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Formulation and Evaluation of Controlled Gas Powered Systems of Captopril Tablets

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ABSTRACT

In the present investigation, an attempt has been made to increase therapeutics efficacy, reduce frequency of administration and improve patient compliance by developing sustained release gastro retentive floating tablets of Captopril using hydrocolloids like hydroxy propyl methylcellulose and Carbopol 934P by effervescent technique using direct compression method. In tablets formulations sodium bicarbonate and citric acid using gas generating agent and HPMC different grade was used to retard the drug release for 24 hrs in stomach. The prepared Gas powered tablets were subjected to post-compressional parameters. Drug compatibility with excipients was checked by DSC and FTIR studies. The stability study conducted 3 months as per the ICH guidelines. In all the formulations, hardness test indicated good mechanical strength, friability is less than 1% indicated that tablets had a good mechanical resistance. The results were revealed that as concentration of HPMC increases there is increase in floating time but release of the drug from all the formulation shows the slow release of Drug, as the concentration of sodium bicarbonate increases there is quick release of drug from all the formulation but the floating time decreases as the concentration of sodium bicarbonate increases so the optimum concentration of HPMC and Sodium bicarbonate is essential in order to achieve good result with respect to both drug release as well as floating time and floating lag time. It has been concluded that Formulation F1 and F4are the excellent formulation as they shows excellent drug release for 24 hrs with minimum floating lag time and more total floating time.

Keywords: Captopril, sodium bicarbonate, citric acid, HPMC, carbopol, controlled gas powered system.

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INTRODUCTION

A controlled drug delivery system is usually designed to deliver the drug in order to maintain blood levels above its minimum effective concentration and below its maximum safe concentration. Controlled Gas Powered System (CGPS) of the present invention is retained for longer periods of time in the stomach (spatial control) than previously known hydrophilic matrix tablets, floating capsules and bioadhesive tablets when these systems are administered with food. Thus, the longer period of gastric retention as compared to other oral controlled drug delivery systems can be attributed to the use of the CGPS as here in described. The CGPS results in release of the drug in to the more absorptive regions of the GIT, is in to the stomach and the small intestine rather than into the large intestine where drug absorption is poor or erratic. This is achieved by adjusting the time period of release for the drug so that it is about the same as or less than the retention time of the tablets at the site of absorption. Thus the system is not transported past the "absorption window" prior to releasing the entire drug, and the maximum bioavailability is attained[1-3]. For designing of CGPS different excipients were used are a gas generating agent (sodium bicarbonate), swelling agent (cross linked CMC), viscolyzing agent (xanthan gum) and a gel forming polymer (sodium alginate). Further, the pharmaceutical composition also contains an additional hydrophilic water soluble polymer (HPMC K4M, and carbopol) such a combination is referred to herein at times as CGPS. The swelling agent used along with super disintegrants which usually function to promote disintegration of tablet by absorbing large amounts of water and there by swelling. This expansion, as well as hydrostatic pressure, causes the tablet to burst. In a tablet which also contains a gas generating component, the generated gas is entrapped and the super disintegrant acts as swelling agent who swells to, preferably, at least twice its original volume. Thus, the composition of gas generating component, the swelling agent which is actually a super disintegrant, and the viscolyzing agent permit the CGPS to act as a controlled drug delivery system. In present research work Captopril is used as a model drug. Captopril is an angiotensin converting enzyme inhibitor; it inhibits the conversion angiotensin I to angiotensin II. As angiotensin II is a vasoconstrictor and a negative feedback mediator for renin activity, lower angiotensin II levels results in a decrease in blood pressure. It has been widely used for the treatment of hypertension and congestive heart failure. Captopril acts orally and the dosage used for the treatment of congestive heart failure ranges from 50 to 150 mg daily. After oral ingestion of a single dose the maximum hemodynamic effect is observed after 45–90 min. The drug is freely water-soluble and it has elimination half-life after an oral dose is 2-3 hrs.

It is stable at pH 1.2, and as the pH increases, the drug becomes unstable and undergoes a degradation reaction. Captopril has been a drug of choice in hypertension management. However, after single oral dosing of the drug, the anti hypertensive action is only effective for 6-8 hrs. Development of a controlled delivery system for captopril would bring many advantages for patients. The drug also undergoes from dose dumping and burst phenomenon (being freely water soluble) when formulated as controlled or sustained release formulation. So present investigation under taken to develop a controlled release oral solid dosage form[4-9]. In the present research work, we are designing Captopril gas powered systems for controlled release using different concentration of natural and synthetic polymers.The compositions of which are given in Table 1.

Table 1: Composition of Captopril CGPS Tablet.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Captopril	25	25	25	25	25	25	25	25	25	25	25	25
Sodiumbicarbonate	30	20	30	40	30	30	30	30	30	30	30	30
Xanthangum	10	10	10	10	5	10	10	10	10	10	10	10
Sodium Alginate	10	20	30	10	10	20	30	20	20	20	20	10
HPMC K4M	50	60	70	70	70	70	70	70	70	70	60	60
HPMC50CPS	-	-	-	-	40	40	40	30	30	40	40	40
HPMC5CPS	-	-	-	-	-	-	-	-	20	20	20	20
MCC	10	10	10	10	10	10	10	10	10	10	10	10
Citric Acid	10	20	10	20	10	10	10	10	10	10	10	10
Lactose	85	75	55	55	40	25	15	35	15	5	15	25
Talc	10	10	10	10	10	10	10	10	10	10	10	10
Total	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**	**250**

**All quantities in mg per tablet, F=formulation codes*

MATERIALS AND METHOD

Captopril drug is procured as a gift sample from Rajesh chemicals, Mumbai, India. HPMCK4M procured as a gift sample from AstraZeneca Pvt Ltd Bangalore.Carbopol 934, xanthan gum (XG), hydroxyl ethyl cellulose (HEC), magnesium stearate and citric acid are purchased from Hi media laboratories Pvt. Ltd, Mumbai. India, Sodium bicarbonate, sodium alginate, lactose, mannitol and talc were purchased from S.D. Fine Chemicals. Mumbai. All other materials used were of pharmaceutical grade.

