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FORMULATIONS AND INVITRO EVALUATION OF BILAYER TABLETS FOR ANTIHYPERTENSION

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ABSTRACT

Aim: Present study is to formulations and evaluations of bilayered antihypertensive drug Captopril tablets by natural polymers

Method: Bilayered Captopril tablets were prepared by direct physical compression method using Guar Gum, Xanthan Gum (Natural), Sodium bicarbonates has a gas generating agent. The developed bilayered tablets are evaluated for physicochemical characters, buoyancy in vitro study, drug content, drug dissolution, Kinetic models, and drug stability studies.

Results: the results are showing satisfactory and within the limits. The bilayered tablets consisting of CIR3 and CSR4 showing good floating property and drug release was found in a sustained manner for 12 hours and follows Higuchi kinetics. The optimised CIR3 and CSR4 bilayered tablet was more stable at various storage conditions.

Keywords: Hypertension Captopril; Gaurgum, Xanthan Gum, Buoyancy and bilayered tablets

INTRODUCTION

The development of oral drug release systems has been novel in gastrointestinal tract. There is sustained release tablet preparations are an alternative to conventional and are more oral preferable tablets. It has better buoyant and floating properties in the gastric fluids and maintains the the retention time in stomach was extended (GRT). These floating dosage form preparation is well known hydrodynamically balanced system (HBS) [1-3]. It has been

preferable for the following conditions, which are enhance the bioavailability in presence of their active materials was in the state of an HBS; (*i*) having a better dissolution and/or stability to overcome the problems in the small intestine fluids, (*ii*) being they are much locally effective in the stomach, (*iii*) being good absorptions only in the stomach part and/or upper part of the small intestine [4].

The drug Captopril is belongs to antihypertensive category and used widely in treatment of hypertension (HTN) and congestive heart failure (CHF). It has been control the conversion of angiotensin-I to angiotensin II by blockade of angiotensin converting enzymes. Its biological t1/2 is 2-3 hours and the duration of action is only 6 to 8 hours, so its clinical use required as twice or thrice day[5-7]. Captopril is more stable at acidic pH 1.2 and if there is pH increases it becomes unstable and degradation. Because of these characters, this drug considered for this study.

MATERIAL AND METHODS

Captopril gift sample obtained from Natco, Hyderabad, India and polymers were received as pharmaceutical grade purchased from S.D. Fine chemicals.

Formulation development of captopril Bilayered Tablets

Captopril bilayered tablets were developed by preparing immediate release layer and sustained release layers individually. Both immediate and sustained release tablets were subjected for various *in vitro* evaluation tests. So that, it can make possible the selection of optimized formulation for each layer. Then, both the optimized formulations were compacted and compressed to get a final captopril bilayered tablet.

Formulation of the Captopril immediate release layer

The Captopril immediate release tablets were geared up by unification of drug with diverse super disintegrants (Crospovidone and Croscarmellose sodium) according to the formulae which have been given in **Table1**. The drug captopril – super disintegrant mixture then combine with MCC for 10 min. Then, magnesium stearate was incorporated in to the above mixture and finally added talc and compressed as a tablet by using tablet punching machine with 8mm flat faced punches. Further, the tablets were applied for various quality control tests such as thickness, weight variation, hardness, friability and tablet disintegration time.

Formulation of the Captopril sustained release layer

The captopril sustained release layer tablets designed by employing the wet granulation method by blending the drug with innate polymers, xanthan gum and guar gum as given in **Table2**. Poly vinyl pyrolidone K30 was employed as a binder to get the wet mass and then it

was sieved using 30# to produce granules. Then, these granules were subjected for drying. Then, the granules were mixed up with lubricant magnesium stearate and compressed as a tablet by using tablet punching machine with 8mm flat faced punches**.** Further, the tablets were applied for various evaluation tests such as thickness, weight variation, hardness, friability FLT, TFT and dissolution studies.

