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# Formulation and Evaluation of Gastric Oral Floating Capsules Containing Captopril

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## Abstract

Captopril an ACE inhibitor has been used widely for the treatment of hypertension and congestive heart failure. The drug is freely water soluble and has elimination half life after an oral dose of 1.7 to 2 hr. It is stable at pH 1.2 and as the pH increases, the drug becomes unstable and undergoes a degradation reaction. Two viscosity grades of hydroxypropylmethyl cellulose (HPMC4000 and 15000 cps) and carbopol 934p were used to prepare captopril floating capsules. In vitro dissolution was carried out in 0.1 N hydrochloric acid at 37°C ± 0.5°C using USP apparatus method. Compared to conventional tablets, release of captopril from these floating capsules was apparently prolonged; as a result, an 8hr controlled-release dosage form for captopril was achieved. Drug release best fit both the Higuchi model and the Korsmeyer and Peppas model, followed by zero order kinetics. Fitting of the release data to the Korsmeyer and Peppas equation was found that, the drug release rate at 6hr (%) ranges from 29.49 ± 3.58 to 57.34 ± 1.842, the diffusion coefficient (n) ranges from 0.24 ± 0.037 to 0.62 ± 0.069. These results indicated that, the release mechanism is by diffusion. Higuchi release model also indicated that the mechanism of drug release is by diffusion. A numerical optimization technique was adapted, which are designed based on $3^2$ full factorial design containing two factors evaluated at three levels and the experimental trials were, performed at all possible combinations. Optimization by desirability function was performed. Optimum formulations were obtained using constraints on drug release at 6hr (%), and diffusion coefficient (n). The optimized formulations were evaluated for the responses. The actual response values were in accordance with the predicted values. Further from the data it is concluded that the mechanism of drug release is by diffusion and follows fickian transport.

**Keywords:** *Captopril, floating, HPMC, carbopol, optimization, release kinetics, Diffusion control release.*

## Introduction

Oral drug delivery system represents one of the frontier areas of controlled drug delivery system. Such a dosage forms having a major advantage of patient compliance. Floating drug delivery system belongs to oral controlled drug delivery system group which are capable of floating in the stomach by bypassing the gastric transit. These dosage forms are also defined as Gastro Retentive drug delivery system or hydrodynamically balanced dosage form or gastric floating drug delivery system, which can float in the contents of the stomach and release the drug in a controlled manner for prolonged period. The release rate will be controlled depending upon the type and concentration of the polymer which swells, leads to diffusion and erosion of the drug.[1,2] Captopril chemically 1-[(2S)-3-mercapto-2-methyl propionyl] –L -proline, is highly active and orally effective ACE inhibitor. The antihypertensive action of captopril may be attributed to a potentiation of the vasodilator substance bradykinin by the prevention of its break down. Captopril is effective in most instances without adjuvant treatment with diuretics. When orally ingested, only about 60-70 % of a normal dose can be absorbed. This incomplete absorption is due to instability of captopril in the alkaline environment because the captopril under goes degradation in the lower part of the gastro-intestinal tract. In view of this absorption characteristic, the hypothesis of current investigation is that if the gastric residence time of captopril containing formulation is prolonged and allowed to float in the stomach for a long period, the oral bioavailability might be increased[3,4]. FDDS or hydrodynamically balanced systems which have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time without affecting the gastric emptying rate. While the system is floating on the

gastric contents, the drug is released slowly at a desired rate from the system. After the release of drug, the residual system is emptied from the stomach. This results in increase in the gastric residence time and a better control of fluctuation in plasma drug concentrations. Based on the mechanism of buoyancy, two distinctly different technologies, i.e., noneffervescent and effervescent systems have been utilized in the development of FDDS[5,6]. 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. Generally the approach to the formulation of such floating dosage forms involves intimate mixing of drug with gel- forming 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. Resultant gel structure then controls the rate of diffusion of solvent-in and drug-out of the dosage form. As the exterior surface of the dosage form goes into solution, the immediate adjacent hydrocolloid layer becomes hydrated and maintains the gel layer. As a result, the drug dissolves in and diffuses out with the diffusing solvent, creating a 'receding boundary' within the gel structure[7,8].