Preparation of CGPS tablet of Captopril[10-12]:

According to present invention, the pharmaceutical composition is prepared by mixing the drug Captopril 25 mg with the gas generating component, the swelling agent, the gas entrapping viscolyzing agent and the optionally included gel forming polymer, citric acid source and lactose

by geometric mixing in mortar and pestle for10 min. The above powder was lubricated with magnesium stearate in mortar and pestle for2min.The lubricated blend was compressed into tablets using 12 stations Rimek tablet compression machine (M/s Karnawati Engg. Ltd. Ahmadabad) using 8 mm punches.

Evaluation of Captopril gas powered tablets[13-15]:

The powder blend was subjected for pre-compressional parameters. The prepared tablets were evaluated for post-compressional parameters as thickness, diameter, weight variation, hardness, friability, drug content, lag time subsequently buoyancy time, *in-vitro* dissolution studies, and stability studies. The thickness of the tablets was measured by Vanier calipers scale. It is expressed in mm. The Tablet hardness has been defined as the force required breaking a tablet in a diametric compression test. A tablet was placed between two anvils of hardness tester, force was applied to the anvils, and the crushing strength that causes the tablet to break was recorded in kg/cm^2.The hardness of tablet of each formulation way measured by using the Pfizer hardness tester. For determination of weight variation the twenty tablets were selected at random and weighed individually. The average weight of 20 tablets was calculated. Individual weights of the tablets were compared with the average weight. The % deviation were calculated and checked for wait variation as per I P.For determination of friability a pre-weighed sample (10 tablets) were placed in the friabilator, and operated for 100 revolutions, then again weighed the tablets and % friability was calculated using the formula.

$$F = \left(1 - \frac{W_0}{W}\right) \times 100$$

Where, W_0 – Weight of tablet before test, and W – Weight of tablet after test

The Drug content can be estimated a tablet potential for efficacy, the amount of drug per tablet needs to be monitored from tablet to tablet, and batch to batch. To perform the test, 10 tablets were crushed using mortar pestle. Quantity equivalent to 100 mg of drug was dissolved in 100 ml 0.1N HCL filtered and diluted up to 50µg/ml, and analyzed spectrophotometrically at 234nm. The concentration of drug was determined using standard calibration curve.

Buoyancy Capacity:

The buoyancy test of tablet was studied by placing them in 200 ml beaker containing 0.1 N HCl. The time in min taken by the tablet to reach the top from the bottom of the containing/ beaker was floating lag time or FLT and the time for which the tablet continuous floats on the surface of the medium way measured as buoyancy time. The swelling properties of HPMC matrices containing drug were determined by placing the tablet matrices in the dissolution test apparatus,

in 900 ml of distilled water at 37 ± 0.5^{0}C paddle rotated at 50 rpm. The tablets were removed periodically from dissolution medium. After draining free from water by blotting paper, these were measured for weight gain. Swelling characteristics were expressed in terms of percentage water uptake (WU %) according to the equation.

***In-Vitro* Dissolution Study[16-18]:**

The *in-vitro* dissolution studied was carried out using USP XXIV Dissolution apparatus No.2 (type) at 50 rpm. The dissolution medium consisted of 0.1N HCL for 2hrs and for subsequent 22 hrs in pH 7.4 Phosphate buffer (900ml) maintained at 37±0.5^{0}C. The release studies were conducted triplet. Adequate of sample 5ml were withdrawn at specific time interval and drug content was determined spectrophotometrically at 234 nm. Percentage drug release was calculated using an equation obtained from a standard curve. Analysis of data was done by using 'PCP Disso V-3' software; India. The graphs of times vs % release were plotted. To ascertain the order and mechanism of drug release the in vitro release data was subjected to various kinetic equations.

Treatment of Dissolution Data with Different Kinetic Equations[19-20]:

To analyse the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi matrix and Pappas. Based on ther-value, the best-fit model was selected.

Characterization of Captopril tablets:

FTIR Studies:

IR spectra for pure drug, F1 and F4 tablets were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR 1615, Perkin Elmer, USA) with KBr pellets.

DSC Studies:

5 mg of Cefixime and F1 and F4 tablets were sealed in perforated aluminium pans for DSC scanning using an automatic thermal analyzer system (Mettler Toledo, USA). Temperature calibrations were performed using indium as standard. An empty pan sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 100C/min from 50-300^0 C.

Stability Studies:

To assess the drug and formulation stability, stability studies were carried out according to ICH guidelines. The most promising CGPS tablet formulation F1 and F4 sufficient no of tablets were packed and sealed in aluminium packing and kept in the stability chamber maintained at 45 ± 1^{0}C / 75 ± 5 % RH for 3 months. Samples were taken at a definite intervals of time for about

Three months for the estimating the drug content, *in-vitro* dissolution and floating behaviour were studies.

RESULT AND DISCUSSION

The Gas powered tablets of Captopril were prepared direct compression technique. The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property. The results of pre-compression parameters were given in **Table 2.**

