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Formulation and evaluation of gastro-retentive drug delivery system of proponolol HCL

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ABSTRACT

This study was conducted to develop gastro retentive floating tablets for Propronolol Hcl is a sulfonylurea used in the treatment of hyperglycemia. Which has rapid and complete absorption after oral administration. Diseased state (Hypertension) influences the gastric emptying rate. The recommended adult oral dosage Propronolol HCl is 100 mg once daily. In present study floating tablets were prepared by using natural polymers as floating agents so as to maintain in buoyancy condition for about 12 hours to achieve maximum bioavailability and to produce local bioavailability. Floating tablets were developed by using natural polymer i.e., Xanthum gum, HPC, and HPMCK4 M. Various precompression parameters were evaluated for formulation blend including Drug excipient compatibility studies by using FTIR studies. Calibration curve was plotted by using 0.1 N HCl as medium. The prepared formulations were evaluated for various post compression parameters like hardness, friability, thickness, weight variation, floating lag time floating buoyancy studies and invitro dissolution studies. Among all the formulations F2 formulation which contains Xanthane gum has shown desired percentage drug release in 12 hours. The In vitro dissolution data were fitted in different kinetic models viz. zero order, first order, Higuchi and Korsemeyer - Peppas equation. Correlation coefficients of formulation F2 showed higher correlation with Peppas $R^2 = 0.993$.

Keywords: Floating drug delivery system, Propronolol Hcl, Natural gums, HPMC & Invitro drug release studies

INTRODUCTION

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost effective manufacturing process [1]. Many of the drug delivery systems, available in the market are oral drug delivery type systems Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug

delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the C_{ss} values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs [2].

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits [3].

Controlled Drug Delivery Systems

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue [4].

Controlled drug delivery or modified drug delivery systems are divided into four categories.

1. Delayed release
2. Sustained release
3. Site-specific targeting
4. Receptor targeting

More precisely, controlled delivery can be defined as:-

1. Sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects.
2. Localized drug action by spatial placement of a controlled release system adjacent to or in the diseased tissue.
3. Targeted drug action by using carriers or chemical derivatives to deliver drug to a particular target cell type.
4. Provide physiologically/therapeutically based drug release system. In other words, the amount and the rate of drug release are determined by the physiological/ therapeutic needs of the body [5].

A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug (Figure 1) [6]. Controlled drug delivery usually results in substantially constant blood levels of the active ingredient as compared to the uncontrolled fluctuations observed when multiple doses of quick releasing conventional dosage forms are administered to a patient.

METHODOLOGY

Determination of Lambda max of Propronolol Hcl

A stock solution of Propronolol Hcl (10 µg/ml) was prepared in 0.1N HCL. The UV spectrum was recorded in the range of 200-400 nm in UV-Visible spectrophotometer and lamda max was determined.

Preparation of standard graph of Propronolol Hcl in 0.1 N Hcl

100mg of drug was dissolved in 100ml of 0.1N Hcl (stock solution-1000 µg/ml). The solutions of concentrations 5 to 25 µg/ml were prepared from above stock solution by appropriate dilution with 0.1 N HCL. The absorbance of each of solution was recorded using UV-Visible spectrophotometer at wavelength of maximum absorption (267nm). The standard graph was plotted by taking concentration (µg/ml) on X-axis and absorbance on Y-axis.

Formulation of floating tablets of Propronolol Hcl

The composition of different formulations of Propronolol Hcl floating tablets are shown in Table no 07**.** Propronolol Hcl, HPMC K14M, Xanthan gum, HPC were passed through sieve no. 80 separately. Sodium bicarbonate was passed through sieve no. 44. All the ingredients were mixed in the proportions shown in Table no.10. The powder blends were lubricated with Magnesium stearate and Talc and mixed for two to three minutes. These lubricated blends were compressed into tablets using 10 mm punch on a multiple punch tablet machine. The compression force was adjusted to obtain tablets with hardness in the range of 4.5 to 5

kg/cm2. Each tablet contained 250 mg of Propronolol Hcl.