**Hydrodynamically Balanced System = (HBS)**

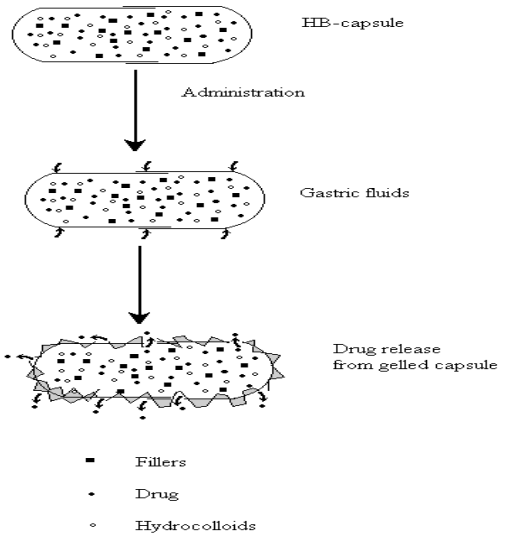



**Fig. 1: Working principles of the floating drug delivery system.**

These buoyant delivery systems utilize matrices prepared with swellable polymers such as Methocel or polysaccharides, e.g., chitosan, and effervescent components, e.g., sodium bicarbonate alone and/or with citric or tartaric acid or matrices containing chambers of liquid that gasify at body temperature. The matrices are fabricated so that upon arrival in the stomach, carbon dioxide is liberated by the acidity of the gastric contents and is entrapped in the jellified hydrocolloids. This produces an upward motion of the dosage form to float on the chyme. The carbon dioxide generating components may be intimately mixed within the tablet matrix, in which case a single–layered tablet is produced, or a bilayer tablet may be compressed. This contains the gas generating mechanism in one hydrocolloid containing layer and the drug in the other layer formulated for a sustained release effect[9,10].

## Material and Methods

Factorial design is an experimental design technique, by which the factors involved and their relative importance can be assessed. In the present study, the runs or formulations, which are designed based on $3^2$ full factorial design containing 2 factors evaluated at three levels and the experimental trials were, performed at all possible combinations.

The two independent formulation variables evaluated include:

Factor A: Amount and type of HPMC ($X_1$) (0, 0.5, 1). Factor B: Amount of carbopol ($X_2$). (0, 20, 40)[11,12].

Two viscosity grades of hydroxy propylmethyl cellulose, HPMC 4000 cps (HPMC 4K) and HPMC 15000 cps (HPMC15K), were used in formulation and their concentration was chosen arbitrarily. This factor was expected to give the effect of change in viscosity of hydroxy propylmethyl cellulose on response parameters. HPMC was chosen as a polymer because of its swelling property and the various viscosity grades of HPMC were reported to have duration of buoyancy for more than 20 hours in 0.1 HCl (density 1.033 g/ml), as well as in distilled water. Amount of HPMC is at three levels as 0, 0.5 and 1. 0, indicates presence of 200 mg of HPMC 4k, 0.5 indicates presence of HPMC 4k and 15k each 100 mg, and 1 indicates the presence of 200 mg of HPMC 15k.Three levels of carbopol 0,20, and 40 were used as factor B. The drug content was calculated to 12.5 mg based on the biological half-life and minimum effective concentration and elimination rate constant. Amount of carbopol was chosen as factor B because of its swelling and adhesive property. $3^2$ full factorial design was considered, according to the model totally 10 experiments were conducted with two replicates of center point[13,14].

The fitting of an empirical polynomial equation to the experimental result facilitates the optimization procedure. The general polynomial equation is as follows:

$$Y = B_0 + B_1X_1 + B_2X_2 + B_3X_3 + \ldots + B_{12}X_1X_2 + B_{13}X_1X_3 + B_{23}X_2X_3 + \ldots + B_{123}X_1X_2X_3.$$

Where,

Y is the response,

$X_1$, $X_2$, $X_3$ are the levels (concentration) of the 1,2,3 factors

$B_1$, $B_2$, $B_3$, $B_{12}$, $B_{13}$, $B_{23}$, $B_{123}$ are the polynomial coefficients.

$B_0$ is the intercept (which represents the response when the level of all factors is low).

Hence, the present research work was to study systematically the effect of formulation variables on the release and floating properties of captopril floating drug delivery system. To achieve this objective, the formulations were prepared in accordance with the designing of experiment (DOE) with two contributing factors called independent formulation variables such as; $X_1$ = Type and amount of HPMC, $X_2$ = Amount of carbopol , the ranges for these were selected based on the literature survey[15,16].

The response (dependent) variables include $Y_1$ = Drug release at 6hr and $Y_2$ = Diffusion co-efficient (n). To select the optimized formulation the numerical optimization by desirability function was applied.

**Table No 1: Actual and coded values of the factors**

| **Model** | **Actual values** | | | **Coded values** | | |
|---|---|---|---|---|---|---|
| **Factor** | **Low level** | **Mid level** | **High level** | **low** | **mid** | **High** |
| Factor -A | (200 mg of HPMC 4K) | (Both 100mg of HPMC 4K and 15K) | (200 mg of HPMC 15K) | -1 | 0 | +1 |
| Factor-B | 0 | 20 | 40 | -1 | 0 | +1 |

**The coded levels are calculated using the following formula:**

$$\text{Level} = \frac{\text{X - The average of the two levels}}{\text{Half the difference of the level}}$$

The capsule weight was fixed at 300 mg. In order to maintain the capsule weight constant, lactose was used as a diluent that does not interfere with the floating properties of the capsule.

