining 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.

\[
\text{% Deviation} = \left( \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \right) \times 100
\]

Table 6.5: Pharmacopoeial specifications for tablet weight variation

<table>
<thead>
<tr>
<th>Average weight of tablet (mg) (I.P)</th>
<th>Average weight of tablet (mg) (U.S.P)</th>
<th>Maximum percentage difference allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 80</td>
<td>Less than 130</td>
<td>10</td>
</tr>
<tr>
<td>80-250</td>
<td>130-324</td>
<td>7.5</td>
</tr>
<tr>
<td>More than</td>
<td>More than 324</td>
<td>5</td>
</tr>
</tbody>
</table>

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.

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.

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

\[
\% \text{ Friability} = \left[ \frac{(W1 - W2)}{W} \right] \times 100
\]

Where, \( W1 \) = Initial weight of three tablets
\( W2 \) = Weight of the three tablets after testing

**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 Amlodipine besylte 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. (As per
the method described by Rosa et al) The tablets were placed in a 100ml 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 N HCl
- **RPM** -- 50
- **Sampling intervals (hrs)** -- 0.5,1,2,3,4,5,6.
- **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:** Added 900ml 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 6
hours and then the medium 0.1 N HCl was taken and process was continued from 0 to 6 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 238 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.

**Zero order release rate kinetics:** To study the zero–order release kinetics the release rate data are fitted to the following equation.

\[ F = K_o t \]

Where, ‘F’ is the drug release at time ‘t’, and ‘K_o’ is the zero order release rate constant. The plot of % drug release versus time is linear.

**First order release rate kinetics:** The release rate data are fitted to the following equation

\[ \log (100-F) = kt \]

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

**Higuchi release model:** To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

\[ F = k t^{1/2} \]

Where, ‘k’ is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

**Korsmeyer and Peppas release model**

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent ‘n’ indicates the mechanism of drug release calculated through the slope of the straight Line.

\[ M_t / M_\infty = K t^n \]

Where, \( M_t / M_\infty \) is fraction of drug released at time ‘t’, k represents a constant, and ‘n’ is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of
Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M/ M_∞) versus log (time) is linear.

**Hixson-Crowell release model**

\[(100-Q_{t})^{1/3} = 100^{1/3} - K_{HC}t\]

Where, k is the Hixson-Crowell rate constant. Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

**SUMMARY**

Gastric emptying of the dosage forms is an extremely variable process and ability to prolong and control the emptying time, which is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms.

Amlodipine besylate is soluble in acidic pH and absorption occurs only in proximal intestine. The aim of the present study was to formulate effervescent floating matrix tablets of Amlodipine besylate to overcome its biological half life (3-4hrs) and to maintain steady state plasma concentration up to 12hrs. A standard concentration of Amlodipine besylate was prepared in 0.1N HCl and the absorbance was measured at 238 nm. Amlodipine besylate is showing good linearity between 5-25 µg/ml with a correlation coefficient of 0.9994.

The floatation was accomplished by incorporation of sodium bicarbonate into a swellable hydrophilic polymer. The optimum concentration of NaHCO₃ is 15 % (50mg). The physicochemical properties of all the formulations were found to be within the prescribed official limits. The formulations containing HPMC K15 M did not show promising results, the drug release was poor, and the in vitro floating time was also found to be less. Formulations containing lower viscosity and concentration of polymer failed to form sufficient gel strength compared to high viscosity and concentration of polymer. Formulations with all HPMC and guargum grades showed retarding of drug release by increasing the polymer concentration. The drug release pattern from the optimized formulations was followed Zero order kinetics with non fickian diffusion mechanism. Formulation F5, gave better-controlled drug release in comparison to the other formulations. It also showed more similarity than F4, F6, F8 & F10 formulations when compared with theoretical release profile.

FTIR study of pure Amlodipine besylate and formulations showed that there is no drug polymer interaction.
CONCLUSION
In the present research work gastro retentive floating formulation of Amlodipine besylate by using various hydrophilic polymers were developed. 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 grades of HPMC and Guar gum as polymeric substances. The formulation blend was subjected to various preformulation 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 HPMC K100 as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 100 mg (F5 Formulation, 99.33% Drug release). whereas in low concentrations the polymer was unable to produce the desired action. The formulations prepared with HPMC K15M 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 zero order mechanism of drug release.

REFERENCES
5. Bhalchandra m. Habade*1 vidyashri kamble1, r. Ramesh2 milind p.wagh3 ” formulation and evaluation of floating drug delivery system of ciprofloxacain”ijprd, 2011; 3(11).
8. Brahmankard m, jaiswal s.b, biopharmaceutics and pharmacokinetics a treatise, 1st ed. Vallabh prakashan; new delhi, 1995; 64-70.
11. Chawla g, gupta p, koradia v, bansal a, gastroretention: a means to address regional variability in intestinal drug absorption, pharm. Tech., 2003; 50-68.
12. Chein y.w, novel drug delivery systems, 2nd ed.: marcel dekker; new york, 1992; 4-56.