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Formulation and Development of Floating Tablet of Highly Water Soluble Drug Using Combination of Hydrophilic and Hydrophobic Polymers

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ABSTRACT

Water soluble drugs if not formulated properly, may release the drug at a faster rate and produce a toxic concentration on administration. Captopril belongs to the class I of biopharmaceutical classification system (BCS) has short half life (~2hrs) shows dose dumping, burst and stability in acidic pH of stomach**.** In this study HPMC K15M and Compritol 888 ATO alone and in combination different proportions using physical mixture and solid dispersion method to prepare floating matrix tablet. The tablets were evaluated for appearance, weight variation, hardness, friability, floating lag time, duration and integrity of matrices, *In-vitro* and In vivo drug release kinetics. IR spectra, thermal behavior and X-ray diffraction pattern of selected solid dispersions were carried out indicating no degradative changes. The rate of release of Captopril from floating matrix tablets containing physical mixtures was found to be affected by the concentration of Compritol 888 ATO increase in the concentration decrease the release. Among the formulations containing solid dispersions of drug with Compritol888 ATO (SPC3c'') give retardation of drug release ($t_{90\%}$ >12) for extended time. All formulations indicated diffusion exponent (n) values in the range 0.4 to 0.6 suggesting Fickian diffusion. The values of 'n' increased with increase in concentration of lipid polymers suggesting a shift in the mechanism of drug release from Fickian to anomalous. All formulations show initial burst release which may due to high water solubility of Captopril. The X-Ray photographs indicated the residence of tablet in stomach for about 5hs.

Keywords: Compritol888 ATO; X-ray diffraction; Solid dispersions

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INTRODUCTION

The design of oral controlled drug delivery system is aimed to achieve increased and predictable bioavailability. The ideal system has single dose for the whole duration of treatment and should deliver the drug directly at the specific site in controlled manner. The real issue in the development of oral controlled release dosage forms is not just to prolong the delivery of drugs more than 12 hours but also to prolong the presence of dosage forms in the stomach or in the upper small intestine. However, this task is difficult due to physiological problems such as fluctuation in gastric emptying process, narrow absorption window of drug and instability in the intestine. These problems could be overcome by altering the physiological state and/or by designing the formulations, which withstand gastric emptying process. Dosage forms with prolonged gastric residence time (GRT), that is gastro retentive dosage forms is essential for drug which exhibits absorption window in stomach, since its spatial and temporal control in specific region of gastrointestinal tract offers intimate contact with absorbing membrane and maximizes drug absorption[1].

Developing oral controlled release tablets for highly water soluble drugs like Captopril with constant release rate has been a challenge to the pharmaceutical technologist. Most of these water soluble drugs if not formulated properly, may release the drug at a faster rate and produce a toxic concentration on oral administration. Hence, it is a challenging task to formulate a suitable tablet dosage form for prolonged delivery of highly water soluble drugs [2].

Captopril has been shown to be effective and safe alone or in combination, in patients with hypertension and congestive heart failure. Captopril is synthetic compound introduced in 1977 and has been used for the treatment of hypertensive diseases, has half-life (2-3 h.) and requires frequent dosing 3-4 tablets daily (dose 12.5-50mg), result in fluctuating drug levels in body. Therefore, the need for slow release formulation of Captopril is justified to overcome this problem (3,4). Captopril belongs to Class I [high solubility and high permeability] of the Biopharmaceutical Classification System (BCS) shows dose dumping and burst phenomenon when formulated as controlled release formulation. Captopril shows stability only in acidic pH of stomach (pH 1-3). This fact may therefore support faster absorption of drug in stomach with higher concentrations entering in plasma and hence improving its bioavailability [5].

Studies have been reported in literature investigating HPMC matrices, also lipid polymers like Compritol, Precirol to control the release of drug [6,7]. Therefore in this study hydrophilic and lipid polymer alone and in combination has been used [8], also different methods like solid dispersion

and physical mixture has been used for the preparation of matrices of Captopril and modulate its release profile.

An objective of the work is to prepare the solid dispersions of Captopril with lipid polymer, to develop the matrix tablet that will remain floating on stomach contents. Provide slow drug release for prolonged period. Exercise better control on release of highly water soluble Captopril from gastro retentive matrix tablets by means of use of suitable combinations of water insoluble and soluble hydrophilic polymers.

MATERIALS AND METHODS

Captopril was gift sample from Lupin Pharmaceuticals, (Aurangabad), Methocel K15 M, Compritol 888 ATO (Glyceryl Behenate) was obtain from Colorcon India Ltd. Goa (Gattefosse), Dicalcium phosphate was gifted by Nu Life Pharmaceuticals, Magnesium Stearate was procured from S.D Fine Chemicals. All other chemicals and reagent used were of analytical grade.

Method

Preparation of physical mixtures

Different formulations (PM1 to PM5) were prepared by direct compression using proportions of drug and lipid polymers viz. 1:1, 1:1.5, 1:2, 1:2.5 and 1:3 (Table. I).The powders were blended together in geometric proportion using glass mortar pastel (9,10).

Table I. Matrix tablets prepared using physical mixtures

Code	Captopril	Compritol 888 ATO	Dicalcium phosphate
P1	25	25	50
P2	25	37.5	37.5
P3	25	50	25
P4	25	62.5	12.5
P5	25	75	-

Note: The total tablet weight was maintained 100mg.