**Formulation of capsules**

The ingredients and drug were passed through 120 # mesh. In each formulation, drug and the ingredients were manually blended homogeneously in a mortar and 300mg of mixture are filled in a '00' size gelatin capsules[17]. The general formula will be as follows:

**Table No 2: Model Formula for Floating Capsules**

| **SI. No** | **Ingredients** | **Quantity per capsule (300mg)** | **Percentage** |
|---|---|---|---|
| 1. | **Captopril** | 12.5 mg | 4.16 % |
| 2. | Hydroxy propyl methyl cellulose | 100-200 mg | 33.3-66.6 % |
| 3. | Sodium bicarbonate | 20 mg | 6.6 % |
| 4. | Carbopol | 20-40 mg | 6.6-13.33 % |
| 5. | Lactose (diluent) to make | 100 mg | 100 % |

**Table No 3: Optimized Formulation- Ingredients Used**

| Ingredients * | Formulation |
|---|---|
| Captopril | 12.5 |
| HPMC 15000cps | 200 |
| Sodium bi carbonate | 20 |
| Carbopol | 40 |
| Lactose | 27.5 |

*All ingredients are in milligrams per capsule.

**Calibration Curve for Captopril**

***Preparation of standard curve of captopril in 0.1 N hydrochloric acid, pH 1.2***

Instrument use Merck 530 UV-Visible spectrophotometer.

100 mg of captopril was accurately weighed into 100ml volumetric flask and dissolved in small quantity of 0.1 N HCl. The volume was made up with the 0.1 N HCl to get a concentration of (1000 µg/ml.) SS-I. From this 10 ml was withdrawn and diluted to 100ml to get a concentration of (100 µg/ml) SS-II.

**Scanning of Drug:** From stock solution (SS-II) 2.5 ml was withdrawn and the volume was made upto 10 ml with 0.1 N hydrochloric acid to get a concentration of 25 µg/ml[18]

## Evaluation Studies[19,20,21]

**Drug Content Estimation**

Accurately weighed quantity (300 mg) of formulation (equivalent to 12.5 mg of captopril) was taken into a beaker and 50ml of 0.1 N HCl was added, and stirred for 2 hrs. The solution was filtered through whatman filter paper No. 40, into a 100ml volumetric flask. The volume was made up with a 0.1 N HCl. From the above solution 2ml was pipetted into a separate 25ml volumetric flask and volume was made up with 0.1 N HCl. The absorbance was measured at 219.6 nm. The drug content was calculated by using the following equation.

Amount of drug present = absorbance $\pm$ intercept/ slope x dilution factor

*Dilution Factor = 25 x 50/ 2 x 1000 / Aver. amt. of drug x 100*

**Duration of Buoyancy**

Duration of buoyancy was observed simultaneously when the dissolution was carried out. The time taken for the capsule to sink to the bottom was noted, this gives the buoyancy of the capsule.

**Weight Variation**

20 Capsules were selected randomly from the lot and weighed individually to check for weight variation. IP limit for weight variation in case of capsules.

**In Vitro Release Profile**

USP XXII dissolution test apparatus II was used. The capsules were placed in the dissolution vessels fitted with paddles. 900 ml of 0.1 N hydrochloric acid solution (pH 1.2) was taken into the jar as dissolution medium and temperature was maintained at $37^0$ C. The paddle was rotated at 50 rpm. 5ml of the dissolution medium was withdrawn at pre determined intervals and fresh dissolution medium was replaced. The samples withdrawn were analyzed by UV method at 219.6 nm against reagent blank (0.1 N HCl).

**Data Analysis (Curve fitting analysis)[22]**

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were fitted into Higuchi model and Korsmeyer-Peppas release model.

***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, 'F' is the amount of drug release, 'K' is the release rate constant, and 't' is the release time.

***Korsmeyer and Peppas release model***

The release rate data were fitted to the following equation,

$M_t / M_\infty = K . t^n$

Where, $M_t / M_\infty$ is the fraction of drug release,

'K' is the release constant,

't' is the release time, and

'n' is the diffusional exponent for the drug release that is dependent on the shape of the matrix dosage form.

***Zero order release rate kinetics***

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

F= K.t

Where 'F' is the fraction of drug release, 'K' is the release rate constant and 't' is the release time.

**Stability Studies**[23]

The International Conference on Harmonization (ICH) Guidelines titled "stability testing of New Drug substance and products" (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America.

ICH specifies the length of study and storage conditions.

