

## DEVELOPMENT AND CHARACTERIZATION OF FLOATING TABLETS OF CAPTOPRIL USING NATURAL POLYMERS

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### ABSTRACT

The present study involved development and characterization of newer floating matrix tablets of Captopril by direct compression method using two different natural polymers like- Xanthan and Guar gum. Powders were evaluated for angle of repose, loose bulk density, tapped density, Carr's index and Hausner ratio whereas the prepared tablets were evaluated for weight variation, thickness and diameter, hardness, friability, drug content, floating lag time, total floating time, hydration behavior, and in vitro dissolution study. The drug release kinetic was fitted in three different mathematical models like- Zero order, Higuchi and Korsmeyer-Peppas model. The results indicate that the drug release mechanism was found fickian diffusion type in most of the formulations. The developed floating tablets of Captopril may be used in clinic for prolonged drug release for at least 24h, thereby improving the bioavailability and patient compliance.

**Key words:** - Captopril, Xanthan gum, Guar gum, Sodium Bicarbonate, Floating Tablet

### 1. INTRODUCTION

Oral administration is the most versatile convenient and commonly employed route of drug delivery for systemic action. (Patel, 2006). Floating drug delivery systems were first described by Davis in 1968. Floating drug delivery systems are used to prolong the gastric residence time of dosage form. The systems to be remain buoyant in the stomach for prolonged period of time without affecting the gastric emptying rate of other contents.

A floating dosage form is useful for those drugs that act locally in the proximal gastrointestinal tract, are unstable in lower parts of GIT, or are poorly absorbed in the intestine. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability (Martinez *et al.*, 2008). Thus the present drug was chosen as suitable candidate for formulation of floating drug delivery system.

The first substance of the ACE inhibitor, Captopril is active in unmodified form. Captopril is rapidly absorbed through GIT but its bioavailability decreases by 30-40% in presence of food. The half life of Captopril is less than 3 hrs. Blood level correlate poorly with clinical response. Captopril, an orally active inhibitor of angiotensin-converting enzyme (ACE) has been used widely for the treatment of hypertension and congestive heart

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failure. The drug is considered as a drug of choice in antihypertensive therapy due to its effectiveness and low toxicity. The drug is stable at pH 1.2 and as the pH increases; the drug becomes unstable and undergoes pseudo first order degradation reaction.

The development of oral controlled release formulations for captopril is somewhat difficult. This difficulty arise from the fact that the drug suffering in vitro and in vivo instability. The drug also suffering from dose dumping and burst phenomenon (being freely water soluble) when formulated as sustained or controlled release formulation. (Nur et al., 2000). In recent years, the value of hydrophilic polymer based matrix tablets as vehicles for controlled release delivery has been increasingly demonstrated with the publication of numerous patents and research papers and their utilization in new products in the market place. (Durig and fassih 2002).

Compressed hydrophilic matrices are commonly used as oral drug delivery systems because of their good compatibility. Drug release from hydrophilic matrix tablets is controlled by formation of a hydrated viscous layer around the tablet which acts as a barrier to drug release by opposing penetration of water into tablet and also movement of dissolved solute out of matrix tablets. (Martinez *et al.*, 2008). In the hydrophilic matrices, drug release process is influenced not only by drug solubility but also by the physical and chemical properties of the gel barrier that forms around the tablet. The extent of matrix swelling, erosion, and diffusion of drug determines the kinetics as well as the mechanism of drug release. (Martinez *et al.*, 2008).

The natural polymers are selected because of their ease of manufacturing, relatively low cost, favorable *in-vivo* performance and versatility in controlling the release of drugs with a wide range of physicochemical properties. The bi-polymeric system in the

dosage form may modify drug release pattern. Absorption windows in the proximal gut can limit the bioavailability of orally administered compounds and can be a major obstacle to the development of controlled release formulations for important drugs. The transit of a drug formulation through the gastrointestinal tract will determine how long a compound will be contact with its preferred absorptive site (Davis, 2005).

The objective of the investigation was to study the utility of using natural polymers (Xanthan gum and guar gum) in the formulation design of floating matrix tablet of captopril and to observe the vitro release characteristics and the kinetic of the prepared formulation.