Table 1: Composition of the Captopril immediate release tablets

Ingredients (mg)	**CIR1**	**CIR2**	**CIR3**	**CIR4**	**CIR5**
Captopril	25	25	25	25	25
MCC	65	63	60	65	63
Crospovidone	4	6	5	-	-
Croscormellose sodium	-	-	2	4	6
Mg.Stearate	2	2	2	2	2
Talc	4	4	4	4	4
Yellow iron oxide	q.s	q.s	q.s	q.s	q.s
Total tablet weight (mg)	100	100	100	100	100

Table 2: Composition of the Captopril sustained release tablets

Ingredients (mg)	**CSR1**	**CSR2**	**CSR3**	**CSR4**	**CSR5**	**CSR6**	**CSR7**	**CSR8**	**CSR9**	**CSR10**
Captopril	25	25	25	25	25	25	25	25	25	25
Guar gum	20	30	40	50	60	-	-	-	-	-
Xanthan gum	-	-	-	-	-	20	30	40	50	60
$NaHCO_3$	20	20	20	20	20	20	20	20	20	20
DCP	60	50	40	30	20	60	50	40	30	20
Crospovidone	10	10	10	10	10	10	10	10	10	10
Mg.Stearate	5	5	5	5	5	5	5	5	5	5
PVP K-30	10	10	10	10	10	10	10	10	10	10

Total tablet weight (mg)	150	150	150	150	150	150	150	150	150	150

Compression of Captopril bilayer Tablet

The Captopril bilayered tablets were developed by direct compression method, the tablet punching machine is with 10 mm flat faced**.** First the die was filled up with the sufficient quantity of the sustained release material and compressed it slightly. Upon this sustained layer, placed the appropriate quantity of the immediate release layer drug powder mixture and punched it in a tablet punching machine at hardness of 6–7kg/cm^2.

Evaluation of Captopril Bilayered Floating Tablet

The captopril bilayered tablets are evaluated for uniformity of weighed 20 tablets, for hardness test Monsanto tester was used, for friability study Roche friabilator was used, for drug content determination assay method was used and for *in vitro* dissolution study was performed with USP- type 2 apparatus and the samples were analysed UV spectrophotometer at 227 nm.

The floating characteristic study was conducted in 100 ml beaker filled with 0.1N HCl. Both FLT and TFT were evaluated by this method.

RESULTS AND DISCUSSION

Captopril bilayered floating tablets were developed to give immediate release layered as well as sustained release layer tablets to obtain the loading dose and maintenance dose, respectively, and to produce the long term therapeutic action[8-9]. Five formulations were developed as immediate release tablets and ten formulations were developed as sustained release tablets. The immediate release tablet formulations (CIR 1-5) were adapted to physicochemical characterization. Tablet weight of the entire immediate release layered tablets consisting in the range of 99.6 - 102.1 mg, and thickness between 2.1 and 2.4 mm, hardness ranging between 4.1-5.0 kg/cm^2. All the tablets exhibited disintegration time between 50-57 sec. The results were shown in table 3. Among all the five immediate release formulations, CIR3 formulation was considered as the optimized formulation (Fig. 4)

All the sustained release formulations (CSR 1-10) instituted to physicochemical analysis. The amount of drug present in all the sustained layered tablets consisting in the range of 92.41-99.86 % . Weights of all the sustained release layer tablets consisting in the range of 149.2 -

153.5 mg, and thickness (mm) between 2.5 and 3.2 and friability values were in the range 0.14-0.35 , hardness ranging between 4.8-5.2 kg/cm^2. As the polymer concentration increases the FLT was also increased[10-12]. Results were shown in table 4.

Dissolution study revealed that CSR4 formulation showed a sustained drug release up to 12 hours. So, CSR4 batch tablets were considered the optimized one among all the ten SR formulations (Fig.5 & Fig.6). The drug release kinetics such as first order, zero order, Peppas and Higuchi model were applied on the optimized batch and the results showed that, it was followed Higuchi model

The selected immediate release layered composition (CIR3) and sustained release layered composition (CSR4) were punched to produce captopril bilayered floating tablet and these bilayered tablet (CBF) were intended to various evaluation tests (Table 5) including FLT, TFT and it was followed Higuchi model release kinetics (Table 6). Further, it was intended for stability studies at various storage conditions for three months and it was stable for a period of 3 months (Table 7).