**Long-Term Testing**: $25^0$ C ± $2^0$ C / 60 % RH ± 5 % for 12 Months.

**Accelerated Testing:** $40^0$ C ± $2^0$ C / 75 % RH ± 5 % for 6 Months. Stability studies were carried out at $25^0$ C / 60 % RH and $40^0$ C / 75 % RH for the selected formulation for 2 months.

➢ **Optimized Formulation 1**

**Method**

The selected formulations were packed in amber-colored bottles, which were tightly plugged with cotton and capped. They were then stored at $25^0$ C / 60% RH and $40^0$ C / 75 % RH for 2 months and evaluated for their physical appearance, drug content and drug excepient compatibility at specified intervals of time.

**Drug-Excipient Compatability Studies**

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation.

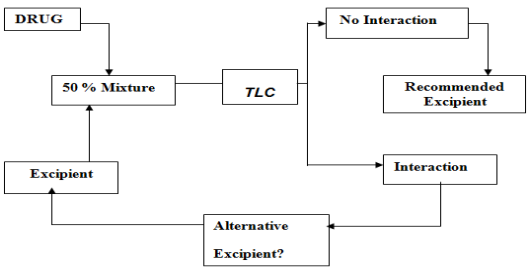



**Figure 2: Schematic representation of compatibility studies**

**Development of chromatogram**

The TLC chamber was saturated with mobile phase for a period of 30 minutes. About 2µl of standard and samples OPT-1 stored at $60^0$ C were spotted separately on the silica gel G plate at a distance of 2cm from the base of the plate. The spots were allowed to dry and then placed in the TLC chamber saturated with mobile phase. The solvent was allowed to run 8cm, the length of the plate and then the plate was removed from the chamber and dried. The plates were sprayed with phenol reagent followed by sodium carbonate solution after 5 minutes. The color developed after 40 minutes were compared with respect to the solute and solvent front. The relative front was calculated using the formula.

$$R_f = \frac{\text{Distance moved by the solute front from the origin}}{\text{Distance moved by the solvent front from the origin}}$$

***Fourier transmission infrared spectrophotometry (FT-IR studies)*:** The FT IR spectra of drug, polymer and optimized formulation. Sample about 5 mg was mixed thoroughly with 100 mg potassium bromide IR powder and compacted under vacuum 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 4000 $cm^{-1}$ to 625 $cm^{-1}$ in a scan time of 12 minutes.

**Scanning Electron Micro Graphs of the Opt-Form**

Scanning electron microscope (SEM) was used to examine for the formulation after the swelling. This was done in order to demonstrate one of the following parameters if any

1. Agglomeration
2. presence or absence of pin holes
3. Particle size and shape.

The samples were dried thoroughly in vacuum dessicator before mounting on a brass specimen studs. The samples were mounted using double sided adhesive tape and gold palladium alloy of 120 $A^0$ thickness was coated on the sample using sputter coating unit in argon ambient of 8-10 with plasma voltage about 2KV and discharge current about 20 MA. The SEM (GSM 35 CF Joel Japan) was operated at low accelerating voltage of about 15 KV with a load current of about 80 MA. The condenser lens position was maintained at a constant level. Working distance was 39 mm; the

photomicrographs were recorded at 500X, 1000X, 3000X and 4000X.

## Results and Discussions

Captopril exhibits peak absorbance at 219.6 nm in 0.1 N hydrochloric acid. Instrument use Merck 530 UV-Visible spectrophotometer. UV scan was taken between the wavelengths 200-400 nm. It gave a peak at 219.6 nm and the same was selected as $\lambda_{max}$ for captopril.

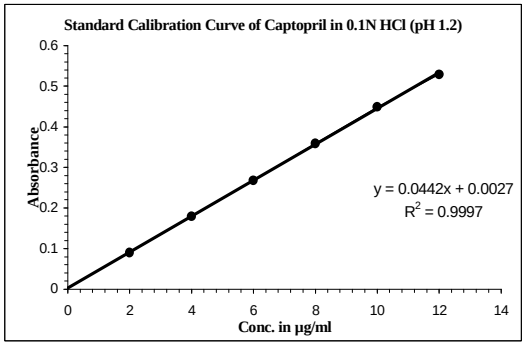



**Figure 3: Standard calibration curve in 0.1N HCl**

Formulations were prepared randomly following $3^2$ full factorial design. The materials used and composition are reported. For floating drug delivery system, the polymers used must be highly swellable in shortest time. Hence, HPMC was chosen as a main swellable polymeric material. In order to study the effect of different viscosity grades, HPMC 4k and 15k were chosen and it was found that, increased viscosity of a polymer prolongs the drug delivery from the dosage form. In order to retain the dosage form in the stomach for a long period of time and to avoid gastric emptying of dosage form, carbopol 934p was included. It was reported earlier that, carbopol belongs to the class of swellable and adhesive polymers and by utilizing this property of carbopol, it was included in the formulation with the intention of adhering the dosage form to the inner wall of the stomach and also possibly to control the release of captopril from the dosage form. Hence, the effect of presence or absence of carbopol was considered as one of the independent factor. Since, the rate of swelling of polymer depends upon the amount of water taken up by the polymer. Hence, sodium bicarbonate ($NaHCO_3$) is added in the formulation which upon contact with HCl liberates carbon-di-oxide ($CO_2$) and expels from the dosage form creating pores, through which the water can penetrate into the dosage form and the rate of wetting of polymer increases and the time required for drug release decreases.