## 2. Material and methods:

Captopril was received as gift samples from Windlas Biotech Limited, Dehradun. Guar gum was obtained from Qualikem Fine Chemicals Pvt. Ltd., New Delhi. Xanthan gum obtained from Pharmasynth Formulation, Limited, Haridwar. Sodium bicarbonate sources.e was procured from Qualikem Fine Chemicals Pvt. Ltd., New Delhi. Lactose was obtained from Glaxosmithkline Pharmaceuticals Limited, Mumbai. Magnesium stearate was obtained from Qualikem Fine Chemicals Pvt. Ltd., New Delhi. All other reagents used in this study were of analytical grade and obtained from standard sources.

### 2.1 Preparation of floating tablets:-

Captopril floating tablets were prepared by the direct compression method using xanthan, guar gum as matrix former and sodium bicarbonate as floating agents. Amounts of various ingredients (mg) used in different formulations of floating tablets are presented in the table. The method was described by Patel et al. Captopril was mixed with the required quantity of polymers containing different ratio of xanthan gum, guar gum,

sodium bicarbonate and lactose in a laboratory cube blender for 15 min. The powder blend was then lubricated with magnesium stearate for additional 3 min and compressed into tablets with manually tablet machine (Rimek, Ahmedabad, India) using 10 mm standard flat faced tools. Compression force was adjusted to obtain tablets with hardness in the range of 3–4 kg/cm<sup>2</sup>. The average diameter of tablets was 10 ± 0.3 mm and thickness 4 ± 0.1 mm.

## 2.2 Evaluation of powder characteristics of floating tablets:-

**Angle of repose:** - Pharmaceutical powders may be broadly classified as free flowing or cohesive. Most flow properties are significantly affected by changes in particle size, density, shape, electrostatic charge and absorbed moisture which may arise from processing or formulation. The frictional forces in a loose powder can be measured by the angle of repose.(Martin et al & Lachman et al.)

It is defined as the bulk powder materials are poured onto a horizontal surface, a conical pile will form. The internal angle between the surface of the pile and the horizontal surface is known as the angle of repose. Material with a low angle of repose forms flatter piles than material with a high angle of repose. In other words, the angle of repose is the angle a pile forms with the ground.

**Table 1.** Relation between Angle of repose and Type of flow

| Angle of repose | Type of flow |
|-----------------|--------------|
| 20              | Excellent    |
| 20-30           | Good         |
| 30-34           | Passable     |
| 40              | Very poor    |

**2.3 Procedure:** - The angle of repose of powder was determined by the funnel method(Ray et al.). The funnel (glass funnel) was fixed at a constant height. The accurately weighed powdered blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose ( $\theta$ ) was calculated by using the following formula-

$$\text{Angle of repose} = \tan^{-1} (h / r)$$

Where, h= height of cone,  
r = radius of the base of heap on the graph paper.

**2.4 Bulk density:** - Bulk density is not an intrinsic property of a material; it can change depending on how the material is handled. For example, a powder poured in to a cylinder will have a particular bulk density, if the cylinder is disturbed; the powder particles will move and usually settle closer together, resulting in a higher bulk density. For this reason, the bulk density of powders is usually reported both as "freely settled" and "tapped" density.

It is defined as the mass of a powder divided by the bulk volume. Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density depends on particle size distribution, powder shape and tendency of the particles to adhere to one another.

**Procedure:** - Loose bulk density was determined using graduated cylinder.(Ray et al.) Accurately weighed (5 gm) of sample was taken and it was transferred in to 100 ml graduated cylinder. The volume of the packing was recorded and the loose bulk density was calculated by the following formula-

$$\text{Loose bulk density} = \frac{\text{Weight of the powder sample}}{\text{Volume of the packing}}$$

**2.5 Tapped bulk density:-** It is defined as the mass of a powder divided by the tapped volume. The tapped bulk density determined using graduated cylinder. The graduated

cylinder was tapped for at least 100 times and the tapped volume of packing was recorded. The tapped bulk density was calculated by the following formula-

**Tapped bulk density =**

**Weight of the powder sample**

**Tapped volume of the packing**

**Carr's index:** - The Carr index is frequently used in pharmaceuticals as an indication of the flowability of a powder. A Carr index greater than 25% is considered to be an indication of poor flowability, and below 15%, of good flowability (Wikipedia).

The **Carr index** is an indication of the compressibility of a powder. It is calculated using following formula.

$$\text{Carr's index (C)} = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

Where,  $\rho_b$  is the loose bulk density of the powder.

$\rho_t$  is the tapped bulk density of the powder.

**Hausner ratio:-** The Hausner ratio is used in a wide variety of industries as an indication of the flowability of a powder. A Hausner ratio greater than 1.25 is considered to be an indication of poor flowability (Wikipedia).