Table 2: Pre-compressional parameters of powdered blend

FC	Bulk	Tapped Density	Carr's Index	Hausner Ratio	Angle of
F1	0.524± 0.05	0.567 ± 0.02	10.12 ± 0.02	1.10± 0.03	22.98 ± 0.19
F2	0.586 ± 0.07	0.532 ± 0.05	9.65 ± 0.04	1.09 ± 0.05	21.56 ± 0.18
F3	0.645 ± 0.02	0.567 ± 0.04	9.66 ± 0.02	1.12 ± 0.08	23.02 ± 0.13
F4	0.579 ± 0.06	0.574 ± 0.07	11.34 ± 0.06	1.13± 0.04	24.12 ± 0.16
F5	0.654 ± 0.04	0.636 ± 0.03	12.22 ± 0.05	1.12 ± 0.06	20.23 ± 0.18
F6	0.526 ± 0.08	0.576 ± 0.09	09.77 ± 0.03	1.08 ± 0.08	22.54 ± 0.13
F7	0.589 ± 0.07	0.587 ± 0.07	11.67 ± 0.07	1.13 ± 0.05	22.91 ± 0.18
F8	0.673 ± 0.06	0.661 ± 0.05	14.84 ± 0.04	1.14 ± 0.08	23.78 ± 0.16
F9	0.704 ± 0.02	0.591 ± 0.03	11.61 ± 0.06	1.12 ± 0.03	20.88 ± 0.17
F10	0.635 ± 0.09	0.584 ± 0.08	13.63 ± 0.13	1.14 ± 0.07	24.75 ± 0.14
F11	0.618 ± 0.08	0.611 ± 0.07	12.15 ± 0.05	1.15 ± 0.04	23.25 ± 0.13
F12	0.595± 0.03	0.569 ± 0.03	13.88 ± 0.08	1.11 ± 0.06	22.14 ± 0.19

*The values represent mean ± S.D; n=3, FC = Formulation Code.

All the formulations were evaluated for various parameters, like thickness, diameter and Hardness of all tablets from batch F1 to F12 are shown in Table 3. In all the formulations, the weight variation of tablets was ranges between 246-255. Weight variation test revealed that the tablets were within the range of Pharmacopoeial limit. Hardness test indicated good mechanical strength, the hardness and percentage friability of the tablets of all the batches remained in the range of 4.2 to 8.6 kg/cm^2 and 0.39 to 0.71 respectively. Friability is less than 1%, indicated that tablets had a good mechanical resistance. Thickness of the tablets was ranges from 5.12 to 5.30 mm. The evaluation parameters were within acceptable range for all the formulations. The results of weight variation, hardness, thickness, friability and were shown in Table 3. The drug content of the tablets was ranges from 98.50 % to99.78 % which is within acceptable limits. The swelling index of the tablets was in the range 31.08 - 59.42 %. The results were shown in Table 3.

Table 3: Post-Compressional properties of CGPS Captopril tablets

FC	Average(mg)	Thickness(mm)	Hardness(kg/cm^2)	Friability(%)	Drug content	Swelling
F1	251 ± 0.03	5.3± 0.03	5.5 ± 0.03	0.52 ± 0.013	99.28 ± 0.55	31.08
F2	253 ± 0.02	5.3± 0.08	6.2 ± 0.05	0.60 ± 0.029	98.70 ± 0.43	34.06
F3	248 ± 0.07	5.3± 0.05	4.2 ± 0.03	0.48 ± 0.051	99.06 ± 0.84	39.95
F4	249 ± 0.04	5.3± 0.07	6.6 ± 0.07	0.64 ± 0.035	99.24± 0.55	41
F5	252 ± 0.05	5.3± 0.04	5.7± 0.07	0.71 ± 0.029	98.50 ± 0.53	46.03
F6	250 ± 0.06	5.3± 0.06	4.9± 0.02	0.39 ± 0.042	98.88± 0.31	49.23
F7	246± 0.02	5.1± 0.05	6.5 ± 0.07	0.52 ± 0.036	99.38± 0.75	50.07
F8	255± 0.04	5.1± 0.04	7.2 ± 0.09	0.658 ± 0.065	98.62± 0.65	52.3
F9	252± 0.02	5.3± 0.07	5.2 ± 0.06	0.69 ± 0.056	98.68 ± 0.64	56.21
F10	247 ± 0.01	5.3± 0.08	7.3 ± 0.09	0.49 ± 0.098	99.26 ± 0.20	52.45
F11	251 ± 0.08	5.1± 0.09	8.6 ± 0.04	0.54 ± 0.067	99.78 ± 0.17	58.75
F12	254 ± 0.03	5.2± 0.06	8.4 ± 0.08	0.57 ± 0.024	98.87 ± 0.42	59.42

*The values represent mean ± S.D; n=3, FC = Formulation Code.

The results of *in vitro* buoyancy time and lag time study (Figures 1- 4) revealed that as the concentration of sodium bicarbonate increases there is increase in total buoyancy time and decrease in lag time. In all the formulations buoyancy time ranges from 1180 - 1440 min and lag time ranges from 0.34 -0.50 min. The formulationF1 shows the lag time of 0.5 min and buoyancy time 1440 min and formulationF4 shows the lag time of 0.34min and buoyancy time 1440 min. Sodium bicarbonate induced CO_2 generation in the presence of dissolution medium (pH1.2 hydrochloric acid buffer). The gas generated is trapped and protected within the gel formed by hydration of polymer, thus decreasing the density of tablet. As the density of tablet falls below 1 the tablet becomes buoyant 18. The results were shown in Table 4.