**Table 4: Drug content values for the formulations, label claim for the drug = 12.5 mg /capsule.**

| **Formulations /Runs** | **Absorbance*** AM ± SD | **Amount of Captopril (DF) (mg / capsule )** | **%Drug content** |
|---|---|---|---|
| 1 | 0.9005 ± 0.126 | 12.65 | 101.2 |
| 2 | 0.9071 ± 0.098 | 12.75 | 102.00 |
| 3 | 0.9172 ± 0.054 | 12.89 | 103.12 |
| 4 | 0.8875 ± 0.021 | 12.47 | 99.76 |
| 5 | 0.9230 ± 0.048 | 12.97 | 103.76 |
| 6 | 0.8959 ± 0.110 | 12.59 | 100.72 |
| 7 | 0.9001 ± 0.090 | 12.65 | 101.20 |
| 8 | 0.8880 ± 0.058 | 12.48 | 99.84 |
| 9 | 0.9285 ± 0.011 | 13.05 | 104.4 |
| 10 | 0.8957 ± 0.069 | 12.59 | 100.72 |

*Average absorbance of 3 trials. SD = Standard deviation.

**Duration of Buoyancy:**

The capsule remained buoyant during the whole process of all dissolution study.

**Table 5: Weight variation of the formulations**

| Formulations /Runs | Average weight of capsule (mg) ± SEM |
|---|---|
| 1 | 429.1 ± 1.28 |
| 2 | 430.0 ± 2.12 |
| 3 | 431.0 ± 1.96 |
| 4 | 434.0 ± 2.52 |
| 5 | 430.2 ± 2.19 |
| 6 | 435.1 ± 2.92 |
| 7 | 431.9 ± 3.96 |
| 8 | 436.5 ± 2.35 |
| 9 | 433.1 ± 2.51 |
| 10 | 433.9 ± 3.46 |

The results obtained were found to be within the IP limit.

**Table 6: Release profile data for Formulation / Run = 10**

Weight of floating capsule = 436mg, Volume of dissolution medium =900ml of 0.1 N HCl, Amount of captopril = 12.59mg

| Time (hrs) | Abs.* | Concn. (mcg/ml) | Amount (mg/5ml) | Amount (mg/900ml) | *CLA (mg)* | CDR (mg) | CDR (%) | |
|---|---|---|---|---|---|---|---|---|
| 0.10 | 0.199 | 4.4412 | 0.0222 | 3.9971 | 0 | .9971 | 31.748 | 0.471 |
| 0.20 | 0.216 | 4.8258 | 0.0241 | 4.3432 | 0.0222 | .3654 | 34.674 | 0.219 |
| 0.30 | 0.318 | 7.1335 | 0.0357 | 6.4201 | 0.0463 | .4665 | 51.362 | 1.893 |
| 1.0 | 0.371 | 8.3326 | 0.0417 | 7.4993 | 0.082 | .5813 | 60.217 | 1.751 |
| 2.0 | 0.411 | 9.2376 | 0.0462 | 8.3138 | 0.1237 | .4375 | 67.017 | 2.124 |
| 3.0 | 0.44 | 9.8937 | 0.0495 | 8.9043 | 0.1699 | .0742 | 72.074 | 1.321 |
| 4.0 | 0.492 | 11.07 | 0.0554 | 9.9631 | 0.2193 | 0.182 | 80.877 | 2.014 |
| 5.0 | 0.532 | 11.975 | 0.0599 | 10.778 | 0.2747 | 1.052 | 87.786 | 1.302 |
| 6.0 | 0.578 | 13.016 | 0.0651 | 11.714 | 0.3346 | 2.049 | 95.701 | 1.089 |
| 7.0 | 0.584 | 13.152 | 0.0658 | 11.836 | 0.3996 | 2.236 | 97.189 | 1.643 |
| 8.0 | 0.602 | 13.559 | 0.0678 | 12.203 | 0.4654 | 2.668 | 100.62 | 1.981 |