The Hausner ratio is a number that is correlated to the flowability of a powder. It is calculated by using following formula-

$$\text{Hausner ratio (H)} = \frac{\rho_t}{\rho_b}$$

Where,  $\rho_b$  is the loose bulk density of the powder.

$\rho_t$  is the tapped bulk density of the powder.

## 2.6 Characterization of floating tablets:-

**Weight variation:** - The tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug.

The weight variation test was determined by the USP XX – NF XV method. The test was carried out by weighing the 20 tablets individually using analytical balance than calculating the average weight , and comparing the individual tablet weights to the average. There was not more than two tablets are outside the percentage limit. The tablets was not differs by more than 2 times the percentage limit.

Table 2. Weight variation tolerances for tablets:-

| Average weight of tablets (mg) | Maximum percentage difference allowed |
|--------------------------------|---------------------------------------|
| 130 or less                    | 10                                    |
| 130-324                        | 7.5                                   |
| More than 324                  | 5                                     |

The percentage of weight variation is calculated by using the following formula.(Ahmed et al).

$$\text{Percentage of weight variation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

**Hardness:** - The resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The instrument measures the force required to break the tablet when the force generated by anvils to the tablet.

Tablet hardness is defined as the load required crushing or fracture a tablet placed on its edge. Sometime it is also termed as tablet crushing strength. The hardness test was performed using Pfizer hardness tester. The diametrical crushing strength test was performed on 10 tablets from each formulation. The tablet is placed between two anvils, force is applied to the anvils, and the crushing strength that just causes the tablet to break is recorded.

**Thickness:** - The diameter and thickness of captopril tablets was performed on 10 tablets from each formulation. The thickness of individual tablets was measured using vernier caliper. It is expressed in mm, which permits accurate measurements and provides information of the variation between tablets. Tablet thickness was controlled within a  $\pm 5\%$  variation of a standard value.

**Friability:** - For each formulation, the friability of 20 tablets was determined using a Roche type friabilator (Erweka, Germany). 20 tablets from each formulation were weighed and tested at a speed of 25 rpm for 4 min. After removing of dusts, tablets were re-weighed and friability percentage was calculated using the following equation. (Emami et al.)

$$\text{Percentage friability} = \frac{W_1 - W_2}{W_1} \times 100$$

Where  $W_1$  = initial weight of tablets  
 $W_2$  = re-weight of tablets

The conventional compressed tablets that lose less than 0.5 to 1.0 % of their weight are generally considered acceptable.

#### **Uniformity drug content:-**

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. Due to increased awareness of physiological availability (Jaimini et al.).

The uniformity of drug content in each formulation was determined by triturating 20 tablets and powder equivalent to average

weight was added in 100 ml of 0.1N hydrochloric acid, followed by stirring for 30 minutes. The solution was filtered through a 0.45 $\mu$  membrane filter, diluted suitably and the absorbance of resultant solution was measured using UV-spectrophotometer at 204.0 nm using 0.1N hydrochloric acid as blank. The average drug content is calculated and the content of the individual tablets was fall within specific limits (97.5 % to 102.0 %) in terms of percentage deviation from the mean.

Drug content was determined according to the following formula-

$$\text{Drug content} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100$$

#### **Floating behavior (Buoyancy lag time determination):-**

The in vitro buoyancy was characterization by floating lag time and total floating time. The in vitro buoyancy was determined by floating lag time, as per the method described by Rosa et al. (Dave et al. 2004). The tablets were placed in a 100 ml beaker containing 0.1 N HCL. The time required for tablet to rise to the surface and duration of time the tablet constantly float was determined as floating lag time and total floating time, respectively.

$$\text{SI} = \frac{\text{Tablet diameter at time (t)} - \text{Initial diameter of tablet}}{\text{Initial diameter of tablet}} \times 100$$

#### **Matrix tablets density:-**

The tablet density is an important parameter for floating tablets. The matrix tablet will float only if its density is less than that gastric fluid (1.004). The apparent densities of the tablets were calculated from their volumes and masses. The tablet density (d) was determined using following equation-

$$d = m / v$$

Where, m = mass of tablet  
v = volume of tablet

The weight and volume reached by the matrix tablets over time was determined by withdrawing the tablets at various time intervals. The tablets were weighed on an analytical balance after slight blotting with tissue paper to remove the excess test liquid. The volume of the tablets was obtained by measuring the height and wide, considering a right circular cylinder form.(Martinez et al., Streubel et al) The volumes V of the

