FORMULATION AND EVALUATION OF HYDRODYNAMICALLY BALANCED CONTROLLED DRUG DELIVERY SYSTEM OF CAPTOPRIL

G. SELVI ARUNKUMAR[1]*, VRUSHABENDRA SWAMY BM [1], P. ARCHANA SWAMY [1], NG. NANJUNDASWAMY [2]

[1]Gautham College of Pharmacy, RT Nagar, Bangalore, Karnataka 560032, India.

[2]Government College of Pharmacy, Subbaiah Circle, Bangalore, Karnataka 560027, India.

ABSTRACT

The present study outlines a systematic approach for design and development of hydrodynamically balanced controlled drug delivery system of captopril with the aid of optimization techniques, utilizing gel forming hydrocolloids like methyl cellulose, ethylcellulose and hydroxyl propyl cellulose. The drug to total polymer content was chosen as 1:5 to 1:7. The tablets were prepared by wet granulation method and were evaluated for duration of Buoyancy, captopril content and release rate profile. A series of such formulation were prepared by using the formulae obtained by optimization technique. From the results obtained it was clear that the formulation G-8 showed maximum buoyancy inferring the influence of high drug to polymer content on the buoyancy of the tablets.

1.INTRODUCTION

A hydrodynamically balanced drug delivery system (HBS) is either a capsule or a tablet designed to prolong gastrointestinal residence time to maximize the drug reaching its absorption site in a solution form and hence ready for absorption (Deshpande,1996). The hydrocolloids used in the HBS tablet on contact with gastic fluid become hydrated and forms a colloidal gel barrier. The mechanism of drug release follows matrix diffusion controlled release process (Chein) Captopril was chosen since it has a short half life, good solubility and stability in gastic fluid, non irritant, non emetic and does not alter gastro-intestinal motility (Deshpande, 1996).

2.MATERIAL AND METHODS

Captopril was obtained as a gift sample from Wockhardt Ltd, and Lupin Laboratories Ltd. The excipients were obtained from BPRL Ltd., Bangalore. Analytical grade chemicals and reagents were used.

Preparation of Hydrodynamically Balanced Tablets (HBS)

The formulae for preparation of HBS tablets were obtained by optimization technique (Users guide). The tablets were prepared by wet granulation method as per table No 1. All the ingredients except Captopril were passed through No 80 prior mixing. The ingredients were weighed separately and mixed to get uniform polymer mixture. The drug was then mixed with the polymer mixture in geometric dilution for a period of 10 minutes. A coherent mass of this mixture was prepared by adding water. This mass was passed through No 16, and the granules dried at 60°C, for one hour. The dried granules passed through No20/44, and lubricated and compressed in RSB4 minipress tablet machine4.

Parameters fixed for a Tablet :

1.	Tablet weight	-	250mg ± 18.5mg
2.	Thickness	-	4.5mm ± 0.5mm
3.	Hardness	-	3.45 ± 0.5kg/Cm^2
4.	Friability	-	not more than 1%

Quantities and ingredients per tablet – Table – 2.

Evaluation of HBS Tablets

The formulations were evaluated for the Captopril content, duration of buoyancy and drug release profiles (or rate).

Estimation of Captropil in Tablets

The tablets were selected in random and average weight was calculated. The tablets were triturated to get fine powder; from the resulting triturate a weight equivalent to 25mg of the drug was taken. The triturate was grind to paste with small amount of gastric fluid. This mixture was suitably diluted, to get desired

*Corresponding author:
selviarunkumar@gmail.com

concentration range. The drug was estimated using Folin ciacalteauis reagent by colorimetric method at 760nm against reagent blank (Emmanuel, 1989). Values are in Table 3.

Formula used:

$$\frac{\text{Sample abs}}{\text{Slope}} \times \text{dilution factor} \times \frac{25}{5} \times \text{Avg.wt of tablet}$$

Response Evaluation

(a) In Vitro Release Profile: The dissolution was conducted as per the method reported by A.K. Hilten and PB Deasey. The dissolution media taken was 750ml of gastric fluid without enzyme maintained at 37° C. The paddle rotated at 50 rpm. About 5ml of media withdrawn and analysed by colorimetric method using Folin's reagent at 760 nm against reagent blank (Menon and Ritchel, 1994).

(b) Duration of buoyancy: Duration of buoyancy was observed simultaneously when dissolution was carried out. The time taken by the tablet to rise to the surface of the media and the time for it to sink to the bottom was noted, which gives the buoyancy of the tablet [Table 5].

