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Formulation and Evaluation of Floating tablet of captopril

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ABSTRACT

The primary objective was to formulate & evaluate gastroretentive floating tablets of the Captopril by using different polymers in different ratios.Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), it isused in the treatment of hypertension. Twelve formulations of floting tablets were prepared by using direct compression method. The evaluation results revealed that all formulations comply with the specification of official pharmacopoeias and/or standard reference with respect to general appearance, content uniformity, hardness, friability and dissolution. Out of all the formulation developed, Formulation 3 gave better-controlled drug release and floating properties in comparison to the other formulations. Hence, developed floating tablets of Captopril are formulated to increase gastric residence time and thereby improve its therapeutic efficacy.

Keywords: Captopril, Direct compression method, Polymers, Formulation, Floating tablet

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1. Introduction

Controlled release drug delivery systems (CRDD) have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity or targeting the delivery of drug to a tissue.

Gastroretentive Drug Delivery Systems:

The development of oral CRDDS has been hindered by the inability to localize the system in the selected regions of the GIT. There has been considerable research over the last decade on the possibility of controlled and site specific delivery to the GIT by controlling the gastro intestinal

transit of orally administered dosage forms using Gastro Retentive Drug Delivery Systems (GRDDS). Such GRDDS possess the ability of retaining the drug in GIT particularly in the stomach for long periods.

Floating DDS (FDDS):

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight (RW) has been reported in the literature.

2. Materials and Methods

Table 1: List of Materials and Suppliers

S.No	Ingredients	Suppliers
1	Captopril	Supplied By Natco Pharma
2	Guargum	SD Fine Chemicals, Mumbai
3	Xanthumgum	SD Fine Chemicals, Mumbai
4	Agar	SD Fine Chemicals, Mumbai
5	Tragacanth	SD Fine Chemicals, Mumbai
6	Sodium bi carbonate	SD Fine Chemicals, Mumbai
7	Citric acid	SD Fine Chemicals, Mumbai
8	MCC	SD Fine Chemicals, Mumbai
9	Talc	SD Fine Chemicals, Mumbai
10	Magnesium stearate	SD Fine Chemicals, Mumbai

Table 2: List of equipments and Companies

S.No	Name of the Equipment	Model
1	Electronic weighing balance	Scale-tec
2	Friabilator	Roche Friabilator Electrolab, Mumbai
3	Laboratory oven	Dtc-00r
4	Compression machine	Cmd(Cadmach)
5	Tablet hardness tester	Pfizer Hardness Tester, Mumbai
6	UV	Labindia Uv 3000+
7	Dissolution apparatus	Electrolab TDT-08L
8	Vernier calipers	Cd-6"Cs

Analytical Method Development

Construction of calibration curve of Captopril in 0.1N HCL:

Procedure: Working standard: 100mg of Captopril was weighed and dissolved in 10ml methanol and then made up to a volume of 100ml with0.1N HCL it gives1000µg/ml concentrated stock solution.

Dilution 1: From the working standard solution 10ml was diluted to 100ml with 0.1NHCL it will give 100µg/ml concentrated solution.

From dilution-1, take 0.2, 0.4, 0.6, 0.8 and 1ml of solution and was diluted up to mark in 10ml volumetric flask to obtain 2, 4, 6, 8 and 10µg/ml concentrated solutions. This solutions absorbance was noted at λ_{max}=242nm

Formulation of gastro retentive floating tablets by direct compression method processing steps involved in direct **compression method:**

The matrix tablets were prepared by following the General Methodology as given below:

All ingredients (except magnesium stearate and talc) were weighed accurately and co sifted by passing through #40 sieve, blended in a Poly Bag for 5 min. The above blendwere lubricated with # 60 Sieve passed Magnesium stearate & talc.The final blend was then compressed into tablets using 16 station tablet compression machine with an average hardness of 7.0 -9.0kg/cm^2, by using 6mm to 8mm die.

Evaluation of Tablets

The formulated tablets were evaluated for the following Pre, post compression quality control studies & In vitro Buoyancy studies and dissolution studies.