#### **Hydration behavior of matrix tablets:-**

##### **Matrices hydration:-**

The Matrices hydration was determined by swelling index, as per the method described by Shishu et al. Apparent radial swelling of the matrices was monitored by immersing the tablet in a beaker containing 250 ml pH 1.2 HCL buffer. The increase in the tablet diameter was measured by vernier caliper at predefined times over a period of 24 h. The dimensions of each matrix were measured using a vernier caliper prior to hydration studies. The swelling index (SI), expressed as a percentage, was calculated from the following equation.

cylindrical tablets were calculated from their heights "h" and radii "r" (both determined with a micrometer gauge) using the mathematical equation for a cylinder.

$$V = \pi r^2 h$$

The results for each time point of three repetitions are registered as an average.

#### **2.7 In-vitro dissolution studies:-**

The in vitro dissolution study of floating tablets was determined by using USP 24 paddle type dissolution apparatus. The dissolution test was performed in 900 ml of 0.1 N HCL at 50 rpm maintained at  $37 \pm 0.5^\circ\text{C}$ . The 5 ml samples were withdrawn at predetermined time intervals for period of 24 hr and replaced with the equal volume of the same dissolution medium. The samples were filtered through 0.45  $\mu\text{m}$  membrane filter,

suitably diluted and the concentration of captopril was obtained by measuring the absorbance at 204.0 nm using double beam UV-Vis spectrophotometer (Systronic). The content of drug was calculated using equation generated from calibration curve. The test was performed in triplicate. Captopril solubility in water at 25 °C is 160mg/ml (Martinez *et al.*, 2008). Therefore, dissolution of 50 mg in 900ml at 37 °C is considered under sink conditions.

### 3. Results and discussion

#### Evaluation of powder characteristic of floating tablets:-

The powders prepared for compression of floating tablets were evaluated for their flow properties. The powder characteristic indicates good flowability with an angle of repose value ranging from 21-26° (Ray *et al.*). The angle of repose of all formulations was found to be the range of  $21.04 \pm 0.57^\circ$  to  $26.10 \pm 0.65^\circ$ .

The bulk density of all the formulation showed acceptable range. The bulk density of these powders was found to be in the range of  $0.22 \pm 0.02$  to  $0.33 \pm 0.03$  gm/cm<sup>3</sup> for all formulations.

The measured tapped density was in the range of  $0.243 \pm 0.042$  to  $0.416 \pm 0.045$  gm/cm<sup>3</sup> for all formulations.

Hausner ratio was found to be in the range of  $1.05 \pm 0.03$  to  $1.24 \pm 0.09$  for all formulations.

Carr's index of powder was found the range of  $05.33 \pm 0.12$  to  $19.68 \pm 0.05\%$  for all formulations. These values indicate that the prepared powder exhibited good flow properties.

#### Physico-Chemical characterization of floating tablets.

The weights of the tablets of all formulations were low standard deviation values, indicating uniformity of weight. The variation in weight was within the range of 5% complying with

pharmacopoeial specification (Indian Pharmacopoeia). The weight variation of different formulations was found to be between +0.0106 to + 0.0437. The hardness for different formulations was found to be between  $3.10 \pm 0.08$  to  $4.26 \pm 0.18$  kg/cm<sup>2</sup>. It was indicate satisfactory mechanical strength. The diameter and thickness of all the formulations were found in the range of  $10.00 \pm 0.03$  to  $10.07 \pm 0.12$  mm and  $3.03 \pm 0.01$  to  $5.01 \pm 0.00$  mm respectively. The friability of all formulation was found to be between  $0.44 \pm 0.05$  to  $0.98 \pm 0.01\%$ . The tablets compressed were stable and having good physical characteristics. The percentage drug content for different tablets formulation varied from  $97.55 \pm 0.05$  to  $99.79 \pm 0.15$  was found to be within limits which indicate uniform drug distribution in all formulations.

In this investigation the gastric floating system employed sodium bicarbonate as a gas forming agent dispersed in matrix. After reacting with hydrochloride acid, sodium bicarbonate creates carbon dioxide whose bubbles were on the surface of the tablets. It was observed that the gas generated is trapped and protected within the gel, formed by hydration of polymers (Xanthan and Guar gum) thus decreasing the density of the tablet below 1 and tablet becomes buoyant.

The tablet floating lag time and total floating time of all formulation was found to be between  $3.03 \pm 0.04$  to  $5.03 \pm 0.12$  (minutes) and  $01.03 \pm 0.04$  to  $24.33 \pm 0.23$  h respectively.