Optimization of gas generating agent

Ingredients	F1	F2	F3
Propronolol Hcl	**80**	**80**	**80**
HPMC K4 M	**100**	**100**	**100**
NAHCO3	**25**	**50**	**75**
Mg.stearate	**3**	**3**	**3**
Talc	**3**	**3**	**3**
MCC pH 102	**Q.s**	**Q.s**	**Q.s**

Table 1: Composition of different floating tablet formulations of Propronolol Hcl

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Propronolol Hcl	80	80	80	80	80	80	80	80	80
Xanthane Gum	60	90	120	-	-	-	-	-	-
HPC	-	-	-	60	90	120	-	-	-
HPMC K4M	-	-	-	-	-	-	60	90	120
$NaHCO_3$	50	50	50	50	50	50	50	50	50
Talc	4	4	4	4	4	4	4	4	4
Magnesium stearate	4	4	4	4	4	4	4	4	4
Microcrystalline cellulose	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s
Total weight	300	300	300	300	300	300	300	300	300

Evaluation of foating tabets of Propronolol Hcl

Preformulation studies (drug-excipient interaction studies, flow properties) were carried out for powder blends to detect any interaction between drug and excipients and to determine the flow properties of ingredients. Prepared tablets were evaluated for post compression parameters like various quality control tests such as Tablet thickness and Diameter, Hardness, Friability, uniformity of weight, content uniformity of drug, drug release and other specific evaluation tests for GFDDS like floating lag time and total floating time.

RESULTS AND DISCUSSION

Standard graph of Propronolol Hcl in 0.1N HCl

The scanning of the volumetric solution of Propronolol Hcl in the ultraviolet range (200-400nm) against 0.1 N HCl blank gave the λ_{max} as 267 nm. The standard concentrations of Propronolol Hcl (5-25 µg/ml) prepared in 0.1N HCl showed good linearity with R^2 value of 0.998, which suggests that it obeys the Beer-Lamberts law.

Table No. 2: Standard curve of Propronolol Hcl

Concentration (µg/ml)	Absorbance
0	0
5	0.168
10	0.328
15	0.481
20	0.635
25	0.785

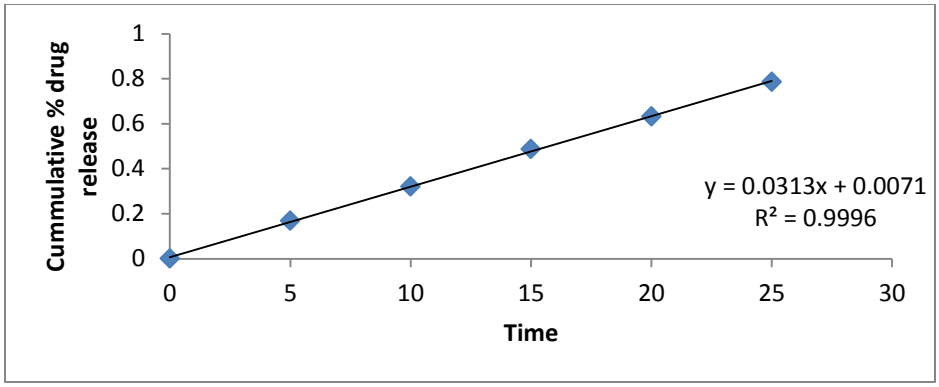

Fig No. 1: Standard curve of Propronolol Hcl

Drug-Excipient Interaction Studies

Fourier Transform Infrared spectroscopic studies (FTIR)

The FTIR spectra of drug, excipients, drug loaded formulation were recorded. The characteristic peaks of the optimized formulation followed the same trajectory as that of the drug alone with minor differences. Thus there may be no drug-excipient interactions. The FTIR spectra were given in figure 14, 15.