Table 3: *In vitro* characterization of Captopril IR tablets

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration time (sec)
CIR1	101.2	4.6±0.10	2.1±0.05	56
CIR2	102.1	4.1±0.23	2.3±0.08	54
CIR3	100.1	5.0±0.21	2.2±0.03	50
CIR4	99.6	5.0±0.25	2.4±0.01	57
CIR5	101.4	4.9±0.15	2.1±0.03	55

Table 4: *In vitro* characterization of Captopril SR tablets

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)	FLT (sec)	TFT (h)	Drug release (%)
CSR1	151.3	4.9±0.10	2.6±0.05	0.21	94.18	15 ± 1	>12	94.56
CSR2	152.1	5.1±0.23	2.7±0.08	0.34	95.32	23 ± 3	>12	95.95
CSR3	149.2	5.1±0.21	2.6±0.03	0.24	97.14	27 ± 5	>12	97.05
CSR4	150.3	5.0±0.25	2.5±0.01	0.35	99.86	18 ± 4	>12	99.96
CSR5	151.1	4.8±0.15	2.8±0.03	0.23	92.41	35 ± 2	>12	93.98
CSR6	153.5	5.2 ±0.23	2.7±0.02	0.3	94.84	45 ± 7	>12	89.20
CSR7	152.3	4.8±0.10	2.8±0.01	0.14	96.28	47 ± 8	>12	90.98
CSR8	149.2	5.1±0.22	3.1±0.03	0.14	97.52	62± 2	>12	66.65
CSR9	151.4	5.2±0.25	2.5±0.04	0.19	99.04	37 ± 4	>12	96.32
CSR10	152.5	5.20±0.28	2.7±0.08	0.28	98.56	49 ± 9	>12	74.19

Table 5: *In vitro* characterization of Captopril bilayered floating tablets

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)	FLT (sec)	TFT (h)	Drug release (%)
CIR3 & CSR 4	250	5.0±0.10	2.8±0.05	0.25	99.18	15 ± 1	>12	99.56

Table 6: The correlation coefficient (R^2) values for optimized formulation

Zero order	First order	Higuchi	Peppas
0.9715	0.7123	0.9915	0.8728

Table 7: Stability studies optimized batch

Parameters	Storage conditions		
	At 2-8°C	**Room temperature**	**At 40°C**

% Cumulative Drug Release	96.10%	98.12	95.73%
Drug Content Uniformity	98.13%	99.65%	98.46%
Color Change	No change	No change	No change

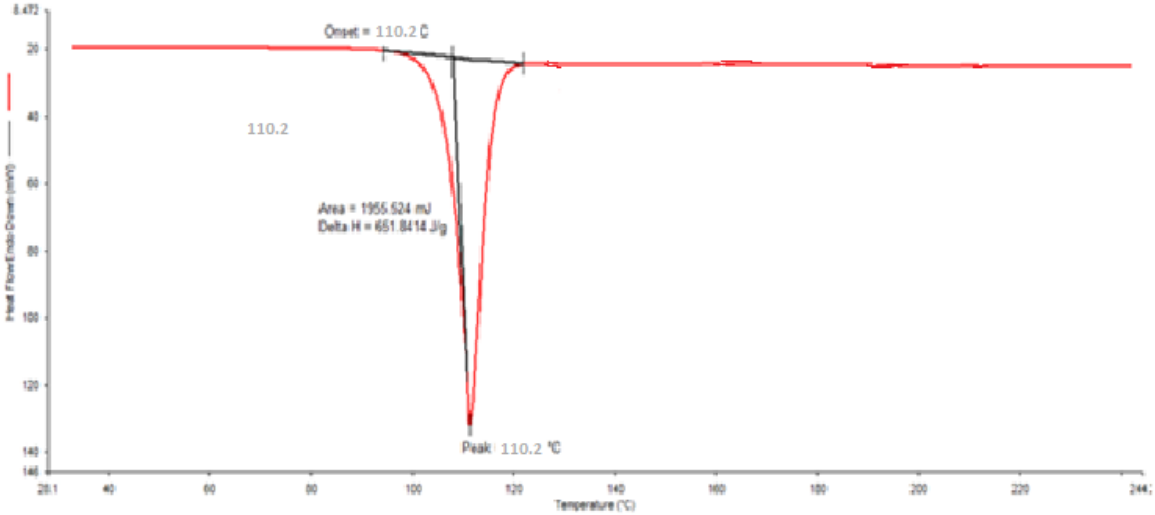

Fig 1: DSC thermogram for Captopril pure drug.