The swelling of the polymers used (Xanthan and Guar gum) were determined by swelling index of the tablet and illustration in figure. The swelling index of all formulation ( except formulation FT<sub>8</sub>) was found to be between  $15.04 \pm 0.31$  to  $77.99 \pm 1.39$  %.

After in-vitro drug release study in 0.1N Hydrochloric acid, it was found that 99.077 %, 71.823%, 92.837%, 97.057%, 89.217%, 98.952%, 85.987%, were release from the formulation FT1 to FT7 respectively. and

97.762%, 96.349%, 93.239%, 95.304%, 95.649%, 93.473%, 88.087% were release from the formulation FT9 to FT15 respectively.

In order to describe the kinetic of the release process of the drug from the formulations three kinetic models such as Zero order, Higuchi model and Korsmerer- Peppas model were used.

**Table 3. Composition of different formulations (mg) of floating tablets**

| BATCH CODE | CAPTOPRIL (mg) | GUAR GUM (mg) | XANTHAN GUM(mg) | SODIUM BICARBONATE (mg) | LACTOSE (mg) | MAGNESIUM STEARATE(mg) |
|------------|----------------|---------------|-----------------|-------------------------|--------------|------------------------|
| FT-1       | 50             | 50            | 50              | 40                      | 150          | 4                      |
| FT-2       | 50             | 50            | 100             | 40                      | 150          | 4                      |
| FT-3       | 50             | 50            | 150             | 40                      | 150          | 4                      |
| FT-4       | 50             | 50            | 200             | 40                      | 150          | 4                      |
| FT-5       | 50             | 100           | 50              | 40                      | 150          | 4                      |
| FT-6       | 50             | 150           | 50              | 40                      | 150          | 4                      |
| FT-7       | 50             | 200           | 50              | 40                      | 150          | 4                      |
| FT-8       | 50             | 50            | -               | 40                      | 150          | 4                      |
| FT-9       | 50             | -             | 50              | 40                      | 150          | 4                      |
| FT-10      | 50             | 100           | 100             | 60                      | 150          | 4                      |
| FT-11      | 50             | -             | 100             | 60                      | 150          | 4                      |
| FT-12      | 50             | 100           | -               | 60                      | 150          | 4                      |
| FT-13      | 50             | -             | 150             | 40                      | 150          | 4                      |
| FT-14      | 50             | 150           | -               | 40                      | 150          | 4                      |
| FT-15      | 50             | -             | 200             | 40                      | 150          | 4                      |

**Table 4. Comparative study of various powder characteristics for formulation FT<sub>1</sub> to FT<sub>15</sub>**

| Batch Code | Angle of repose ( $\theta$ ) | Bulk density (gm/cm <sup>3</sup> ) | Tapped density (gm/cm <sup>3</sup> ) | Hausner ratio (H <sub>R</sub> ) | Carr index (I <sub>C</sub> ) |
|------------|------------------------------|------------------------------------|--------------------------------------|---------------------------------|------------------------------|
| FT-1       | 21.04±0.57                   | 0.22±0.02                          | 0.263±0.012                          | 1.19±0.09                       | 16.34±0.02                   |
| FT-2       | 23.08±0.59                   | 0.22±0.08                          | 0.243±0.042                          | 1.06±0.12                       | 09.46±0.45                   |
| FT-3       | 21.36±0.38                   | 0.23±0.07                          | 0.250±0.125                          | 1.07±0.04                       | 06.08±0.09                   |
| FT-4       | 25.32±0.61                   | 0.23±0.02                          | 0.247±0.063                          | 1.05±0.03                       | 05.33±0.12                   |
| FT-5       | 24.45±0.12                   | 0.23±0.07                          | 0.277±0.004                          | 1.16±0.10                       | 13.82±0.52                   |
| FT-6       | 22.79±0.21                   | 0.27±0.01                          | 0.312±0.021                          | 1.12±0.11                       | 11.36±0.30                   |
| FT-7       | 23.92±0.69                   | 0.26±0.01                          | 0.294±0.101                          | 1.10±0.21                       | 09.62±0.10                   |
| FT-8       | 22.47±0.09                   | 0.30±0.07                          | 0.333±0.011                          | 1.09±1.01                       | 08.85±0.09                   |
| FT-9       | 25.96±0.71                   | 0.31±0.06                          | 0.384±0.002                          | 1.21±0.05                       | 17.39±0.03                   |
| FT-10      | 26.10±0.65                   | 0.33±0.03                          | 0.416±0.045                          | 1.24±0.09                       | 19.68±0.05                   |
| FT-11      | 25.53±0.59                   | 0.29±0.02                          | 0.344±0.031                          | 1.18±0.04                       | 15.31±0.20                   |
| FT-12      | 21.38±0.08                   | 0.27±0.12                          | 0.322±0.021                          | 1.17±0.41                       | 14.82±0.09                   |
| FT-13      | 22.26±0.05                   | 0.30±0.08                          | 0.370±0.005                          | 1.20±0.12                       | 17.17±0.05                   |
| FT-14      | 21.51±0.24                   | 0.26±1.12                          | 0.299±0.006                          | 1.14±0.22                       | 13.02±0.04                   |
| FT-15      | 25.96±0.69                   | 0.24±0.04                          | 0.280±0.126                          | 1.12±0.04                       | 11.43±0.09                   |