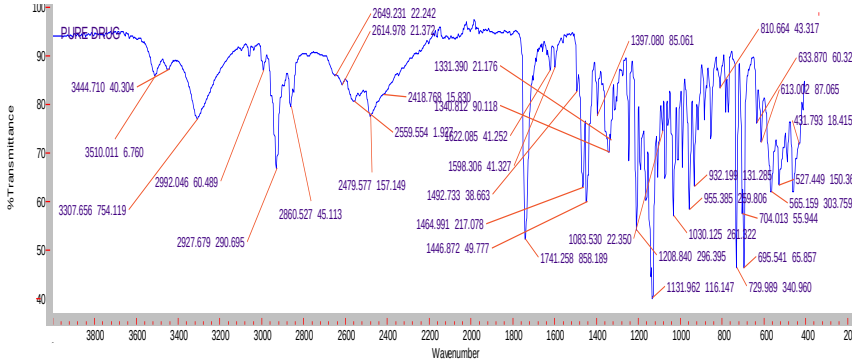

Fig No 2: FTIR spectra of Propronolol Hcl

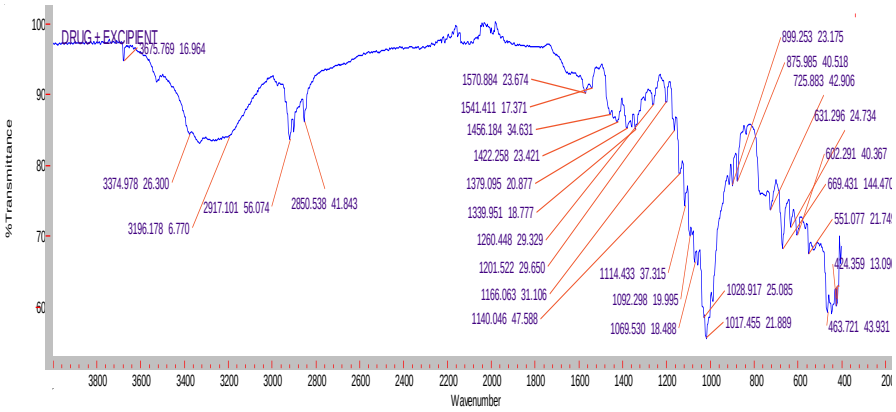

Fig. No 3: FTIR spectra of optimized formulation

Flow properties of floating tablet blends

Table 3: Results of Precompression Flow Properties of Propronolol Hcl

Formulationcode	Angle of repose (Ɵ)	Bulk density(gm/cm3) gm/cm3) (gm/cm3)	Tapped density(gm/cm3)	Carr's index (%)	Hausner ratio (HR)
F1	21.01	0.47	0.55	14.54	1.17
F2	23.8	0.54	0.61	11.87	1.12
F3	25.74	0.55	0.63	12.68	1.14
F4	23.33	0.54	0.64	17.67	1.18
F5	25.24	0.51	0.62	17.72	1.21
F6	27.12	0.53	0.61	13.11	1.15
F7	28.08	0.59	0.67	16.43	1.13
F8	23.12	0.48	0.57	15.78	1.18
F9	25.45	0.55	0.61	16.54	1.10

Post compression parameters of floating tablets of Propronolol Hcl

Table 4: Results of Post Compression Properties Propronolol Hcl -of Floating Tablets

Formulation Code	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Drug Content (%)	Weight variation(mg)
F1	4.1	4.5	0.53	99.89	299.6
F2	4.5	4.4	0.54	98.93	298.1
F3	4.9	4.5	0.48	102.63	299.8
F4	4.6	4.6	0.64	95.56	302.8
F5	4.8	4.7	0.48	96.96	304.7
F6	4.5	4.6	0.69	100.5	297.8
F7	4.7	5.0	0.42	98.7	301.5
F8	4.8	4.8	0.64	90.54	304.5
F9	4.8	4.6	0.55	96.5	301.5

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Table 5: Results of *In vitro* Buoyancy study of Propronolol Hcl Floating Tablets

Formulation code	Buoyancy Lag Time (sec)	Total Floating Time (hrs)
F1	90	10
F2	80	>12
F3	88	8
F4	82	>9
F5	95	>12
F6	100	>12
F7	90	9
F8	82	>12
F9	104	>8