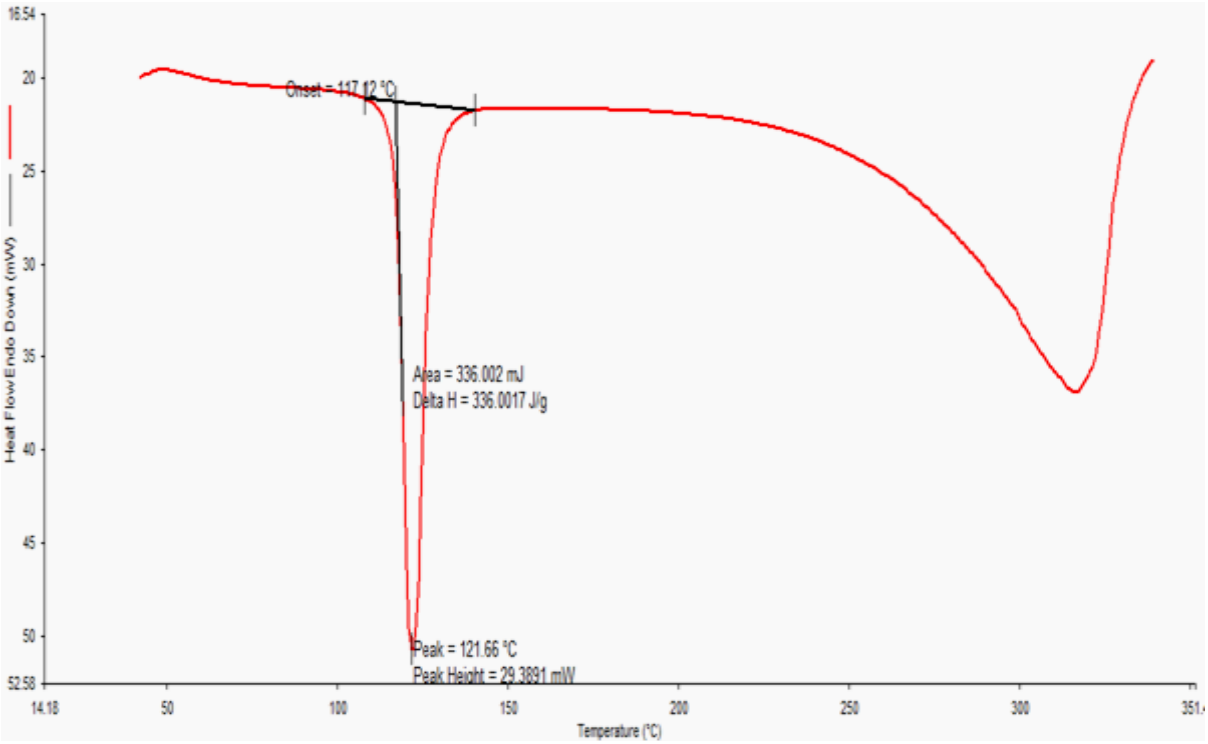

Fig2: DSC thermogram for Captopril + Excipients.

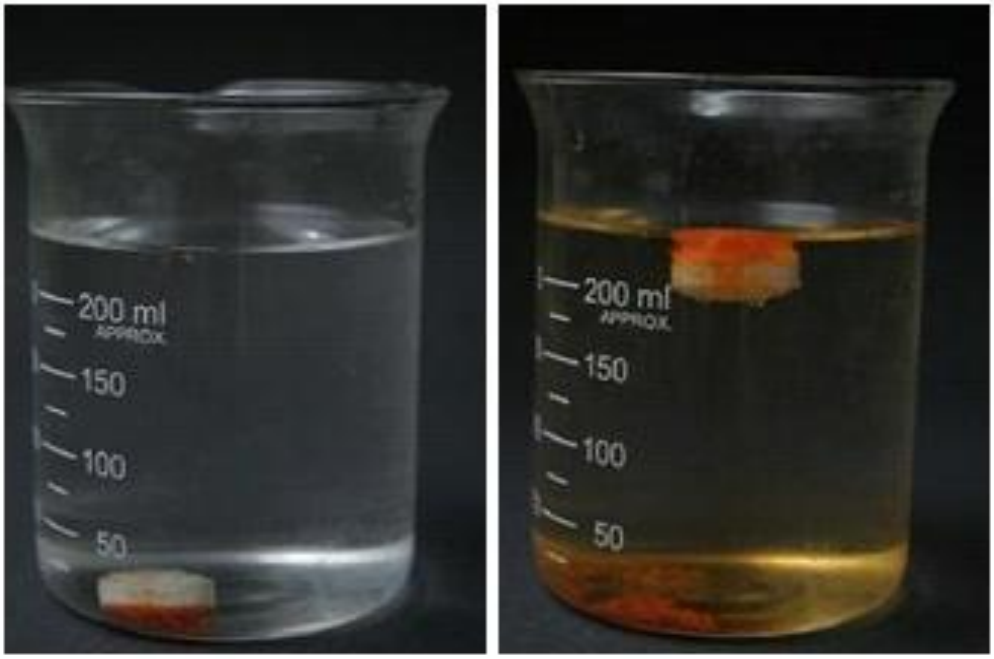

Fig 3: *In vitro* buoyancy study of Captopril bilayered floating tablet.