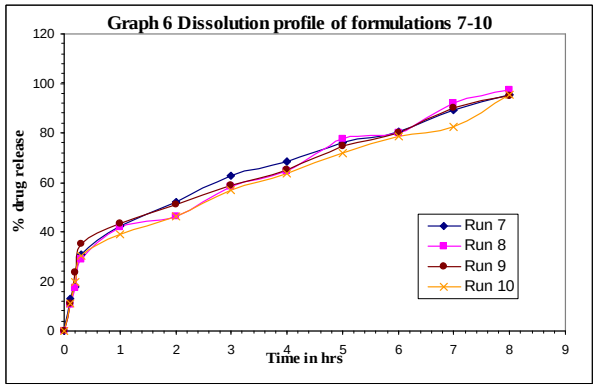



**Figure 4: Dissolution profile of optimized floating capsules**

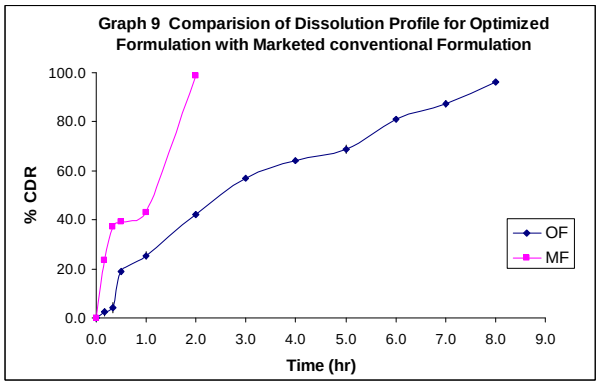



**Figure 5: Dissolution profile of optimized formulation with marketed preparation**

**Table 7: Curve fitting data for optimized formulation**

| Kinetic Models | OPT- Formulation |
|---|---|
| **Peppas Model** | |
| K | 25.42 ± 1.821 |
| N | 0.5438 ± 0.04099 |
| $R^2$ | 0.9861 |
| **Higuchi Model** | |
| K | 31.99 ± 1.084 |
| $R^2$ | 0.9608 |
| **zero order release Model** | |
| K | 13.49 ± 0.7255 |
| $R^2$ | 0.903 |

OF = optimized formulation, MF = marketed formulation

**Drug Excipient Compatibility Studies**

Thin layer chromatography was carried out to check for the possible Drug excipient interaction. The $R_f$ values of the drug and the drug-excipient were almost similar indicating that there was no interaction. Hence, it can be concluded that the drug captopril was found to be compatible with the excipients used in the formulation, as shown in figure no.2.

After comparing the IR spectra, we conclude that there was no significant interaction between the captopril and polymers and hence found to be compatible with the excipients used in the formulation are reported.

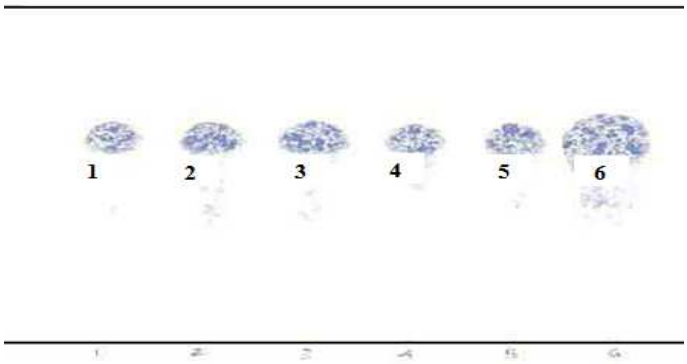



**Figure 6: Picture of TLC profile of compatibility studies after 8 weeks.**

**Table 8: $R_f$ values of Compatibility studies**

| SL No | Contents | $R_f$ values |
|---|---|---|
| 1. | Captopril | 0.6375 |
| 2. | Captopril + HPMC 15K | 0.6375 |
| 3. | Captopril + HPMC 4K | 0.6375 |
| 4. | Captopril + Lactose | 0.6375 |
| 5. | Captopril + Sod. Bicarbonate | 0.6375 |
| 6. | Captopril + carbopol | 0.6375 |