Table No. 6: In vitro drug release profile of Propronolol Hcl

Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	18.45	13.3	11.34	37.2	24.2	18.4	11.08	23.28	6.12
1	24.16	22.5	19.28	40.2	38.8	23.4	17.56	36.12	12.04
2	32.37	29.5	21.17	55.3	45.4	433.4	23.88	42.28	23.48

3	43.21	43.3	26.28	59.5	54.2	46.5	32.56	54.27	28.57
4	50.34	52.1	33.28	62.4	68.3	52.7	44.52	67.29	32.32
5	56.28	57.8	42.20	79.6	75.2	59.8	49.16	74.28	37.62
6	65.23	63.3	47.18	81.8	86.2	61.4	52.96	80.16	43.96
7	71.26	65.7	52.19	93.8	92.3	73.4	56.08	85.32	52.4
8	78.73	71.3	58.48	102.7	99.6	75.6	61.68	92.16	57.04
9	82.18	81.3	66.18			83.3	65.72	97.26	64.08
10	95.34	89.5	72.19			87.7	70.92	103.29	68.76
11		92.1	75.27			90.3	72.92		77.8
12		99.8	82.14			93.4	81.34		80.5

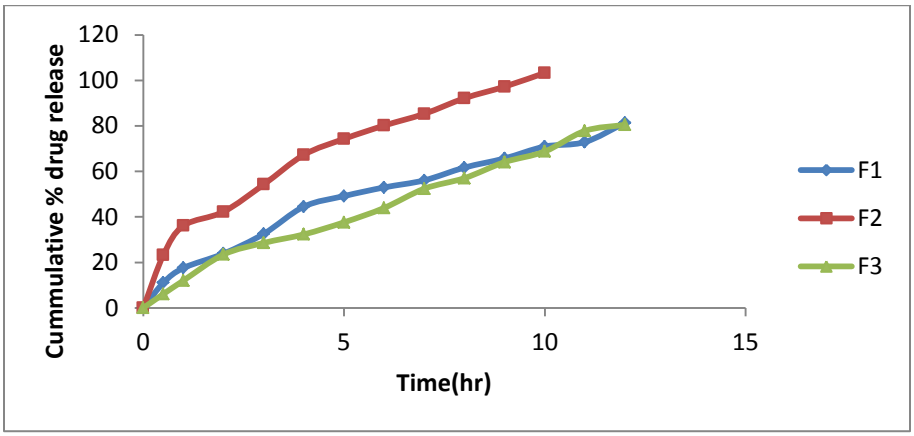

Fig No 4: Invitro drug release data from formulation with HPMC K 4 M

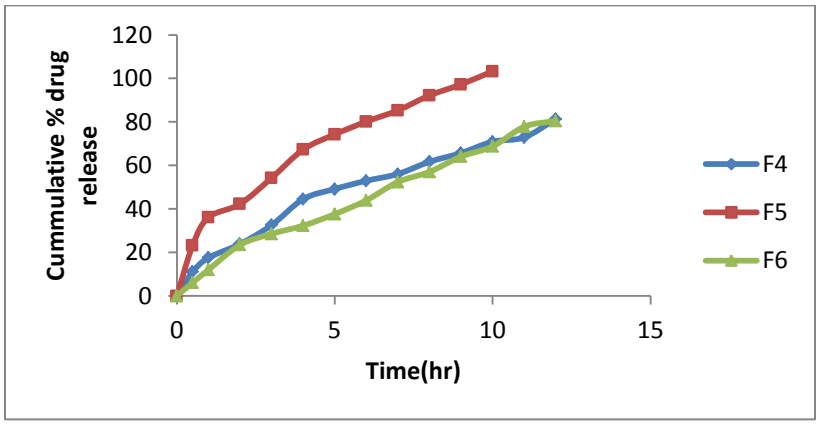

Fig No 5: Invitro drug release data from formulation with HPC

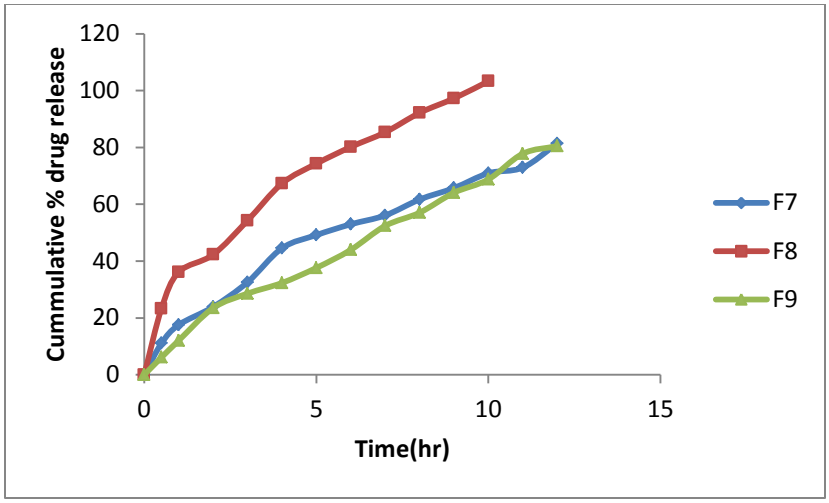

Fig No 6: Invitro drug release data from formulation with Xanthane gum

In vitro dissolution studies of all the formulations of Propronolol Hcl were carried out in 0.1 N HCl. Percentage drug release was calculated at one hour time intervals for 12 hours. The