**Table 5. Physico-Chemical Characterization of Captopril Floating Tablets**

| Batch Code | Weight variation    |                       | Hardness (kg/cm <sup>2</sup> ) | Diameter (mm) | Thickness (mm) | Friability (%) | Drug Content Uniformity (%) |
|------------|---------------------|-----------------------|--------------------------------|---------------|----------------|----------------|-----------------------------|
|            | Average weight (mg) | Highest (%) deviation |                                |               |                |                |                             |
| FT-1       | 344.11±2.34         | + 0.0104              | 3.10±0.08                      | 10.00±0.04    | 3.46±0.04      | 0.69±0.05      | 98.12±0.25                  |
| FT-2       | 394.80±1.84         | + 0.0294              | 4.03±0.14                      | 10.00±0.03    | 4.03±0.01      | 0.50±0.01      | 98.54±0.26                  |
| FT-3       | 444.63±2.14         | + 0.0437              | 4.21±0.09                      | 10.01±0.08    | 4.43±0.06      | 0.53±0.03      | 98.83±0.11                  |
| FT-4       | 494.42±1.68         | + 0.0239              | 4.06±0.11                      | 10.01±0.02    | 5.01±0.00      | 0.84±0.01      | 98.95±0.03                  |
| FT-5       | 394.42±1.43         | + 0.1179              | 4.13±0.12                      | 10.06±0.04    | 4.03±0.01      | 0.98±0.00      | 99.79±0.15                  |
| FT-6       | 444.04±1.32         | + 0.1079              | 4.03±0.17                      | 10.01±0.08    | 4.47±0.03      | 0.44±0.05      | 98.75±0.04                  |
| FT-7       | 494.42±1.68         | + 0.0228              | 3.17±0.04                      | 10.02±0.05    | 4.93±0.05      | 0.84±0.02      | 97.91±0.06                  |
| FT-8       | 294.27±5.10         | - 0.0389              | 3.34±0.33                      | 10.06±0.04    | 3.03±0.01      | 0.72±0.09      | 98.10±0.02                  |
| FT-9       | 294.27±5.12         | + 0.0842              | 4.13±0.12                      | 10.07±0.04    | 3.03±0.01      | 0.98±0.01      | 97.45±0.05                  |
| FT-10      | 464.16±1.40         | - 0.0149              | 3.20±0.24                      | 10.01±0.04    | 4.53±0.02      | 0.63±0.05      | 99.16±0.04                  |
| FT-11      | 363.78±1.93         | + 0.0422              | 3.17±0.07                      | 10.07±0.12    | 3.43±0.05      | 0.84±0.09      | 97.81±0.35                  |
| FT-12      | 363.78±1.93         | + 0.0134              | 3.14±0.03                      | 10.01±0.08    | 3.62±0.02      | 0.57±0.02      | 99.26±0.01                  |
| FT-13      | 394.80±1.84         | + 0.0235              | 4.26±0.18                      | 10.05±0.04    | 4.03±0.01      | 0.64±0.06      | 98.54±0.07                  |
| FT-14      | 394.40±1.43         | - 0.1361              | 4.03±0.15                      | 10.06±0.03    | 4.04±0.04      | 0.45±0.08      | 98.95±0.09                  |
| FT-15      | 444.04±1.32         | + 0.0106              | 4.06±0.09                      | 10.01±0.07    | 4.47±0.03      | 0.46±0.04      | 97.91±0.03                  |