In vitro Buoyancy studies:

a. **Floating Lag Time (FLT):** A tablet was placed in a 100 ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as the Floating Lag Time (FLT).
b. **Total Floating Time (TFT):** A tablet was placed in a 100 ml beaker containing 0.1N HCl. The duration of time up to which the tablet constantly floats on the dissolution medium was noted as the Total Floating Time (TFT).
c. **Matrix integrity:** During the period of TFT the swelled matrix tablets were observed for integrity. For 12 hrs

In vitro Dissolution Study:

900 ml of 0.1N HCl was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of 37^0C±0.5^0C. A tablet was placed in the vessel and was covered; the apparatus was operated up to 12 hrs at 50 rpm. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium and were analyzed spectrophotometrically at λ_{max} =242 nm using a UV-spectrophotometer (Lab India).

Fourier Transform – Spectroscopy:

FT-IR spectra were recorded on samples prepared in potassium bromide disks using thermon electron FTIR. Samples were prepared in potassium bromide discs by means of a hydrostatic press. The scanning range was 400 to 4000 cm^{-1} and the resolution was 4 cm^{-1}. IR spectroscopy has been to quantify the interaction between drug and carrier FTIR spectra of pure Captopril, Captopril: Agar(1:4) (MM), Captopril: Xanthumgum(1:4) (MM) and best Formulation are shown in figs.

In-vitro Release Kinetics Studies:

The analysis of drug release mechanism from a pharmaceutical dosage form is important but complicated process and is practically evident in the case of matrix systems. The order of drug release from FDDS was described by using zero order kinetics or first order kinetics. The mechanism of drug release from FDDS was studied by using Higuchi equation and the Peppa's-Korsemeyer equation.

3. Results and Discussion

Construction of Standard calibration curve of Captopril in 0.1N HCL:

The absorbance of the solution was measured at 242nm, using UV spectrometer with 0.1N HCl as blank. The values are shown in table no 13. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml.

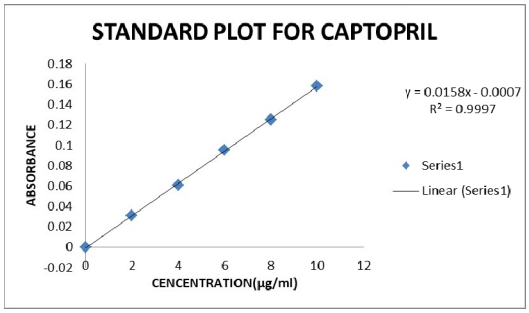

Fig 1: Standard calibration curve of Captopril in 0.1N HCl

Pre compression studies:

The Captopril floting tablets were evaluated for their flow properties like the bulk density and the tapped density for all formulations were found to be almost similar. The Carr's index and Hausner's ratio were found to be in the range of ≤ 18 and 1.0 to 1.23 respectively, indicating good flow and compressibility of the blends. The angle of repose for all the formulations was found to be in the range of 31.29-37.27° which indicating passable flow (i.e. incorporation of glidant will enhance its flow).

Post compression Studies:

The post compression parameters showed on variation in weight was within the limit. The thickness of tablets was found to be between 3.39-3.56 mm. The hardness for different formulations was found to be between 7.80 to 8.35 kg/cm^2, indicating satisfactory mechanical strength. The friability was < 1.0% W/W for all the formulations, which is an indication of good mechanical resistance of the tablet. The drug content was found to be within limits 98 to 102 %.

In vitro dissolution Studies:

Among the different control release polymers, Guargum was showing highest drug release retarding capacity. F3 was showing the satisfactory results. For F3 formulation diffusion exponent n value is in between 0.45 to 0.89 so they are following non fickiananmolous diffusion model. Higuchi plots for F3formulation is having good correlation values so the drug is releasing diffusion mechanism.