Preparation of solid dispersions of Captopril and lipid polymers by melt granulation (11**):**

Formulations SMC1 to SMC5 were prepared by weighing Compritol 888 ATO and heated in porcelain dishes on boiling water bath to melt the polymers (Compritol 888 ATO M.P. 65–77° C). Weighed quantities of Captopril were added to the molten polymer with stirring to form uniform dispersion. The molten mass was then cooled with continuous stirring to room temperature (25-30°C); the solids so obtained were pulverized in mortar and graded by passing through sieve (No.16). The resulting granules were lubricated with magnesium stearate and evaluated for flow properties. (Table II.) .The appropriate quantities of physical mixtures, solid dispersions of Captopril, Dicalcium phosphate (DCP) as diluents and other excipients were compressed into matrix

tablets using S.S punches (diameter 6 mm) on rotary tablet press. The weight of all tablets was maintained 100mg (12,13). Physical mixtures and solid dispersions of Captopril were evaluated for bulk density, tapped density, compressibility index, angle of repose [14,15.]

Table II. Matrix tablets prepared using solid dispersions

Code	Captopril	Compritol 888 ATO	Drug: Polymer
SMC1	25	25	1:1
SMC2	25	37.5	1:1.5
SMC3	25	50	1:2
SMC4	25	62.5	1:2.5
SMC5	25	75	1:3

Note: The total tablet weight was maintained 100mg.

Matrix tablets prepared using solid dispersions were blended with HPMC K15M, sodium bicarbonate and DCP [16,17,18]:

The solid dispersions of Captopril prepared with Compritol 888 ATO of selected formulations were further blended with variable percentage of HPMC K15M (Table. III) [19,22]

Table III. Formulation of matrix tablets containing HPMC K15M, sodium bicarbonate and solid dispersion of Captopril

Code	Drug: Compritol 888 ATO	HPMC %	Sodium bicarbonate (%)	DCP (%)
SMC1a''	1:1	20	15	45
SMC1b''	1:1	30	15	35
SMC1c''	1:1	40	15	25
SMC2a''	1:1.5	20	15	40
SMC2b''	1:1.5	30	15	30
SMC2c''	1:1.5	40	15	20
SMC3a''	1:2	20	15	35
SMC3b''	1:2	30	15	25
SMC3c''	1:2	40	15	15
SMC4a''	1:2.5	20	15	30
SMC4b''	1:2.5	30	15	20
SMC4c''	1:2.5	40	15	10
SMC5a''	1:3	20	15	25
SMC5b''	1:3	30	15	15
SMC5c''	1:3	40	15	5

Weight of blend was maintained 250mg.

Evaluation of modified matrix tablets for floating characteristics

The matrix tablets of all formulations were evaluated by physical tests like appearance & dimensions, weight variation, hardness, friability and performance tests like uniformity of drug content, and *In-vitro* drug release kinetics. The floating matrix tablets were evaluated for their floating behavior in terms of following properties using 900 ml of 0.1 N HCl (37±1 ºC) in USP

dissolution apparatus (Type II) like floating lag time, duration of floating and integrity of matrices [20,22,24,25].

In vivo Study of Experimental Floating Tablets

In vivo Study was carried out using X-Ray photography technique. All the experimental procedures and protocols used in this study were reviewed and approved by the Institutional Animal Ethical Committee (IAEC) of Padmashri Dr D.Y. Patil Institute of Pharmaceutical Science & Research, Pimpri, Pune, constituted in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. The Placebo floating tablet was administered to the Newzealand white rabbit weighing 2-2.5kg with aid of 3-4 ml water. The lateral view of rabbit stomach was taken by using Digital X-Ray machine (Semens, make-200 MA). Floating tablets were compared with the conventional placebo (125mg) (21,23).

Characterization of selected formulations

Characterization of selected solid dispersions was carried out using IR spectrometry, determination of thermal behavior by Differential Scanning Calorimetry (DSC) (26) and X-ray diffraction pattern (XRD).

RESULT AND DISCUSSION

Melting point of Captopril was in the range 104±2°C. The UV spectra of Captopril in both distilled water and 0.1 N HCl indicated λ max at 205nm. The UV absorption data and concentration estimates of Captopril in the two solvents exhibited good linearity over the range of 0-32 mcg/ml. Hence, Captopril was found to obey Beer- Lambert's law.

Infrared spectrometric characterization of Captopril

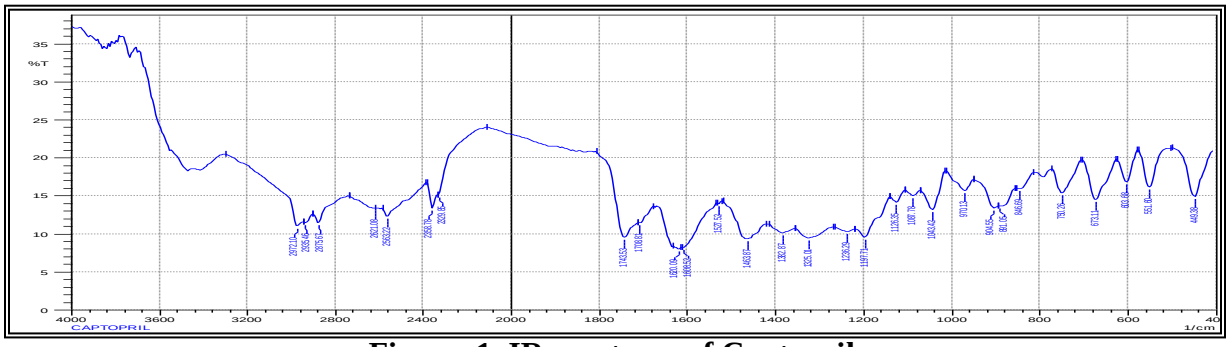

Figure. 1. IR spectrum of Captopril

Differential Scanning Calorimetry

The thermogram of Captopril revealed sharp melting endotherm at 105.84°C which is close to its melting point. Also no decomposition was observed up to 250°C (26)(Figure. 2).