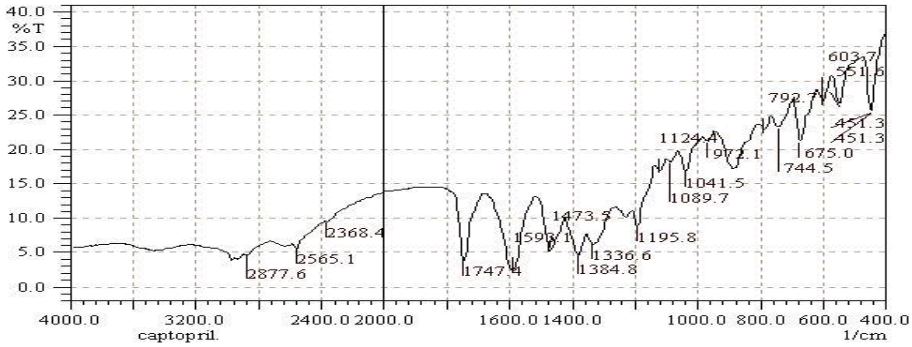



**Figure 7: IR SPECTRUM OF CAPTOPRIL**

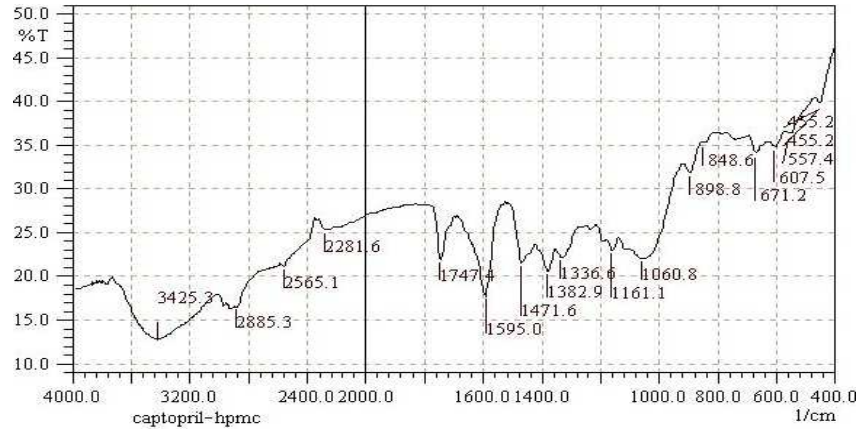



**Figure 8: The IR spectra obtained for captopril-HPMC formulations.**

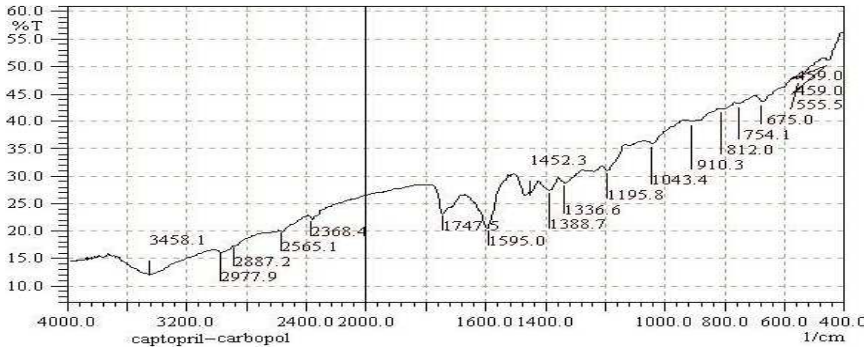



**Figure 9: The IR spectra obtained for captopril-carbopol formulations.**

**Stability Studies**

The optimized formulations were tested for 8 weeks at the storage conditions of $25^0$ C and $40^0$ C at 60 % RH and 75 % RH, were analyzed for their drug content. The residual drug contents of optimized formulation were found to be within the permissible limits. The capsules were also subjected to Thin Layer Chromatography (TLC) to determine compatibility of the drug with the adjuvant used in the capsules. The TLC profiles showed that the Rf values of the drug did not change, revealing no interaction between the drug and adjuvant. The capsules showed satisfactory physical stability at $25^0$ C and $40^0$ C at 60% RH and 75% RH respectively. The physical appearance did not change considerably.

**Table 9: Stability Data of Optimized Formulations**

| Time in weeks | Formulation –1 | Stored at 25° C/ 60% RH | Formulation –1 | Stored at 25° C/ 60% RH |
|---|---|---|---|---|
| | Physical Appearance | % Drug Content | Physical Appearance | % Drug Content |
| 0 | +++ | 97.58 | +++ | 98.59 |
| 2 | +++ | 96.98 | +++ | 97.53 |
| 4 | +++ | 97.95 | +++ | 97.31 |
| 6 | +++ | 96.98 | +++ | 96.23 |
| 8 | ++ | 95.75 | ++ | 94.74 |