variation in drug release was due to different types of polymers and different concentrations of polymer in all the formulations. Among these formulations, formulation F2 gave desired release in first hour for loading dose and also retarded the drug release for 12 hours (99.8%). Hence, the formulation F2 was considered as most promising formulation among all the formulations.

Table No 7: Kinetics of In-vitro dissolution studies of optimized formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining
0	0	0			2.000				100
13.3	0.5	0.707	1.124	-0.301	1.938	26.600	0.0752	-0.876	86.7
22.5	1	1.000	1.352	0.000	1.889	22.500	0.0444	-0.648	77.5
29.5	2	1.414	1.470	0.301	1.848	14.750	0.0339	-0.530	70.5
43.3	3	1.732	1.636	0.477	1.754	14.433	0.0231	-0.364	56.7
52.1	4	2.000	1.717	0.602	1.680	13.025	0.0192	-0.283	47.9
57.8	5	2.236	1.762	0.699	1.625	11.560	0.0173	-0.238	42.2
63.3	6	2.449	1.801	0.778	1.565	10.550	0.0158	-0.199	36.7
65.7	7	2.646	1.818	0.845	1.535	9.386	0.0152	-0.182	34.3
71.3	8	2.828	1.853	0.903	1.458	8.913	0.0140	-0.147	28.7
81.3	9	3.000	1.910	0.954	1.272	9.033	0.0123	-0.090	18.7
89.5	10	3.162	1.952	1.000	1.021	8.950	0.0112	-0.048	10.5
92.1	11	3.317	1.964	1.041	0.898	8.373	0.0109	-0.036	7.9
99.8	12	3.464	1.999	1.079	-0.699	8.317	0.0100	-0.001	0.2