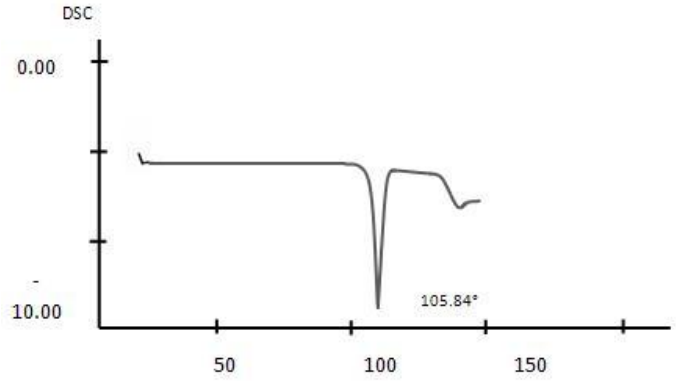

Figure. 2. DSC thermogram of Captopril

X-ray diffraction pattern

The diffractogram of Captopril indicated numerous high intensity reflections between 15-20 2θ values demonstrating the crystalline nature of drug (Figure. 3).

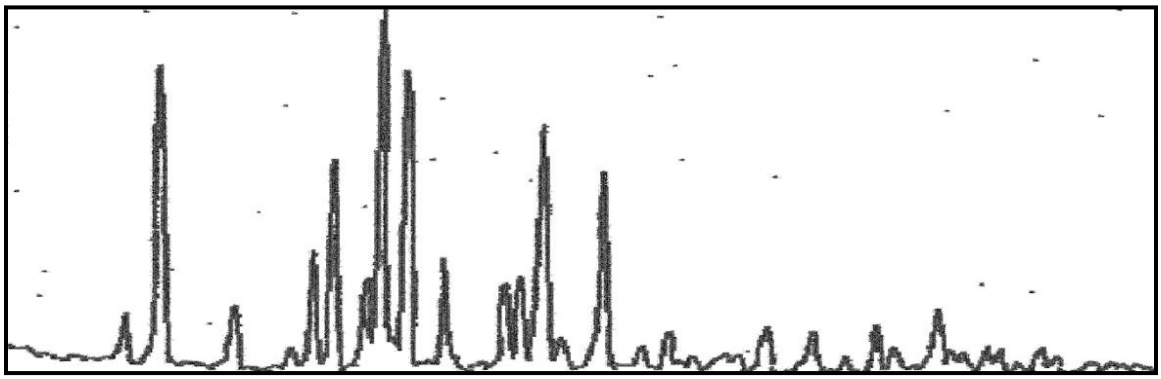

Figure. 3. X-ray diffractogram of Captopril

Characterization of selected solid dispersions

Infrared characterization: The IR spectra of solid dispersions of Captopril prepared with matrix forming polymer Compritol 888 ATO are reported in Figure.4.

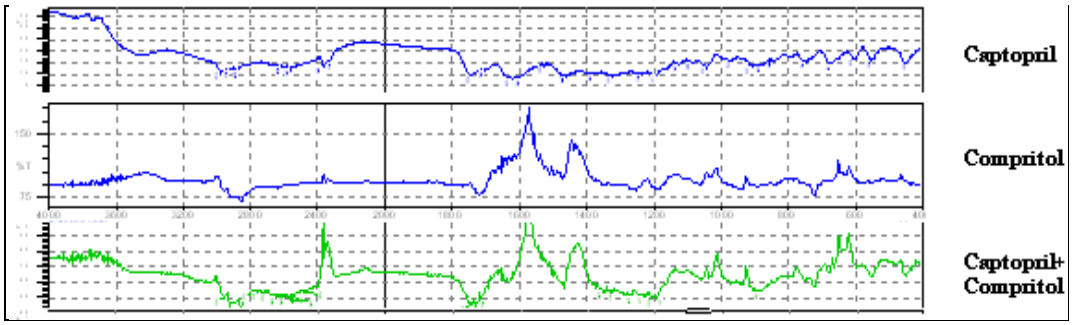

Figure. 4. IR spectra of drug, polymers and selected solid dispersions

Differential Scanning Calorimetry

The thermograms of solid dispersions of Captopril prepared using melt granulation technique as shown in **Figure. 5.**

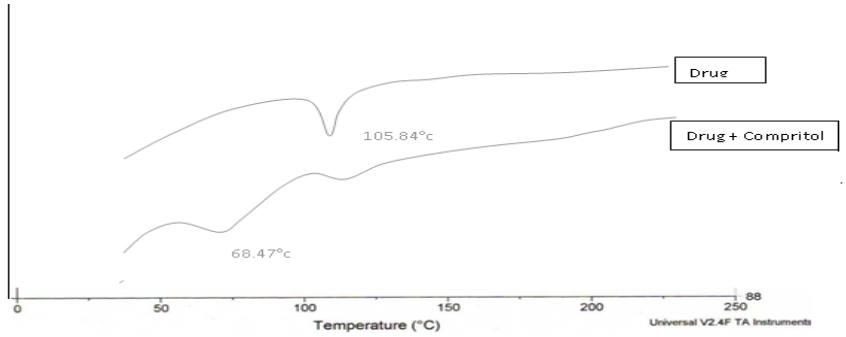

Figure. 5. Thermogram of Captopril its solid dispersions Compritol

These findings of thermogram are suggestive of probable changes in crystallinity of Captopril when prepared as the solid dispersion.