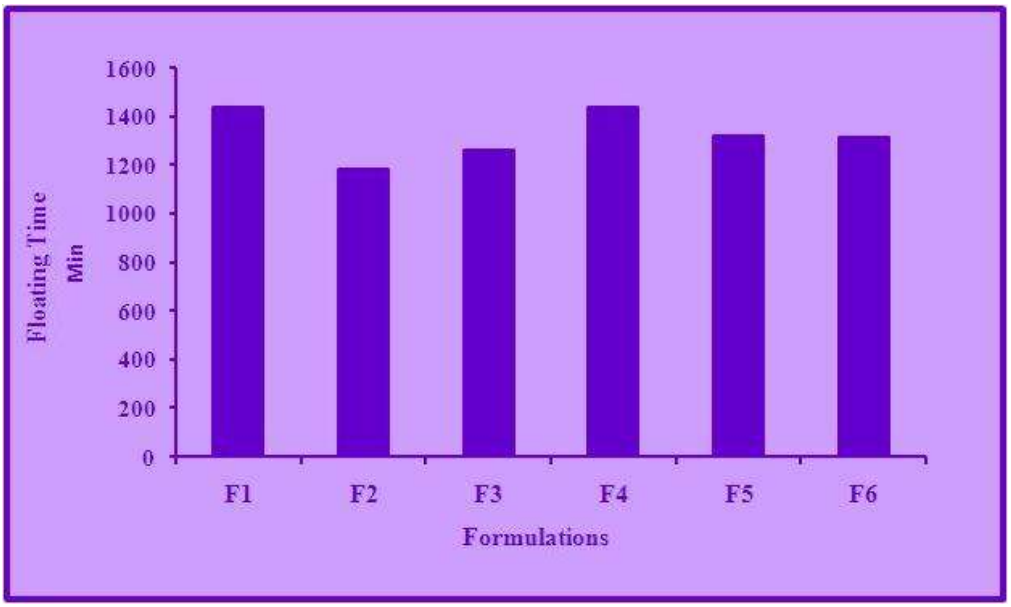

Figure 1: Floating Time Vs Formulation F1-F6

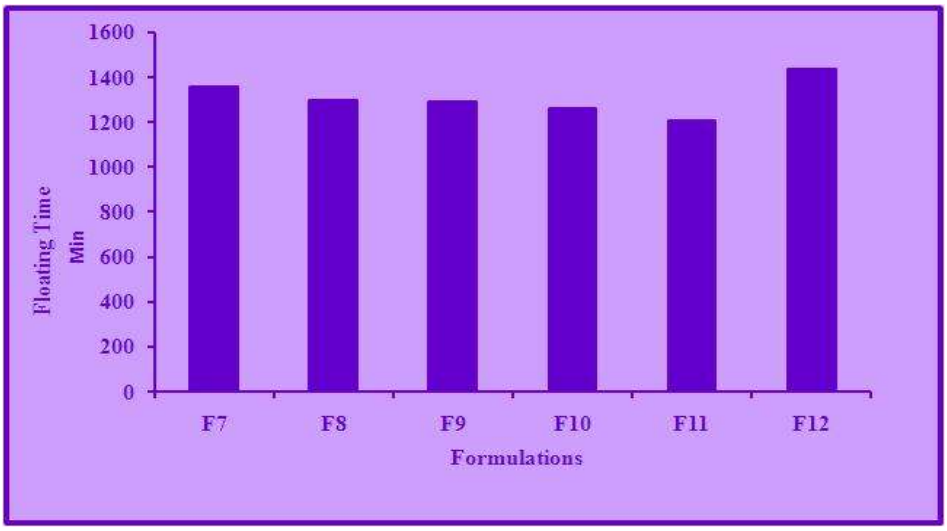

Figure 2: Floating Time Vs Formulation F7-F12

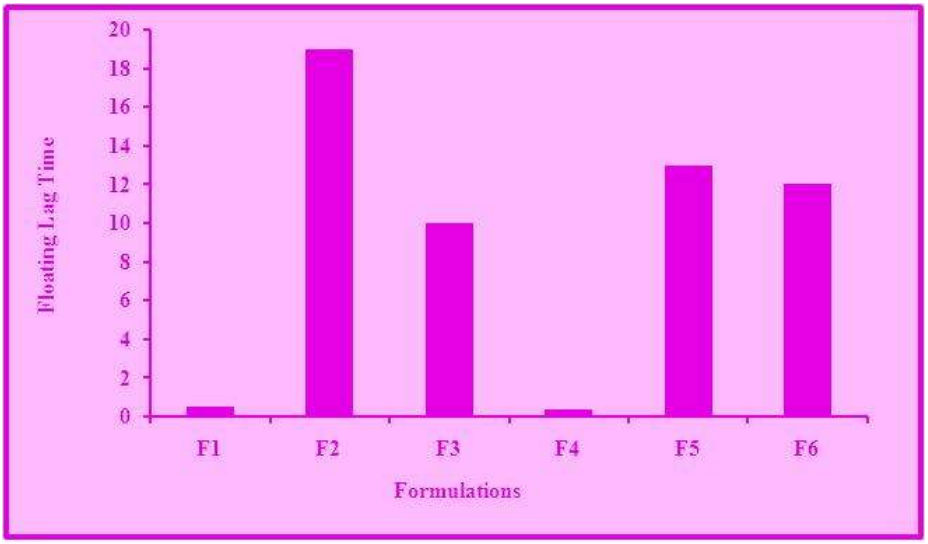

Figure 3: Floating Lag Time Vs Formulation F1-F6

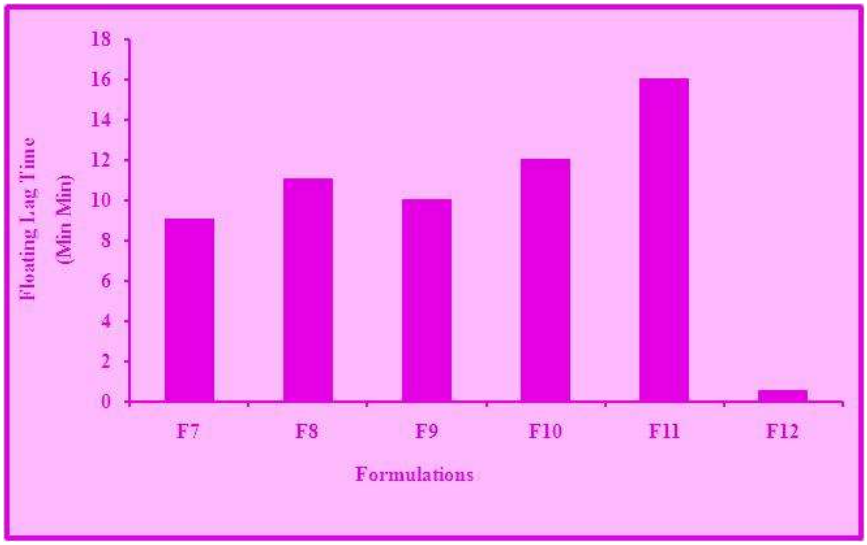

Figure 4: Floating Lag Time Vs Formulation F6-F12

Table 4: Floating ability of various CGPS Captopril tablets

FC	Floating Lag time (min)	Floating duration
F1	0.5	1440
F2	19	1180
F3	10	1260
F4	0.34	1440
F5	13	1320
F6	12	1310
F7	9	1360
F8	11	1300
F9	10	1290
F10	12	1260
F11	16	1210
F12	0.6	1440

*The values represent mean ± S.D; n=3, FC = Formulation Code.