+++ = same as on zero day, ++ slight change in color

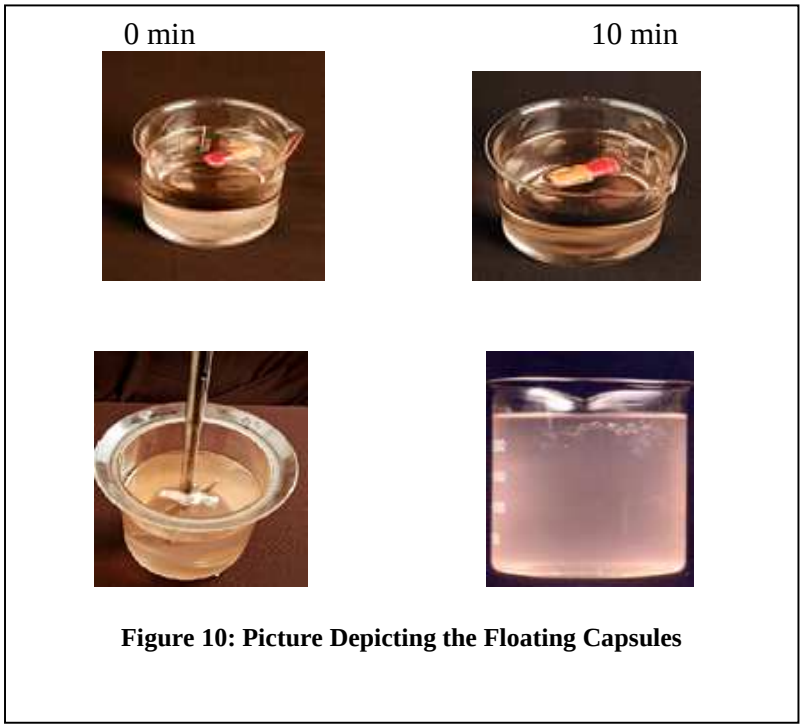
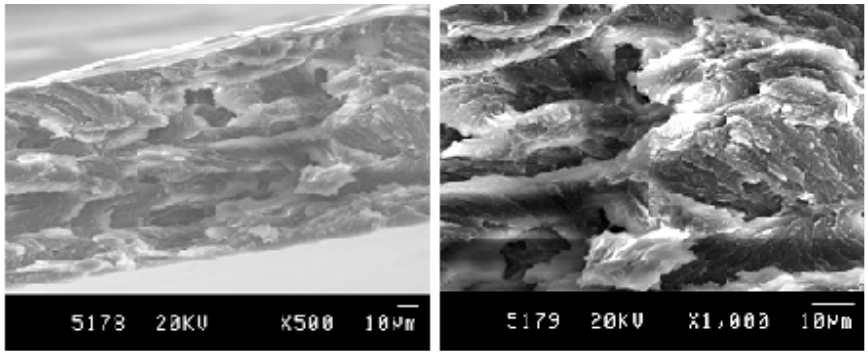


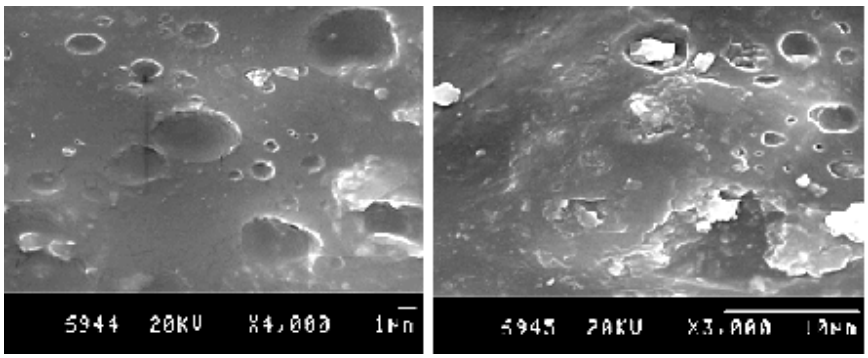

**Figure 10: Picture Depicting the Floating Capsules**

**Scanning Electron Microscope**

In figure 10 the picture depicts the cross section and pore formation of the gelled matrix of a capsule after swelling in the dissolution medium. Hence it prove integrity of the membrane after swelling, this ensures the flow of drug through the gelled matrix capsule is by diffusion mechanism which is further confirmed by curve fitting data where in 'n' lies between 0.24 to 0.52 and follows Fickian-diffusion transport.




**Picture depicting cross sectional view of the gelled matrix**




**Picture depicting pore formation of gelled matrix**

**Figure 10: Photographs Showing the Scanning Electron Microscopy of Gelled Matrix**

## Conclusion

Captopril is an example of a drug, which is degraded in colon. The gastric retentive drug delivery devices may be used for sustained and controlled drug delivery of such drugs. From the results it can be concluded that, as the polymer ratio increases in the formulation the release decreases which may be due to increased strength of the gel matrix of the HPMC. Similarly, presence of carbopol in the formulation also decreases the drug release, which may be attributed due to increased imbibition of water into polymer. Similarly, increases the swelling of carbopol which holds the water inside the matrix and thus decreases the release of drug from the dosage form.

Further it is concluded that, by the application of optimization technique, optimized formulation can be obtained with minimum expenditure of time and money. Gastric retention time can be increased for a drug like captopril, by formulating it in a floating dosage form, which enhances the absorption of captopril in the stomach hence giving the desired pharmacological effect. Thus the objective of my work of formulating a floating dosage form of captopril by using optimization technique has been achieved with success. Hence, the so developed formulation holds promising for other drugs which has an absorption window in the upper part of the stomach.

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