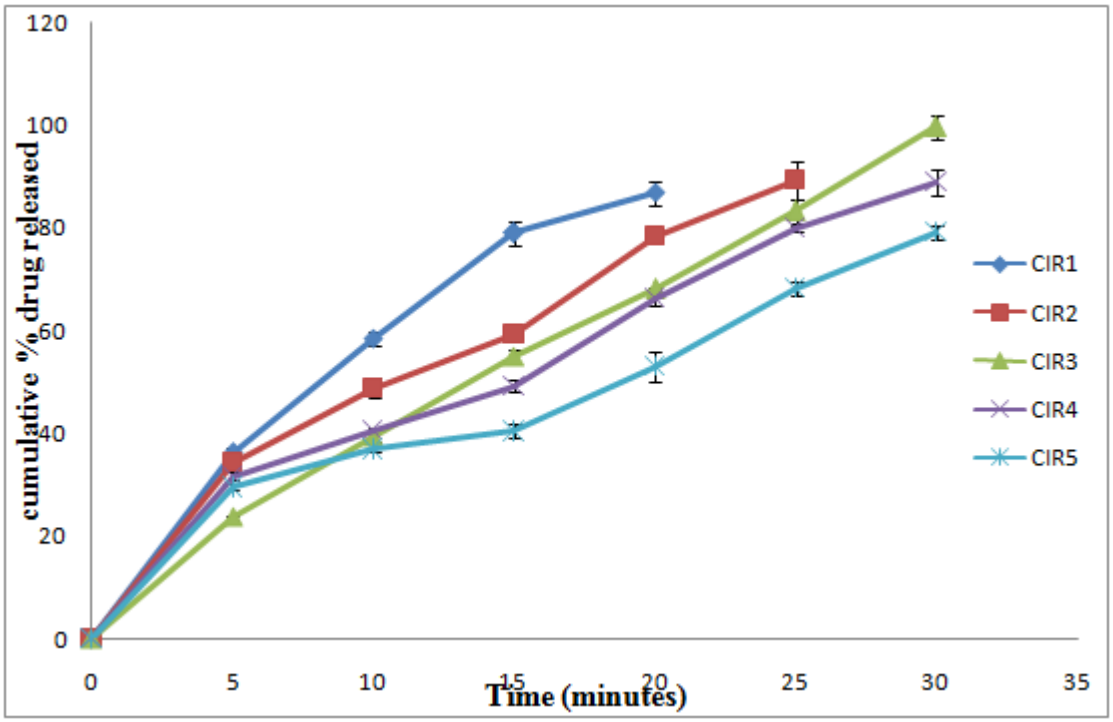

Figure 4: Drug release profiles of Captopril immediate release tablets (CIR1-CIR5) (Mean ± SD)