3.RESULTS AND DISCUSSION

An effort was made to formulate a hydrodynamically balanced controlled drug delivery system of Captopril utilizing gel forming hydrocolloids. The polymer to drug ratio was varied by utilizing optimization technique. The resulting formulae were used to develop various formulations. The run (8), that is formulation G-8, was found to show the maximum buoyancy, indicating the influence of polymer on buoyancy. The greater the amount of hydrocolloid, greater is the buoyancy.

4.ACKNOWLEDGEMENTS

I am extremely grateful to Prof N.G. Nanjundaswamy, Prof M Laksmana and Prof. M.S.Srinath for their valuable help and encouragement for the present work.

Table No. 1: The quantities for the different ingredients in the formulations of Design I

Ingredients	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Run 7	Run 8	Run 9
Captropil	30	30	30	30	30	30	30	30	30
Methyl cellulose	80	96	91.08	109.04	112	134.4	127.26	152.72	118.12
Ethyl Cellulose	30	30	13.63	13.63	42	42	19.1	19.1	22.5
Hydroxy propyl Cellulose	40	24	45.54	27.26	56	33.6	63.63	38.12	39.37
Micro crystalline	65	65	65	65	5	5	5	5	35
Magnesium Stearate	5	5	5	5	5	5	5	5	5

All ingredients are in mg.

Table No. 2: Quantities of ingredients per tablet and their percentage for Design I

Sl No	Ingredients	Qty/Tablet (mg)	Percentage
1	Captopril	30	12
2	Methylcellulose	80-153	32-61.2
3	Ethylcellulose	14-42	5.6-16.8
4	Hydroxypropyl Cellulose	25 – 65	10 – 26
5	Microcrystalline Cellulose	05 – 65	2 – 26
6	Magnesium stearate	5	2

Table.3: Captopril contents in the formulation of design I

Formulation Code	Trial 1	Trial 2	Trial 3	Avg. Captopril content (mg) ± SD	Assay (%)
G1	30.12	30.07	30.08	30.09 ± 0.0265	100.03
G2	29.56	29.52	29.3	29.46 ± 0.1400	98.20
G3	30.1	30.06	30.05	30.07 ± 0.0265	102.23
G4	29.84	29.87	29.96	29.89 ± 0.0624	99.53
G5	29.72	29.81	29.78	29.77 ± 0.0458	99.23
G6	29.58	29.57	29.53	29.56 ± 0.0265	98.53
G7	29.50	29.49	29.42	29.47 ± 0.0436	98.23
G8	30.28	30.32	30.33	30.31 ± 0.0265	101.03
G9	30.20	30.15	30.19	30.18 ± 0.0265	100.60