X-ray diffraction

To confirm this probability of changes in crystallinity of Captopril in solid dispersion, the X-ray diffraction patterns of each of drug, polymers and solid dispersions were studied (Figure. 6)

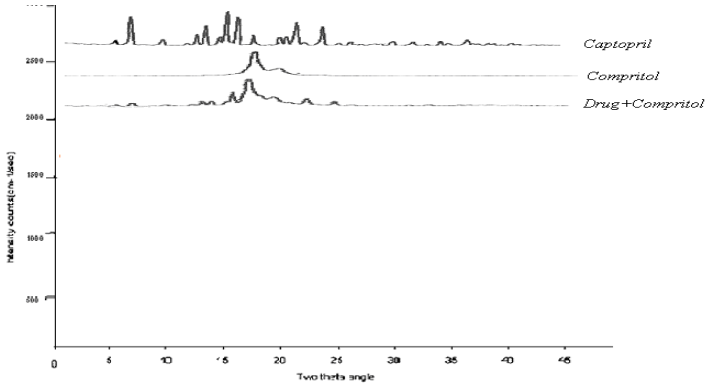

Figure. 6. X-Ray diffraction patterns of drug , polymer and its solid dispersions

The UV, IR spectrophotometric analysis and DSC, X-ray diffraction pattern supported the identity and purity of Captopril.

Characterization of physical mixtures and solid dispersions

Table IV. Flow characteristics of various blends of powder

Code	Loose Bulk Density* gm/ml	Tapped Bulk Density* gm/ml	Carr's Index (%)	Angle of Repose*(Ø)
P1	0.46±0.03	0.60±0.02	23.52	33.86±0.04
P2	0.41±0.04	0.57±0.03	29.82	34.21±0.05
P3	0.41±0.02	0.52±0.03	21.15	32.27±0.01
P4	0.42±0.03	0.53±0.03	20.75	33.15±0.02
P5	0.43±0.04	0.57±0.03	24.56	31.34±0.02
SMC1	0.46±0.03	0.55±0.05	14.98	16.28±0.05
SMC2	0.45±0.03	0.53±0.03	14.76	16.86±0.06
SMC3	0.44±0.04	0.52±0.03	16.00	17.51±0.03
SMC4	0.44±0.02	0.51±0.04	13.74	15.91±0.04
SMC5	0.38±0.03	0.46±0.02	15.90	15.25±0.03

SMC1a''	0.50±0.01	0.57±0.02	12.50	27.75±0.03
SMC1b''	0.44±0.01	0.50±0.02	12.00	24.93±0.01
SMC1c''	0.44±0.01	0.52±0.01	15.38	20.96±0.02
SMC2a''	0.40±0.01	0.44±0.01	10.10	27.14±0.04
SMC2b''	0.40±0.03	0.47±0.02	16.00	23.98±0.01
SMC2c''	0.44±0.02	0.50±0.02	12.00	22.19±0.04
SMC3a''	0.40±0.03	0.44±0.03	10.10	22.47±0.02
SMC3b''	0.44±0.02	0.50±0.03	12.00	21.38±0.03
SMC3c''	0.40±0.01	0.43±0.02	8.08	21.75±0.03
SMC4a''	0.40±0.02	0.45±0.02	12.12	21.55±0.02
SMC4b''	0.44±0.01	0.50±0.01	12.00	26.00±0.06
SMC4c''	0.40±0.02	0.44±0.03	9.09	27.14±0.04
SMC5a''	0.36±0.01	0.40±0.03	10.0	24.01±0.02
SMC5b''	0.44±0.02	0.50±0.02	12.0	22.19±0.04
SMC5c''	0.40±0.01	0.44±0.01	10.10	23.14±0.04

From the values of loose bulk density, tapped density, Carr's index and angle of repose for physical mixtures with lipid polymer are suggestive of passable flowability and that of solid dispersions are suggestive of excellent flowability.