The tablet floated with less lag time due to high concentration of gas generating agent. It was observed that paddle speed affected the floating properties of tablet. However, some results revealed that, as the concentration HPMC K4M increased, total floating time increased, this is because of increased gel strength of matrices, which prevents escape of evolved carbon dioxide from matrices, leading to decreased density of the formulations. As the density of tablets falls below 1 the tablet become buoyant. From the above results concluded that linear relationship exists between swelling process and viscosity of polymer. So the presence of optimum amount of HPMC K4M, $NaHCO_3$, and citric acid is important in achieving good floating time and minimum floating lag time. Incorporation of sodium bicarbonate helps to produce carbon dioxide gas which entrapped inside the hydrophilic matrices leads to increase in volume of dosage form resulting in lowering of density and dosage form starts to float. As the amount of polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent ($NaHCO_3$) increases the drug release increases and at the same time floating lags time decreases. The detailed *in-vitro* release data of all the formulations were given in Table 5. At the end of 12 hrs and 24 hrs. The formulation Fl - F4 prepared with only HPMC K4M showed tablet floating time in the range of 1140 min to 1440 min respectively, The releases of Captopril from all the formulations were in the range of 38 ± 0.87 to 49.53 ± 0.83 at the end of 6 hrs and 63.12 ± 0.23 to 74.41± 2.30 at the end of 12 hrs and 70.97 ± 0.34 to 88.60 ± 0.24 at the end of 18 hrs and 78.98 ± 0.89 to 99.66 ± 0.76 at the end of 24 hrs. Hence, F2, F3 formulation did not follow the principle of floating for the desire period of time. While the F1 and F4 follow the principle of floating at desired period of time as well give the best in Vitro

drug release profile. The detailed *in-vitro* data were plotted for percentage drug released Vs time as shown in Figure 5. The formulations F5-F8, which are prepared by using HPMC K4M, HPMC 50cps The releases of Captopril from all the formulations were in the range of 32.34 to 44.96% at the end of 6 hrs and 59.24 to 68.90% at the end of 12 hrs and 70.76 to 80.11% at the end of 18 hrs and 87.15 to 95.07% at the end of 24 hrs. These formulations follow the principle of floating for the desire period of time. The detailed *in-vitro* data were plotted for percentage drug released Vs time as shown in Figure 6. The formulations F9-F12 which are prepared by using HPMC K4M and HPMC K4M and HPMC 50 cps, the releases of Captopril from all the formulations were in the range of 30.72 to 46.02% at the end of 6 hrs and 55.81 to 68.59% at the end of 12 hrs and 66.95 to 81.27% at the end of 18 hrs and 78.39 to 99.19% at the end of 24 hrs. The detailed *in-vitro* data were plotted for percentage drug released Vs time as shown in Figure 7.

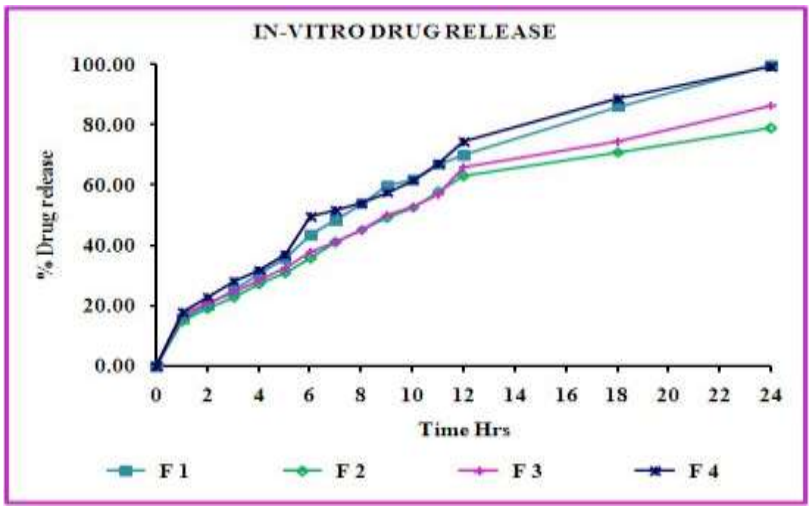

Figure 5: Comparative drug release profile of formulations F1 to F4.

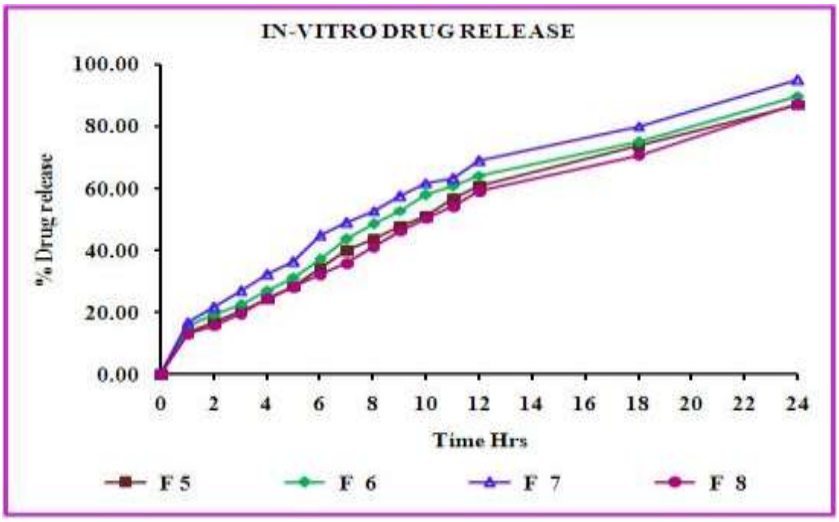

Figure6: Comparative drug release profile of formulations F5 to F8.