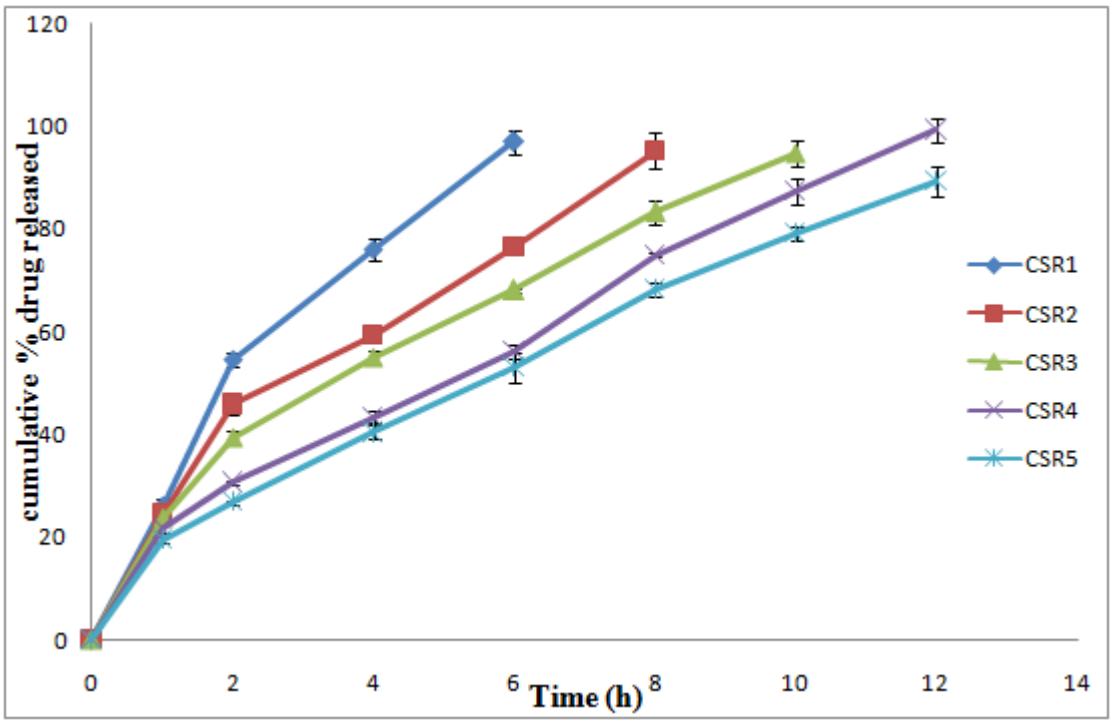

Figure 5: Drug release profiles of Captopril sustained release tablets prepared with guar gum (CSR1-CSR5) (Mean ± SD)

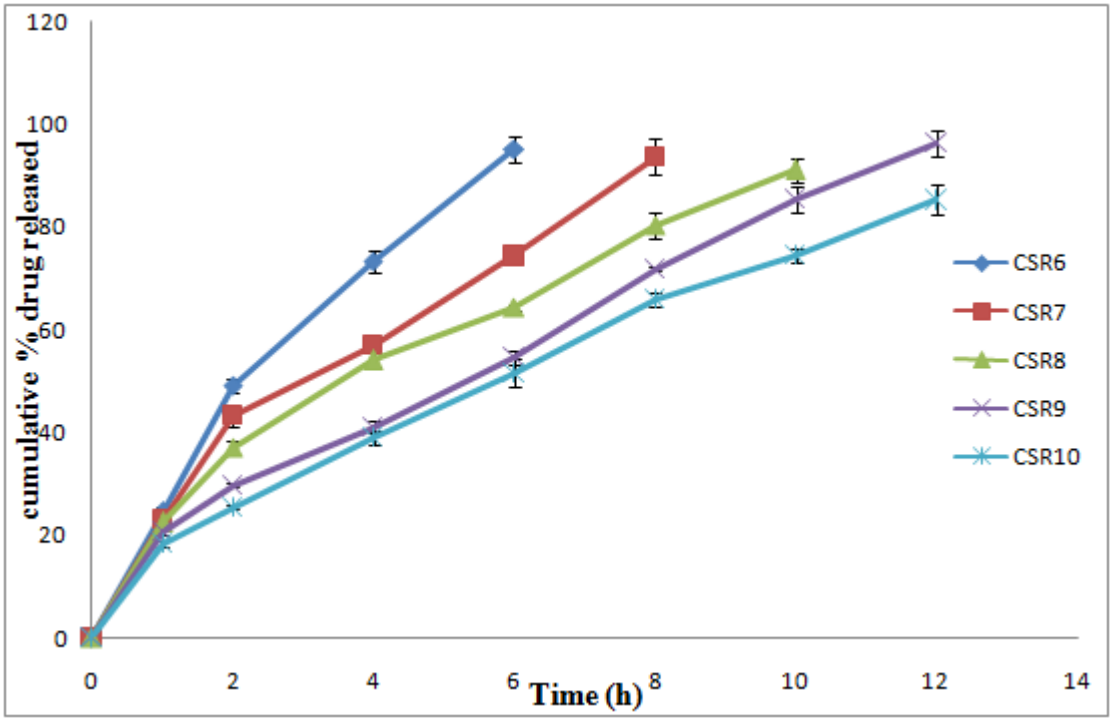

Figure 6: Drug release profiles of Captopril sustained release tablets prepared with xanthan gum (F6-F10) (Mean ± SD)

CONCLUSION

Captopril floating bilayered tablets were developed successfully and all the tablet formulation were intended for various physical evaluations and all are showing acceptable ranges with the pharmacopeia specifications. The optimized captopril bilayered tablets were stable for three months at various storage conditions

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CONFLICT OF INTEREST

Authors have no conflict of interest.

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