Table V. Characterization of matrix tablets

Code	Diameter (mm)*	Thickness (mm)*	Average Weight*	Hardness (kg/cm^2)*	Friability (%)**	% Drug content*
P1	6.24±0.13	3.19±0.03	100±2.2	3.0	0.65	93.07±0.48
P2	6.10±0.18	3.23±0.02	102±1.9	3.0	0.66	94.01±0.51
P3	6.12±0.09	3.25±0.03	104±1.6	3.0	0.75	96.00±0.65
P4	6.21±0.10	3.27±0.03	103±3.1	3.5	0.66	98.10±0.15
P5	6.11±0.21	3.25±0.01	103±1.9	3.0	0.71	99.12±1.20
SMC1	6.20±0.04	3.25±0.03	100±3.4	3.5	0.23	98.65±0.17
SMC2	6.12±0.02	3.29±0.02	102±2.6	3.5	0.10	95.36±0.04
SMC3	6.16±0.03	3.29±0.02	102±3.7	4.0	0.20	96.54±0.20
SMC4	6.14±0.03	3.25±0.04	103±2.7	3.5	0.10	97.35±0.16
SMC5	6.08±0.10	3.28±0.04	105±2.5	4.0	0.14	98.88±0.10
SMC1a''	8.11±0.09	4.36±0.02	248±6.1	4.5	0.75	99.07±0.48
SMC1b''	8.15±0.02	4.38±0.01	251±4.6	4.5	0.62	99.01±0.51
SMC1c''	8.12±0.05	4.32±0.03	253±3.9	4.5	0.58	99.00±0.65
SMC2a''	8.09±0.03	4.30±0.02	247±5.2	5.0	0.73	99.12±1.20
SMC2b''	8.05±0.1	4.41±0.02	245±4.8	4.5	0.70	98.45±0.85
SMC2c''	8.20±0.04	4.35±0.03	252±3.5	4.5	0.68	99.56±0.75
SMC3a''	8.04±0.06	4.40±0.02	255±2.5	4.5	0.89	97.98±0.58
SMC3b''	8.12±0.12	4.37±0.02	253±2.3	5.0	0.84	98.51±0.65
SMC3c''	8.06±0.08	4.37±0.03	250±1.8	5.0	0.74	98.68±0.20
SMC4a''	8.14±0.13	4.33±0.04	249±1.5	5.0	0.54	97.51±0.58
SMC4b''	8.12±0.11	4.34±0.03	247±1.9	4.5	0.49	99.50±0.69
SMC4c''	8.08±0.08	4.33±0.04	251±2.1	4.5	0.48	98.15±0.35
SMC5a''	8.09±0.07	4.40±0.01	249±2.6	4.5	0.44	97.68±0.48
SMC5b''	8.12±0.03	4.41±0.02	250±2.4	4.5	0.68	99.56±0.75
SMC5c''	8.14±0.08	4.39±0.03	251±2.5	5.0	0.55	98.45±0.85

Appearance of matrix tablets possessed uniform appearance with no defects such as capping, chipping or lamination. The percentage deviation from average tablet weight for all the formulations was found to be within the specified limits (±7.5 %). The Hardness was in the range 3.0 to 3.5 kg/cm^2 suggesting good mechanical strength. The friability was found to be less than 1% i.e. within specified limits. The drug content values ranged between 93.07 - 99.12% i.e. within the limits (90% to 110% of labeled amount).

Characterization of floating properties for matrix tablets of Captopril

Table VI. Floating characteristics of matrix tablets containing solid dispersions and hydrophilic polymer at 15% concentration of Sodium bicarbonate

Code	Floating lag time (Minutes)
SMC1a"	1.5
SMC1c"	1.0
SMC5a"	1.3
SMC5c"	1.0

Lag time: reduced significantly as compared to the tablets containing 15% gas generating agent.

Duration of floating: > 12 hours.

Integrity of matrices**:** excellent, all tablets intact throughout the duration of studies (>12h)

***In vitro* release study of Captopril from matrix tablets**

The rate of release of Captopril from matrix tablets containing physical mixtures, solid dispersions , solid dispersions with variable % of HPMC K15M, was shown in (Table.VII, VIII Figure. 7, 8, 9 ,10,11,12 and 13).

Table VII. % Release data from Captopril matrix tablets prepared with physical mixtures

Time	Formulation code				
(h)	P1	P2	P3	P4	P5
0.5	64.27 ± .54	53.68 1.22	49.50 0.58	41.59±0.84	32.05± 1.22
1	70.94 ± .37	67.19±0.82	52.73±1.28	46.19±0.89	39.27± 1.17
2	76.40±1.83	72.61 ±0.90	63.40±0.78	51.61±0.77	43.93± 0.60
3	93.69±1.47	82.90 ±1.10	73.91±0.79	59.67±1.23	51.86±1.00
4	-	95.48 ±1.40	90.44±0.49	74.95±0.86	65.28±0.86
5	-	-	98.82±0.85	94.12 0.80	79.80±1.19
6	-	-	-	-	97.62±2.46
$t_{50\%}$	0.3	0.4	0.9	2.6	3
$t_{90\%}$	2 .4	3.8	3.9	4.8	5.8

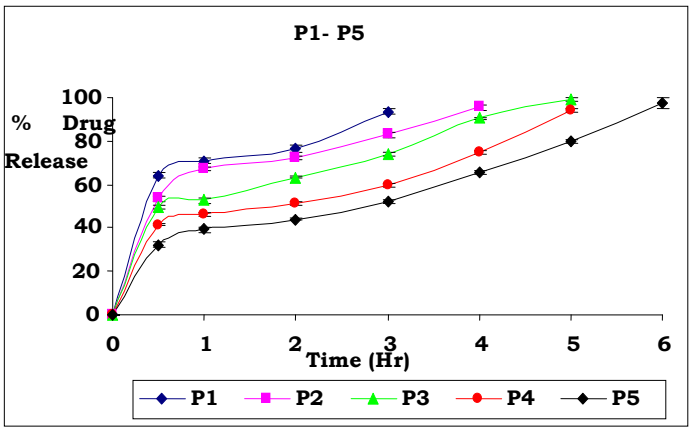

Figure. 7. *In vitro* release from matrix tablets prepared with physical mixtures