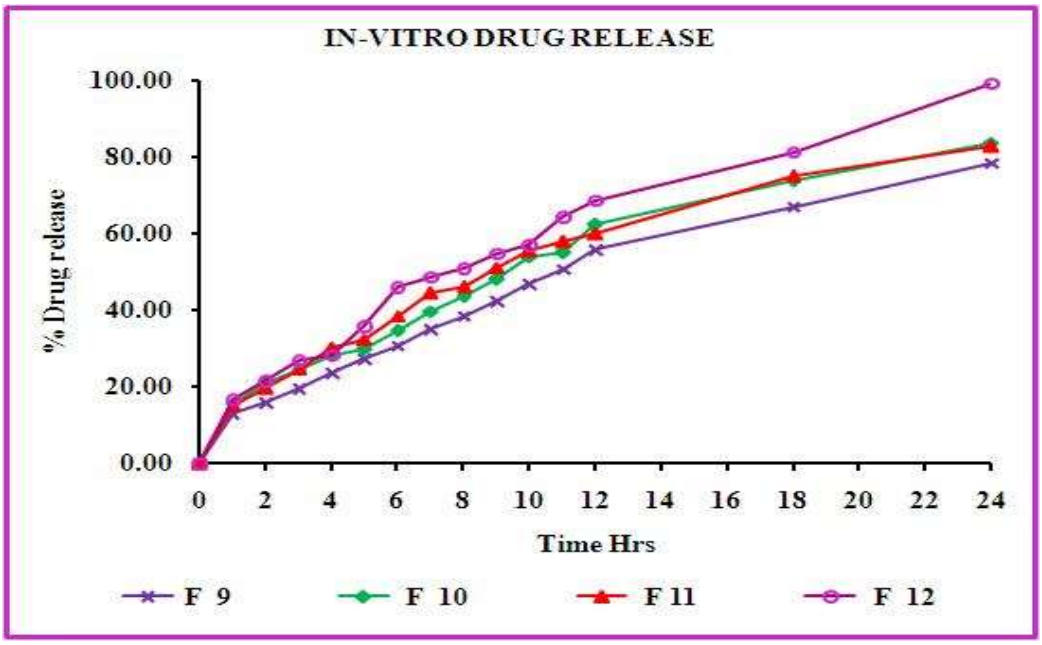

Figure7: Comparative drug release profile of formulations F9 to F12

Table 5: *In-vitro* drug release data at the end of 6, 12, 18 and 24 hrs from CGPS Captopril tablets

FC	%drug release	%drug release	%drug release	%drug release
F1	43.56 ± 0.65	70.63 ± 0.70	86.02 ± 0.65	99.66 ± 0.76
F2	35.73 ± 0.34	63.12 ± 0.23	70.97 ± 0.34	78.98 ± 0.89
F3	38 ± 0.87	65.89 ± 0.98	74.37 ± 0.86	86.47 ± 0.99
F4	49.53 ± 0.83	74.41 ± 2.30	88.60 ± 0.24	99.30 ± 1.55
F5	34.44 ± 0.12	61.04 ± 0.54	73.82 ± 0.52	87.15± 1.23
F6	37.22 ± 0.57	64.22 ± 1.64	75..15. ± 0.99	89.96 ± 1.83
F7	44.96 ± 0.74	68.90 ± 0.34	80.11± 1.23	95.07 ± 0.34
F8	32.34 ± 0.73	59.24 ±2.01	70.76 ± 0.22	87.28 ± 0.71
F9	30.72 ±1.93	55.81 ± 0.89	66.95± 0.48	78.39 ± 0.92
F10	34.52 ± 0.25	62.36 ± 0.46	73.66 ± 0.95	83.66 ± 0.09
F11	38.48 ± 0.35	58.89 ±0.64	74.87 ± 0.29	82.66 ± 0.67
F12	46.02 ± 0.65	68.59 ±0.76	81.27 ± 0.39	99.19 ± 0.23

* All values are expressed as mean ± SD, n=3, FC= Formulation codes.

The kinetic study results suggest that, the drug was released by mixed order kinetics. To ascertain, the drug release mechanism the *in-vitro* release data were also subjected to Higuchi's diffusion equation the r- values (Table 6) of all the formulations were 0.9705 to 0.9897. It suggests that the drug released by diffusion mechanism. The formulations are also treated to Peppa's plots by taking log percent drug release versus log time. The plots are found to be fairly linear and the regression values (n value) of all formulations ranges (Table 6) from lowest 0.7460 to highest 0.9960.

Table 6: Curve Fitting Analysis for Different Formulations.

FC	Zero order (R)	First order (R)	Higuchi's (R)	Korsmeyer– Peppa's	
				R	N
F1	0.9331	0.9898	0.9835	0.9859	0.746
F2	0.9031	0.9844	0.9787	0.9785	0.750
F3	0.9309	0.987	0.9816	0.9757	0.784
F4	0.9221	0.9726	0.9842	0.9815	0.996
F5	0.9508	0.9866	0.9746	0.9771	0.841
F6	0.9292	0.9806	0.9780	0.9715	0.844
F7	0.9176	0.9534	0.9896	0.9875	0.838
F8	0.9606	0.9744	0.9705	0.9784	0.816
F9	0.9519	0.9947	0.9762	0.9822	0.972
F10	0.9341	0.9922	0.9784	0.9761	0.786
F11	0.9142	0.9968	0.9897	0.9890	0.965
F12	0.9393	0.9892	0.9830	0.9800	0.988

*All values are expressed as mean ± SD, n=3, FC= Formulation codes.