**Table 6. Physic-chemical Characterization of Matrices of Captopril Floating Tablets**

| Batch Code | Total Weight of Tablet (mg) | Floating Lag Time (minutes) | Total Floating Time (hours) | Matrix Integrity | Buoyancy on Disturbing |
|------------|-----------------------------|-----------------------------|-----------------------------|------------------|------------------------|
| FT-1       | 344.11±2.34                 | 4.06±0.09                   | 24.16±0.23                  | +                | Float                  |
| FT-2       | 394.80±1.84                 | 4.16±0.12                   | 24.03±0.04                  | +                | Float                  |
| FT-3       | 444.63±2.14                 | 3.25±0.25                   | 24.05±0.05                  | +                | Float                  |
| FT-4       | 494.42±1.68                 | 3.33±0.23                   | 24.33±0.23                  | +                | Float                  |
| FT-5       | 394.42±1.43                 | 4.03±0.04                   | 24.33±0.23                  | +                | Float                  |
| FT-6       | 444.04±1.32                 | 4.06±0.09                   | 24.03±0.04                  | +                | Float                  |
| FT-7       | 494.42±1.68                 | 4.03±0.04                   | 24.33±0.23                  | +                | Settle                 |
| FT-8       | 294.27±5.10                 | 3.06±0.04                   | 01.03±0.04                  | -                | Settle                 |
| FT-9       | 294.27±5.12                 | 3.33±0.23                   | 24.16±0.23                  | +                | Float                  |
| FT-10      | 464.16±1.40                 | 3.03±0.04                   | 24.03±0.04                  | +                | Float                  |
| FT-11      | 363.78±1.93                 | 5.03±0.12                   | 24.16±0.23                  | +                | Float                  |
| FT-12      | 363.78±1.93                 | 3.33±0.23                   | 24.06±0.04                  | -                | Settle                 |

|       |             |           |            |   |        |
|-------|-------------|-----------|------------|---|--------|
| FT-13 | 394.80±1.84 | 3.10±0.08 | 24.03±0.04 | + | Float  |
| FT-14 | 394.40±1.43 | 3.03±0.04 | 07.10±0.08 | - | Settle |
| FT-15 | 444.04±1.32 | 4.03±0.04 | 24.03±0.07 | + | Float  |

**Table 7. Hydration behavior of floating tablets (batch FT<sub>1</sub> to FT<sub>7</sub>)**

| Batch No.  | Swelling index  |                 |                 |                 |                 |                 |                 |
|------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|            | FT <sub>1</sub> | FT <sub>2</sub> | FT <sub>3</sub> | FT <sub>4</sub> | FT <sub>5</sub> | FT <sub>6</sub> | FT <sub>7</sub> |
| Time (hrs) |                 |                 |                 |                 |                 |                 |                 |
| 0.0        | 0.00            | 0.00            | 0.00            | 0.00            | 0.00            | 0.00            | 0.00            |
| 1          | 15.08±3.94      | 15.98±4.18      | 18.51±0.93      | 16.71±1.54      | 20.18±4.59      | 18.51±3.91      | 19.45±1.01      |
| 2          | 22.04±2.03      | 24.04±3.12      | 25.45±2.05      | 25.06±0.64      | 30.21±3.41      | 26.04±4.12      | 22.04±2.05      |
| 4          | 39.26±5.34      | 29.15±0.59      | 35.41±3.45      | 33.43±1.39      | 40.32±3.05      | 35.36±3.49      | 29.00±0.39      |
| 6          | 50.24±0.49      | 41.61±0.85      | 55.54±1.59      | 41.01±3.54      | 51.50±1.56      | 43.59±5.59      | 38.51±4.01      |
| 8          | 64.03±2.05      | 49.31±0.41      | 61.31±0.24      | 47.05±4.31      | 59.31±3.58      | 54.07±0.04      | 49.31±2.19      |
| 10         | 69.09±1.09      | 63.45±3.49      | 68.50±0.61      | 50.45±6.48      | 64.04±4.01      | 64.08±4.59      | 56.01±0.56      |
| 12         | 72.91±0.59      | 69.51±0.63      | 71.31±0.75      | 54.64±3.35      | 70.02±0.56      | 69.89±3.01      | 69.08±0.87      |
| 18         | 76.05±0.13      | 72.42±0.59      | 76.49±3.46      | 58.41±2.48      | 73.49±0.39      | 72.05±5.61      | 74.53±1.05      |
| 24         | 77.15±0.12      | 75.03±0.19      | 77.53±5.39      | 75.10±3.67      | 76.21±0.48      | 76.31±3.05      | 77.99±1.39      |