Table VIII. % Release data of Captopril from matrix containing solid dispersions

Time	Formulation code				
(h)	SMC1	SMC2	SMC3	SMC4	SMC5
0.5	18.70±1.16	16.20±1.74	17.70±0.39	11.11±0.32	8.66±0.84
1	21.05±0.85	17.09±1.21	19.45±1.03	13.78±0.71	9.76±0.59
2	24.46±0.81	22.2±0.35	21.66±0.24	18.16±1.40	10.82±0.24
3	28.00±0.57	24.45±0.80	22.53±0.27	20.81±0.78	13.25±0.57
4	32.94±0.96	26.12±0.87	23.82±0.47	22.45±0.85	15.75±0.57
5	37.20±0.84	28.68±1.40	25.39±0.53	24.78±0.60	18.20±0.32
6	42.06±1.36	30.89±1.54	27.71±0.17	26.50±0.61	21.44±0.52
7	45.09±1.44	33.58±0.40	31.55±0.60	29.37±0.55	24.90±0.46
8	48.93±2.10	37.75±0.79	34.42±0.48	32.82±0.54	28.62±0.59
9	51.77±1.16	40.97±1.06	37.92±0.94	36.30±0.22	31.47±0.60
10	54.71±0.46	45.30±1.20	41.27±0.75	39.09±0.29	34.12±0.80
11	57.83±0.60	50.09±1.40	45.65±1.08	42.18±0.10	37.06±0.74
12	61.90±1.16	56.64±1.74	49.18±0.39	46.27±0.32	39.14±0.84
$t_{50\%}$	8.4	11	>12	>12	>12
$t_{90\%}$	>12	>12	>12	>12	>12

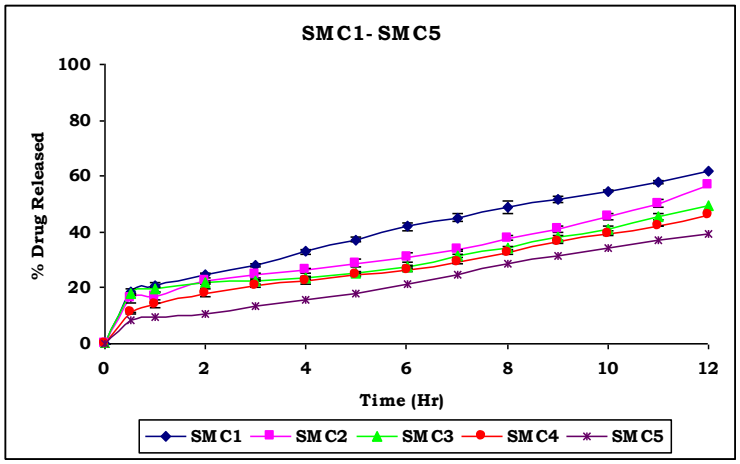

Figure. 8. *In vitro* release of Captopril from matrix containing solid dispersions

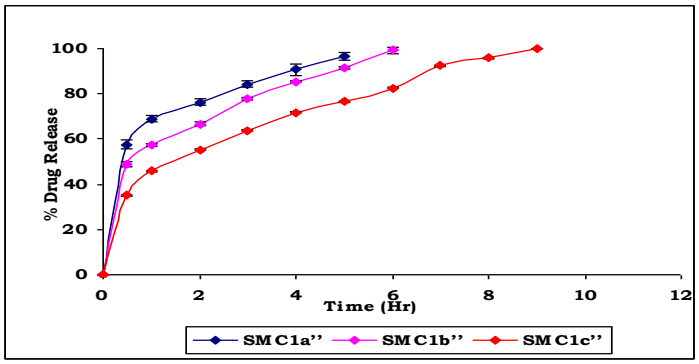

Figure. 9. *In vitro* drug release from matrix tablets containing (Captopril: Compritol=1:1), variable % of HPMC K15M

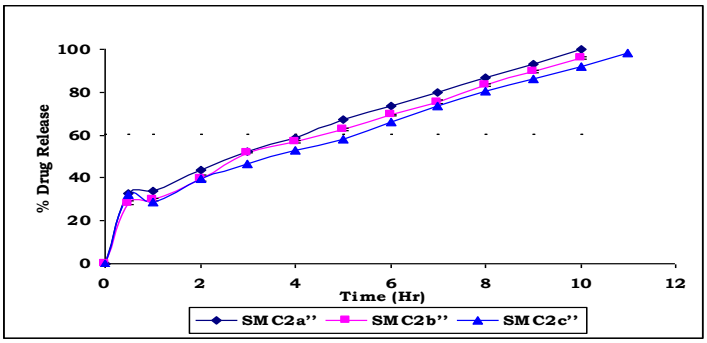

Figure.10. *In vitro* drug release from matrix tablets containing (Drug: Compritol =1:1.5), variable % of HPMC K15M

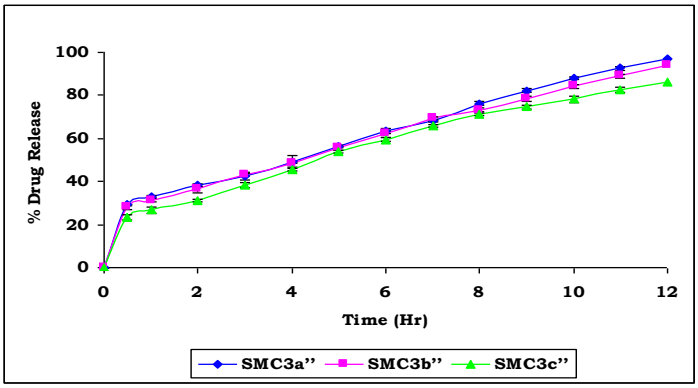

Figure.11. *In vitro* drug release from matrix tablets containing (Drug: Compritol =1:2), variable % of HPMC K15M