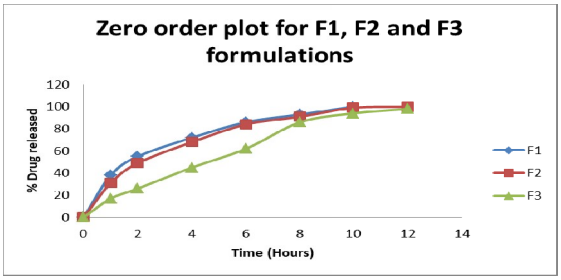

Fig 2: Comparative dissolution profile for F1, F2 and F3 formulations

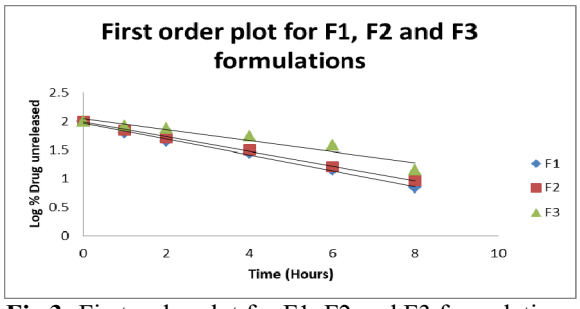

Fig 3: First order plot for F1, F2 and F3 formulations

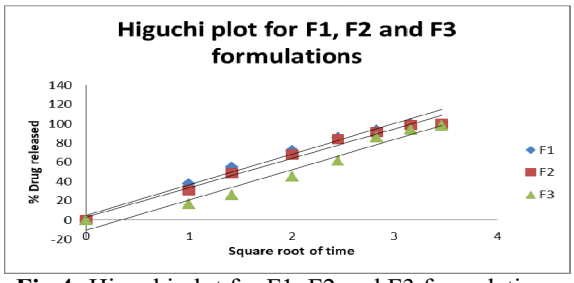

Fig 4: Higuchi plot for F1, F2 and F3 formulations

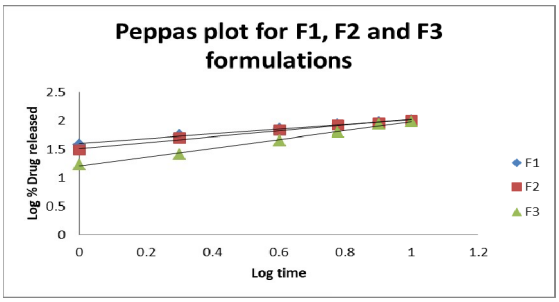

Fig 5: Peppas plot for F1, F2 and F3 formulations

Fourier Transform – Spectroscopy:

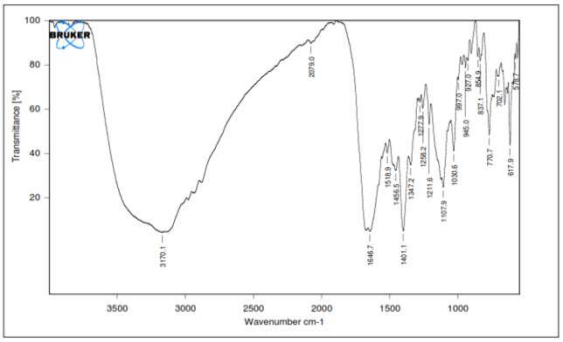

Fig 6: FTIR plot for Captopril

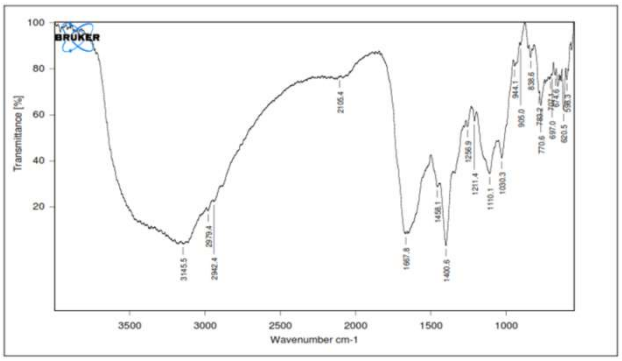

Fig 7: FTIR plot for Best formulation

Table 3: Formulation of Captopril floating tablets by direct compression method

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Captopril	100	100	100	100	100	100	100	100	100	100	100	100
Guargum	20	40	60	-	-	-	-	-	-	-	-	-
Xanthumgum	-	-	-	20	40	60	-	-	-	-	-	-
Agar	-	-	-	-	-	-	20	40	60	-	-	-
Tragacanth	-	-	-	-	-	-	-	-	-	20	40	60
Sodium bicarbonate	30	30	30	30	30	30	30	30	30	30	30	30
Citric acid	10	10	10	10	10	10	10	10	10	10	10	10
MCC	106	86	66	106	86	66	106	86	66	106	86	66
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg.stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total weight (mg)	270	270	270	270	270	270	270	270	270	270	270	270

Table 4: Standard Calibration graph values of Captopril in 0.1N HCl

Concentration (µg / ml)	Absorbance
0	0
2	0.031
4	0.061
6	0.095
8	0.125
10	0.158

Table 5: Pre compression studies of Captopril floating tablets

Formulation Code	% weight variation	Thickness (mm)	Hardness (Kg/cm^2)	% Friability	% Drug Content
F1	Pass	3.46	8.32	0.28	100.31
F2	Pass	3.55	8.16	0.22	100.03
F3	Pass	3.53	8.17	0.16	99.56
F4	Pass	3.46	8.25	0.19	99.93
F5	Pass	3.42	8.17	0.07	99.52
F6	Pass	3.51	8.35	0.31	100.67
F7	Pass	3.47	7.8	0.39	100.94
F8	Pass	3.56	8.09	0.16	99.52
F9	Pass	3.39	8.28	0.26	100.34
F10	Pass	3.55	8.35	0.24	99.4
F11	Pass	3.41	7.86	0.17	100.78
F12	Pass	3.52	8.19	0.12	100.38

*Test for Friability was performed on single batch of 20 tablets

Table 6: In vitro Buoyancy Studies of Captopril floating tablets

Formulation Code	Floating lag time(sec) n = 3	Total floating time; n = 3	Matrix Integrity up to 12hrs.n = 3
F1	20	Up to 8	-
F2	36	Up to 12	+
F3	35	Up to 12	+
F4	24	Up to 14	+
F5	40	Up to 14	+
F6	80	Up to 15	+
F7	51	Up to 3	-
F8	42	Up to 4	-
F9	53	Up to 6	-
F10	20	Up to 12	+
F11	20	Up to 12	+
F12	30	Up to 12	+

Table 7: In-vitro Dissolution results for formulation trails

Time (hrs)	% Drug released											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	38	31	17	25	18	15	53	48	35	35	30	23
2	55	49	26	34	29	24	96	84	64	50	44	39
4	72	68	45	59	43	37	100	95	79	64	58	51
6	86	84	62	68	65	52		100	91	82	76	69
8	93	91	86	79	77	65			100	89	83	78
10	100	99	94	88	84	79				95	89	85
12		100	98	93	91	86				100	96	90

4. Conclusion

The present work concluded that floating Tablets of Captopril are formulated to increase gastric residence time and thereby improve its therapeutic efficacy. Guargum was respectively showed better Sustained drug release of Captopril.When drug:polymer concentration increases the release rate decreases this is because of reason when the concentration of polymer increases the diffusion path length increases. FTIR spectroscopic studies were carried out in order to establish compatibility between drug and excipients. The result was concluded that there were no chemical intraction between drug and the excipients used. Formulated tablets showed satisfactory results for various Post compression evaluation parameters like: tablet thickness, hardness, weight variation, floating lag time, total floating time, content uniformity and *in vitro* drug release. Formulation F3 gave better-controlled drug release and floating properties in comparison to the other formulations. The release pattern of the F3 formulations was best fitted to Korsmeyer-Peppas model, Higuchi and first-order model. The most probable mechanism for the drug release pattern from the formulation was non-Fickian diffusion or anomalous diffusion.

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