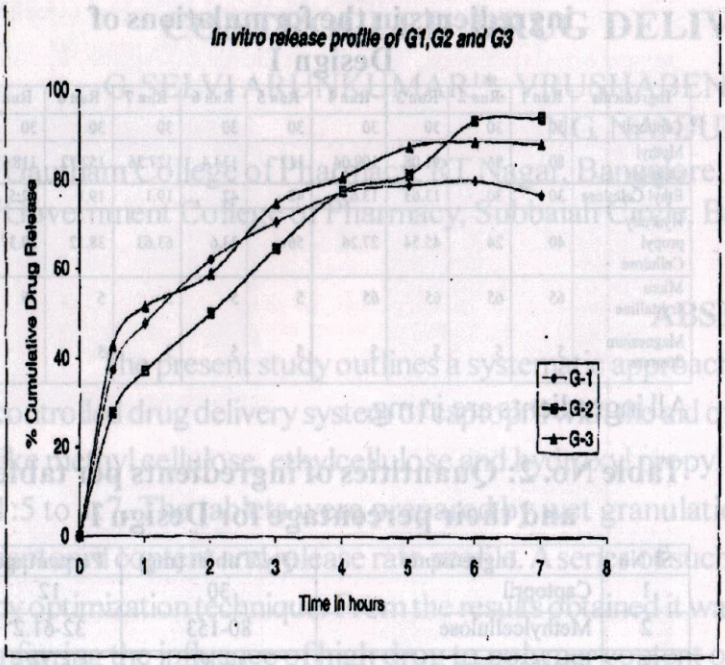
Table-4: In Vitro Release Studies

Time	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Run 7	Run 8
0.5	37.44±1.4	27.86±1.9	42.82±1.4	23.69±1.0	23.25–1.08	17.97±1.9	19.66–1.0	17.5±1.06
1	47.85±1.4	37.34±0.9	51.67±0.92	31.39±1.6	32.05–2.8	25.7±2.8	31.26–1.100	24.01±0.9
2	62.08±1.4	50.15±1.4	58.97±0.9	42.9±1.0	43.62–1.4	40.58±3.3	41.84–4.59	33.7±1.05
3	70.51±1.8	64.68±1.9	74.88±1.9	52.88±1.43	54.18–1.9	50.65±1.4	55.23–1.0	44.5±1.4
4	77.39±1.9	77.67±1.4	80.72±1.9	63.46±0.95	65.35–1.9	58.61±1.4	66.5±1.9	49.11±1.4
5	78.97±1.3	81.46±1.6	87.67±1.4	74.64±1.59	80.3±1.42	70.42±0.94	80.6±1.1	53.68±1.4
6	80.02±1.9	94.47±1.6	88.78±1.4	78.36±1.92	80.9±2.8	77.42±0.9	87.6±1.078	62.5±1.3
7	76.79±1.9	94.08±1.4	88.28±1.8	74.0±1.8	79.26–2.4	80.1±1.4	90.44–1.4	67.72±1.9

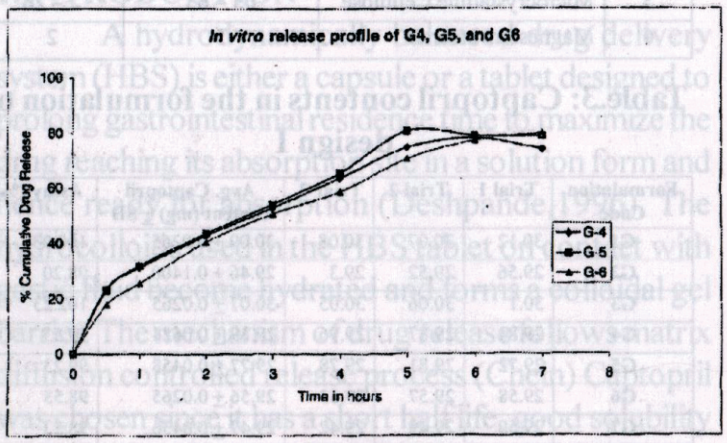
Table -5: Duration of buoyancy for runs of Design I

Formulation code	Duration of buoyancy in hours			
	Trial 1	Trial 2	Trial 3	Mean ± SD
G1	4.80	5.20	5.00	5.00 ± 0.200
G2	5.32	5.20	4.78	5.10 ± 0.284
G3	2.50	2.30	2.19	2.33 ± 0.157
G4	4.80	5.21	4.69	4.90 ± 0.274
G5	6.00	5.72	5.68	5.80 ± 0.174
G6	7.10	7.35	7.30	7.25 ± 0.132
G7	7.40	7.45	6.75	7.20 ± 0.391
G8	8.50	8.40	7.85	8.25 ± 0.350
G9	5.35	5.45	4.80	5.20 ± 0.350

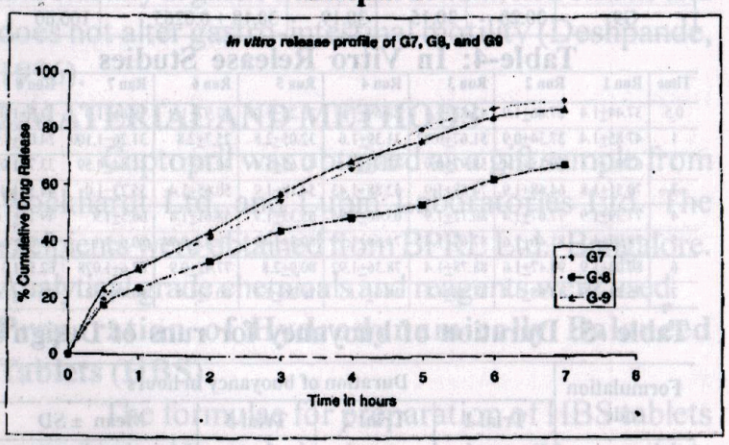
Graph-1



Graph-2



Graph -3



REFERENCES

Chein Y W, Oral drug delivery systems, In novel drug delvery systems, Vol.50.

Deshpande A.A, et al., controlled release drug delivery systems for prolonged gastic residence, An over view, Drug dev.Ind.Pharm., 22(6), 1996, 531-539.

Emmanuel J, Halankar and Surendra D, A sensitive spectro colorimeter method for the estimation of captropril and its formulatios, Indian Drugs, 26(6), 1989, 319-320.

Menon A, Ritchel, Development and evaluation of monolithic floating dosage form for Furosemide, J.Pharm.Sci., 88(2), 1994, 239-245.

Section -3, Two level full factorial tutorials, design expert software, version 6.0, user's guide.