FTIR study:

The IR spectrum of the pure drug Captopril sample and formulations F1 and F4 were shown in Figure 8.The drug Captopril contains carboxylic acid group and carbonyl group this is evident from its IR studies where in OH group of the carboxylic acid give a broad peak at 3119 cm^{-1} this is the characteristic peak of the free carboxylic acids. C=O absorption of amide group is noticed at 1625 cm^{-1}. The carbonyl group of carboxylic acid is found to resonate at 1750 cm^{-1} the C-H of the drug residue absorbed at 2980 and 2951 cm^{-1} indicates their aliphatic nature. Same drug was taken for formulation with HPMC, Na CMC and carbopol whose IR spectra gave number of O-H and carboxylic acid residues. In the IR spectrum suggesting that the characteristic absorption peaks of the drug have not under gone any change. Either suggesting that drug and HPMC mixture has not undergone any chemical interaction but produce only physical mixtures to facilitate for the drug solubility because HPMC contain number of hydroxyl group.

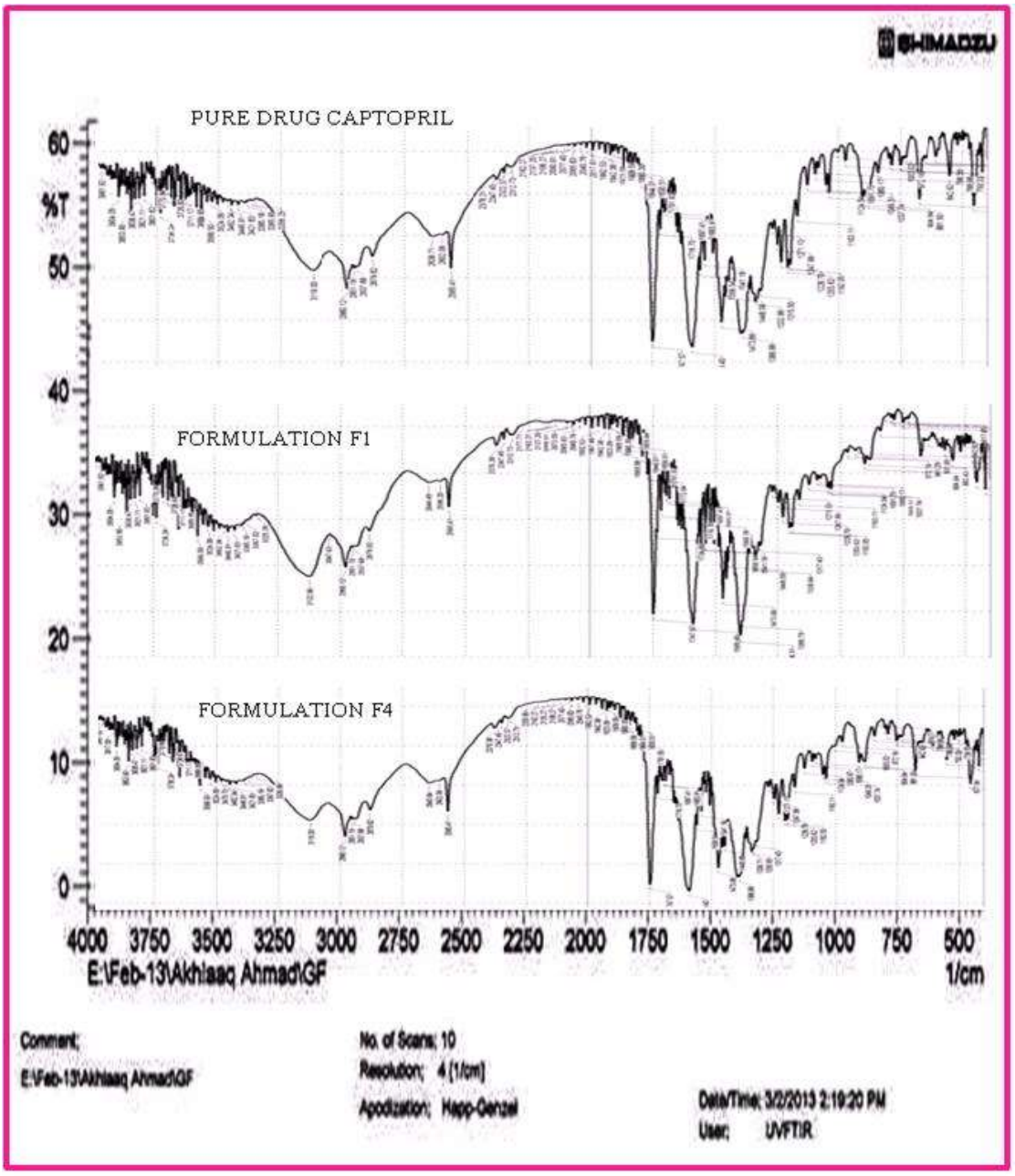

Figure7: IR spectra of pure drug Captopril and optimized formulations F1 and F4

DSC study:

The pure drug Captopril sample and formulations F1 and F4 were shown in Figure 9 where subjected to DSC, the drug captopril has given a strong melting point at 110^{o}C but it started melting at 105^{0}C completed at 115^{0}C suggesting that this commercial sample contain little impurities. When the polymer containing drug and HPMC formulation F1 has taken for DSC studies little change in the melting range was observed where it has started melting at 105^{0}C giving a strong melting range at 108^{0}C this decrease suggested that the drug and polymer has made an physical mixture effecting for the decrease in the range of absorption of drug this

indicate the chemical reaction has not taken place between drug and HPMC. The formulation F4 is taken for studies is drug and polymers HPMC and NACMC since the polymer is sodium content melting range is wide enough where in process of melting has started at 90^0C give melting range at 103^0C completed at 111^0C indicating that the compound containing inorganic salt give always long range. When polymer was prepared with drug and carbopol resulting polymer give absorption ranged which is identical with the drug it self suggesting that during the process of formulation the chemical reaction has taken place shown in Figure 9. The above study with IR as well as DSC in this case drug carbopol is not undergoing any chemical reaction with polymer used. The physical mixture so prepared will help for the solubility of the drug to make the drug available for physic chemical reaction to produce the desired effect.