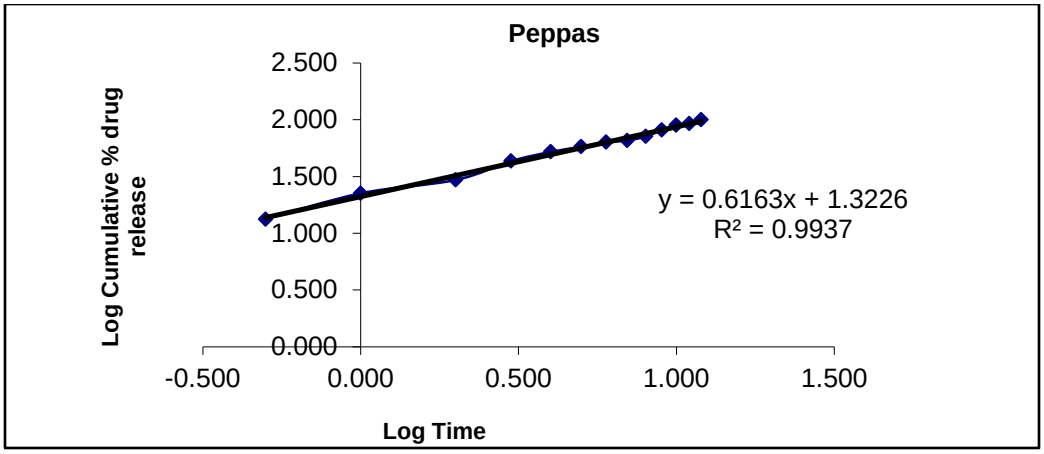

Fig No 7: Kinetic release plot - Korsemeyers peppas plot

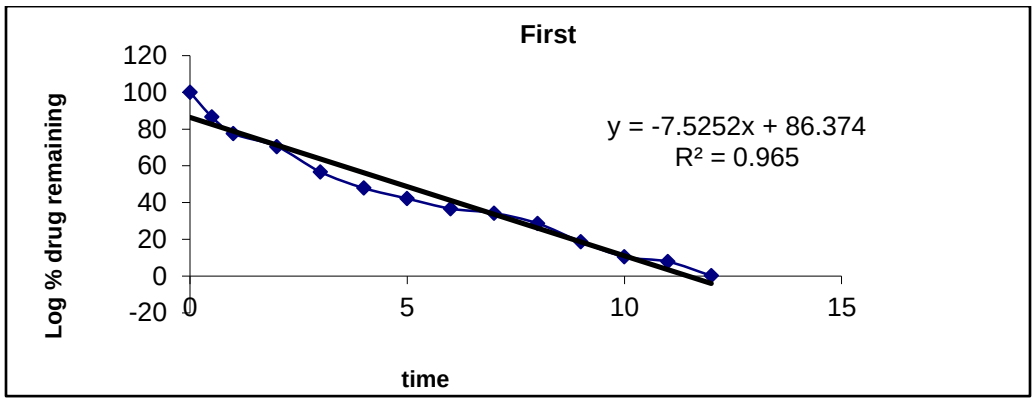

Fig No 8: Kinetic release plot - First order plot

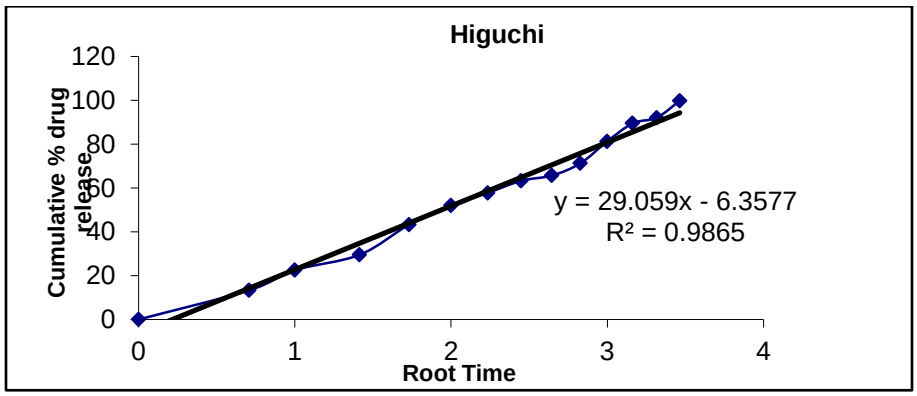

Fig No 9 : Kinetic release plot - Higuchi plot

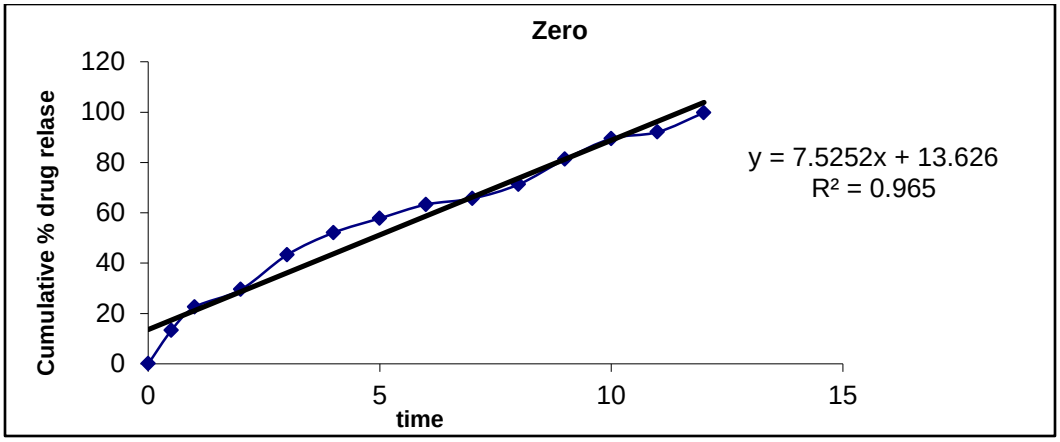

Fig No 10: Kinetic release plot - Zero order plot

The In vitro dissolution data were fitted in different kinetic models viz. zero order, first order, Higuchi and Korsemeyer - Peppas equation. Correlation coefficients of formulation F2 showed higher correlation with Peppass (R^2 = 0.993).

CONCLUSION

The conclusion drawn from the present studies of all the formulations of Propronolol Hcl were carried out in 0.1 N HCl. The variation in drug release was due to different types of polymers and different concentrations of polymer in all the formulations. Among these formulations, formulation F2 gave desired release in first hour for loading dose and also retarded the drug release for 12 hours (99.8%). Hence, the formulation F2 was considered as most promising formulation among all the formulations.

REFERENCES

[1]. Basak SC, Rao NK, Manavalan R and Rao RP: Development and in vitro evaluation of an oral floating matrix tablet formulation of ciprofloxacin, Indian J Pharm Sci., 66(3), 2004, 313-316.
[2]. Brahmankar DM and Jaiswal SB: Biopharmaceutics and Pharmacokinetics a Treatise. Vallabh Prakashan, 1995, 336-337.