**Table 8. Hydration behavior of floating tablets (Batch FT<sub>9</sub> to FT<sub>15</sub>)**

| Batch No.  | Swelling index  |                  |                  |                  |                  |                  |                  |
|------------|-----------------|------------------|------------------|------------------|------------------|------------------|------------------|
|            | FT <sub>9</sub> | FT <sub>10</sub> | FT <sub>11</sub> | FT <sub>12</sub> | FT <sub>13</sub> | FT <sub>14</sub> | FT <sub>15</sub> |
| Time (hrs) |                 |                  |                  |                  |                  |                  |                  |
| 0.0        | 0.00            | 0.00             | 0.00             | 0.00             | 0.00             | 0.00             | 0.00             |
| 1          | 17.05±0.01      | 16.05±0.31       | 15.04±0.31       | 40.01±0.05       | 17.81±0.01       | 50.01±2.93       | 16.01±0.04       |
| 2          | 23.99±0.59      | 24.38±1.59       | 22.81±0.59       | 44.09±0.87       | 24.05±0.56       | 55.08±0.82       | 23.91±0.59       |
| 4          | 33.51±3.01      | 36.56±2.35       | 39.56±1.39       | 50.03±1.36       | 35.01±1.36       | 59.03±1.23       | 36.49±1.41       |
| 6          | 40.00±4.06      | 43.05±0.38       | 46.41±2.01       | 55.04±2.47       | 39.06±2.48       | 61.06±2.82       | 40.51±1.39       |
| 8          | 43.05±5.39      | 49.95±3.51       | 48.59±3.05       | 66.03±2.49       | 42.58±4.79       | 65.39±0.51       | 45.31±1.54       |
| 10         | 52.59±1.25      | 63.81±2.67       | 56.11±0.38       | 71.05±3.08       | 51.08±3.81       | 68.51±1.56       | 52.09±2.31       |
| 12         | 60.21±6.81      | 68.53±2.87       | 59.24±5.31       | 74.00±0.43       | 59.58±4.31       | 71.05±2.01       | 59.69±3.14       |
| 18         | 66.05±3.59      | 72.91±0.21       | 72.05±4.82       | 79.03±0.34       | 66.68±1.08       | 76.71±3.12       | 65.99±3.05       |
| 24         | 84.01±4.01      | 75.86±0.53       | 82.99±0.59       | 79.93±3.14       | 83.34±2.83       | 79.53±3.02       | 83.23±1.08       |

**Table 9. Model fitting analysis of drug release**

| Batch code       | Zero order | Higuchi plot | Korsmeyer-Peppas model |
|------------------|------------|--------------|------------------------|
|                  | $R^2$      | $R^2$        | n                      |
| FT <sub>1</sub>  | 0.8947     | 0.9890       | 0.7650                 |
| FT <sub>2</sub>  | 0.9220     | 0.9936       | 0.6324                 |
| FT <sub>3</sub>  | 0.9940     | 0.9452       | 1.2343                 |
| FT <sub>4</sub>  | 0.9988     | 0.9371       | 0.8911                 |
| FT <sub>5</sub>  | 0.9699     | 0.9678       | 0.6544                 |
| FT <sub>6</sub>  | 0.9926     | 0.9560       | 1.2126                 |
| FT <sub>7</sub>  | 0.5733     | 0.9154       | 0.4687                 |
| FT <sub>9</sub>  | 0.9563     | 0.9379       | 0.7828                 |
| FT <sub>10</sub> | 0.9191     | 0.9751       | 0.8999                 |
| FT <sub>11</sub> | 0.9909     | 0.9711       | 0.8656                 |
| FT <sub>12</sub> | 0.9878     | 0.9694       | 0.8404                 |
| FT <sub>13</sub> | 0.9846     | 0.9543       | 0.8196                 |
| FT <sub>15</sub> | 0.9973     | 0.9536       | 1.2817                 |

#### 4. Conclusion:

From all above finding it can be concluded that, an optimized oral controlled drug4. delivery system for captopril was developed via floating tablets prepared using a combination of natural polymers (Guar gum and Xanthan gum) to regulate the drug release5. in the upper part of gastrointestinal tract. The in-vitro dissolution studies carried out with the floating tablets of captopril prepared by Direct compression method suggests that tablets may deliver the drug at the site of its maximum6. absorption, thereby increasing the bioavailability as well as reduce the gastrointestinal side effects of the drug.

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