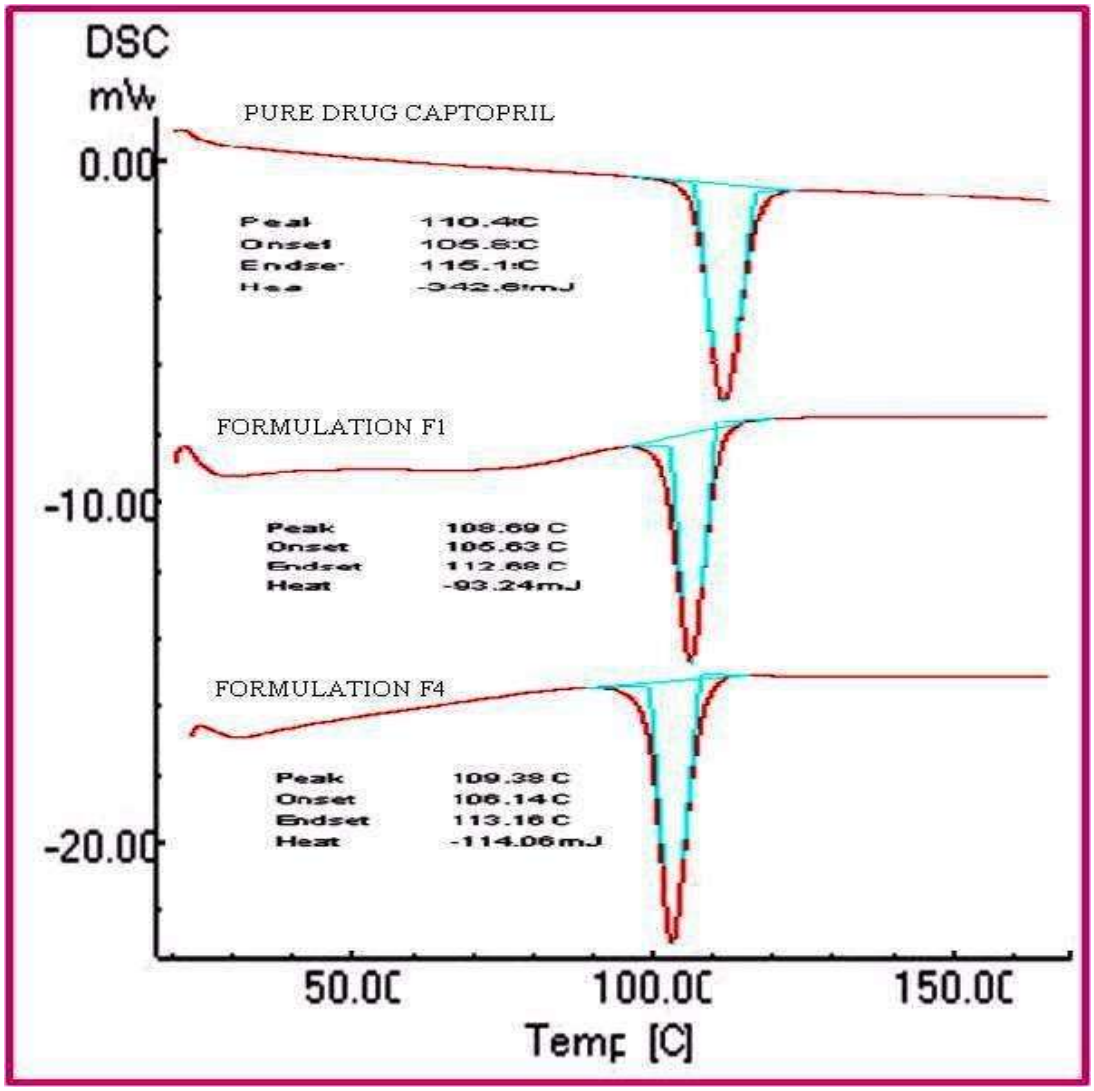

Figure 9: DSC Thermograms of pure drug Captopril and optimized formulations F1 and F4

The most promised formulations were selected stability studies. Three month stability studies were performed as per ICH guidelines at a temperature of $45^0 \pm 1^0$C over a period of three month on the promising CGPS tablet formulation F1, F4. Sufficient number of tablets (10) were packed in aluminum packing and kept in stability chamber maintained at 45 ± 1^0 C / 75 ± 5 % RH for 3 months. Samples were taken at 30 days intervals for drug content estimation. At the end of three months period, the estimation of drug contents are shown in tables 7 and 8.The stability study conducted for optimized formulation F1 and F4 as per the ICH guidelines for three months and the formulation F1 and F4 were found to be stable.

Table 7: Drug Content Data of Stability FormulationF1

Sl. No.	Trial No	1st Day (%)	30th Day (%)	60th Day (%)	90th Day (%)
1.	I	99.96	99.83	99.87	99.87
2.	II	99.93	99.45	99.91	99.88
3.	III	99. 76	99.63	99.55	99. 76
4.	Mean	99.88	99.63	99.86	99.83

*All values are expressed as mean± SD, n=3.

Table 8: Drug Content Data of Stability FormulationF4

Sl. No.	Trial No.	1st Day (%)	30th Day (%)	60th Day (%)	90th Day (%)
1.	I	99.64	99.62	99.71	99.59
2.	II	99.79	99.69	99.92	99.78
3.	III	99. 71	99.75	99.81	99.87
4.	Mean	99.71	99.68	99.81	99.69

*All values are expressed as mean± SD, n=3.

CONCLUSION

From study it is evident that a promising gas powered controlled release floating tablets of Captopril can be developed to increase gastric residence time and thereby increasing its bioavailability. Further detailed investigations are required to establish efficacy of these formulations and fix the required dose.

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