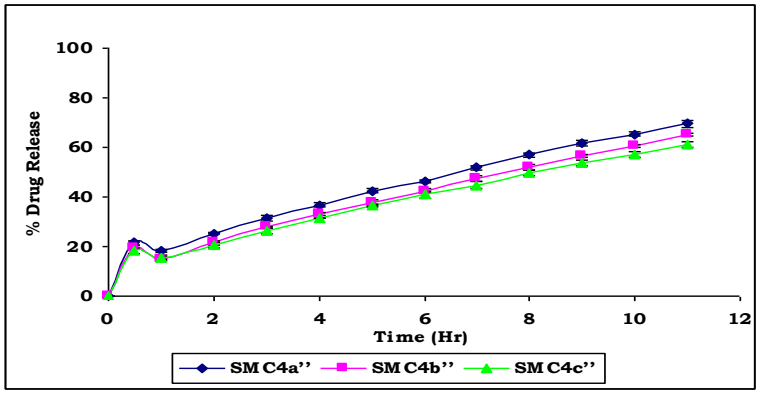

Figure.12. *In vitro* drug release from matrix tablets containing (Drug: Compritol =1:2.5), variable % of HPMC K15M

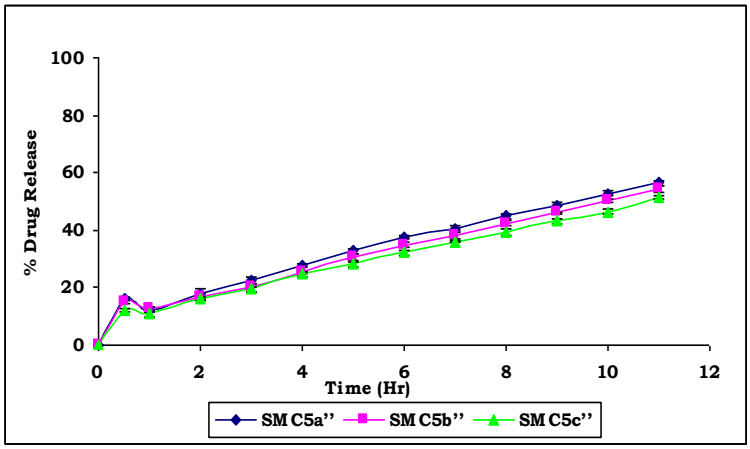

Figure.13. *In vitro* drug release from matrix tablets containing (Drug: Compritol =1:3) variable % of HPMC K15M

The rate of release of Captopril from matrices containing physical mixtures was found to be affected by the concentration of lipid polymer. Increase in the concentration decrease the release of Captopril from Compritol 888 ATO .The same is reflected in the values of $t_{50\%}$ and $t_{90\%}$. The retardation was proportional to the amount of polymers used. Comparison between $t_{50\%}$ and $t_{90\%}$ values for release of Captopril from matrices, the formulations containing solid dispersions with lipid polymer (1:2, SPC3c'') give retardation of drug release for extended time. The retardation of drug release was observed to decrease as compare to the tablets containing only solid dispersions of drug with water insoluble polymer. This may be due to inclusion of hydrophilic HPMC K15M. Due to hydrophilic nature, dissolution fluid easily gets penetrated into matrices, than those containing solid dispersion alone. This helps in dissolution of drug along with floating characteristics.

Kinetic treatment to the dissolution data of matrix tablets

The dissolution data for matrix tablets containing solid dispersions of lipid polymers was fitted to various release kinetic models viz. Zero order, First order, Higuchi Matrix, Hixon Crowel and Korsemeyer Peppas model. Rate constants (K), correlation coefficients (R) and release exponent obtained for various models are listed in Table IX.

The model that gives high 'R' value is the best fit model for the release data. It was found that Higuchi matrix was the best fit model for majority of the formulations except the SMC5 which followed the first order kinetics. All the formulations indicated diffusion exponent (n) values in the range 0.4 to 0.6 suggesting Fickian diffusion mechanism. The values of 'n' increased with increase in concentration of lipid polymers suggesting a shift in the mechanism of drug release from Fickian to anomalous. All the formulations except SMC5 gave initial burst release which

may due to high water solubility of Captopril.

Table IX. Kinetic treatment to the dissolution data Captopril from matrix tablets