[3]. Chein YW: Novel Drug Delivery Systems. Marcel Dekker, Second Edition 1992.
[4]. Jain NK: Controlled and Novel Drug Delivery. CBS Publishers and Distributors, First Edition 1997.
[5]. Vyas SP and Khar RK: Text Book of Controlled Drug Delivery. Vallabh Prakashan, First Edition 2002.
[6]. Samip Shah and Shridhar Pandya A Novel approach in Gastro Retentive Drug Deivery System: Floating Drug Delivery System International Journal of Pharmaceutical Sciences and Reaserch l(6), 2010.
[7]. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating Drug Delivery Systems: A Review. AAPS PharmSciTech. 06(03), 2005.
[8]. Streubel A, Siepmann J, Bodmeier R. "Floating matrix tablets based on low density foam powder: effect of formulation and processing parameters on drug release". Eur J arm Sci. 18, 2003, 37-45.
[9]. Rocca DJG,Omidian H, Shah k. Progresses in gastroretentive drug delivery systems, Business Briefing, Pharmatech 2003, 152-156.
[10]. Tortora GJ and Grabowski SR: Principles of Anatomy and Physiology. John Willey and Sons, 10, 2002.
[11]. Wilson KRW, Waugh A.Anatomy and Physiology in Health and Illness, London: Churchill Livingstone, 2, 1996.
[12]. P. Grubel et al, Gastric emptying of non-digestible solids in the fasted dog, J.Pharm.Sci., 76, 1987, 117 –122.
[13]. Baumgartner S, Kristi J, Vrecer F, et al .O Int J Pharm 195, 2000, 125-3.Garg.S, Sharma S. Pharmatech. 2000, 160 – 66.