Code	Zero order		First Order		Matrix		Hixon Crowel		Korsemeyer Peppas	
	k	R	k	R	k	R	k	R	n	k
SMC1	5.4514	0.9153	-0.0749	0.9784	15.933	0.9907	-0.0223	0.9639	0.4994	15.749
SMC2	4.3871	0.9036	-0.0559	0.9560	12.818	0.9791	-0.0171	0.9436	0.4623	13.612
SMC3	4.0316	0.8411	-0.0501	0.9156	11.847	0.9671	-0.0155	0.8916	0.3748	15.966
SMC4	3.7732	0.9361	-0.0461	0.9711	10.985	0.9846	-0.0144	0.9622	0.5393	10.020
SMC5	3.1440	0.9840	-0.0373	0.9886	8.996	0.9456	-0.0117	0.9883	0.6440	6.480
SMC1a''	19.7095	0.7103	-0.5148	0.9785	42.609	0.9690	-0.1169	0.9484	0.2871	56.851
SMC1b''	16.7553	0.8117	-0.5040	0.8992	38.526	0.9906	-0.1040	0.9719	0.3741	46.411
SMC1c''	13.1540	0.8726	-0.2752	0.9703	31.973	0.9983	-0.0691	0.9772	0.46	34.048
SMC2a''	10.0858	0.9259	-0.4141	0.6362	28.239	0.9903	-0.0629	0.9196	0.5123	27.216
SMC2b''	9.6149	0.9401	-0.2147	0.9396	26.856	0.9882	-0.0521	0.9821	0.5547	23.866
SMC2c''	8.9760	0.9390	-0.2188	0.8981	26.110	0.9819	-0.0505	0.9691	0.5356	24.417
SMC3a''	8.5251	0.9316	-0.1759	0.9569	24.836	0.9846	-0.0444	0.9821	0.5034	24.233
SMC3b''	8.2736	0.9271	-0.1589	0.9777	24.136	0.9889	-0.0414	0.9877	0.5099	23.313
SMC3c''	7.7875	0.9458	-0.1376	0.9931	22.644	0.9854	-0.0372	0.9930	0.5700	19.380
SMC4a''	6.3402	0.9545	-0.0954	0.9909	18.379	0.9765	-0.0275	0.9874	0.5636	15.809
SMC4b''	5.8141	0.9664	-0.0836	0.9900	16.786	0.9671	-0.0245	0.9885	0.5954	13.461
SMC4c''	5.5054	0.9622	-0.0768	0.9909	15.922	0.9715	-0.0228	0.9868	0.5798	13.212
SMC5a''	5.0085	0.9731	-0.0673	0.9918	14.422	0.9621	-0.0202	0.9896	0.6277	10.808
SMC5b''	4.7309	0.9767	-0.0624	0.9901	13.601	0.9576	-0.0189	0.9890	0.6185	10.349
SMC5c''	4.4301	0.9836	-0.0571	0.9937	12.721	0.9596	-0.0174	0.9931	0.6717	8.739

***In Vivo* study of floating behavior of experimental matrix tablet [22]**

For this study the floating tablet containing 15% sodium bicarbonate was selected because at this concentration of sodium bicarbonate the tablets have showed efficient floating properties as shown in Figure No. 15-18 in contrast with the conventional tablet which had already made its passage out of the stomach within 2h (Figure No. 14). The SMC5c'' was the selected tablet contained highest percentage of polymer. For this study the quantities of all ingredients were reduced to half of original weight and drug quantity was replaced with barium sulphate.

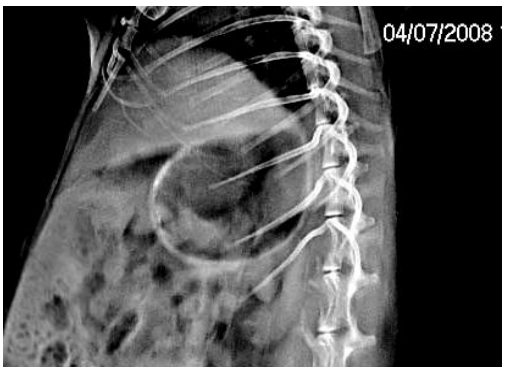

Figure.14 .Conventional tablet in stomach after 2 h

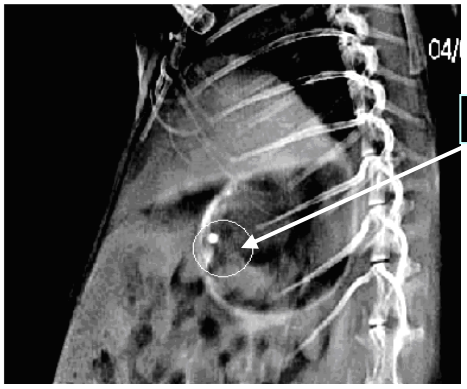

Figure. 15. Position of floating tablet in stomach after 1 h

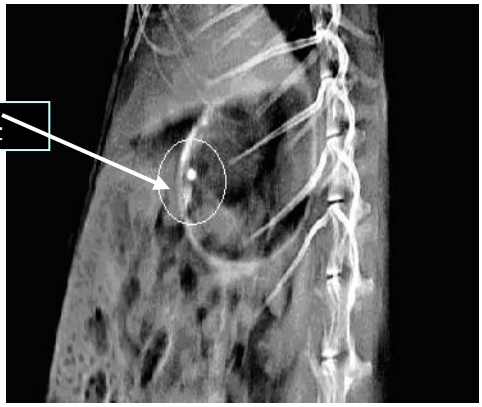

Figure.16. Position of floating tablet in stomach after 5 h

In Vivo study of floating behavior of matrices of Captopril by X-Ray photographs of the experimental tablets indicated the residence of tablet in the stomach of animal for about 5hrs. Thus the selected formulation of Captopril SMC5c'' was successful in overcoming the gastro intestinal transit mechanism over an extended period.

CONCLUSION

The floating matrices of Captopril prepared using solid dispersions with Compritol, HPMC K15M and sodium bicarbonate; shows buoyancy with lag time of 5-6 minutes with controlled drug release over 12 hrs. This delay in floating is attributed to hydrophobic nature and low wettabilty of polymers thus overcome the problem of variable and unpredictable lag time for floating, control over *in vitro* release, minimized initial burst release. The retardation of drug release decrease as compare to the tablets containing only solid dispersions of drug with water insoluble polymer is due to inclusion of hydrophilic HPMC K15M as the dissolution fluid easily gets penetrated into hydrophilic matrices, than those containing solid dispersion alone.

This work can be extended for design of multiple unit FDDS in future for drugs with high water solubility, with variety of water insoluble materials as lipids, waxes

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