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Development and Evaluation of Gastroretentive Controlled Release Polymeric Suspensions Containing Ciprofloxacin and Carbopol Polymers

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ABSTRACT

Considering the importance of drug release pattern from polymers, controlled release oral formulations of Ciprofloxacin were prepared using two grades of Carbopol polymer such as C934 and C940. The objective of the present study was to design and compare the release characteristics of those suspensions. The results indicated that the dissolution of Ciprofloxacin was faster in acidic buffer of pH 1.2 than in phosphate buffer of pH 7.2. In the acidic buffer, the values of the regression coefficient suggested that both the formulations followed Korsmeyer Peppas model release kinetics whereas those values, in the phosphate buffer, indicated that the release kinetics of the formulation containing C934 (F1) were according to Korsmeyer Peppas model and the formulation containing C940 (F2) followed first order release kinetics. Considering the n values for Peppas model, both the formulations showed Fickian diffusional release pattern in acidic buffer suggesting usual molecular diffusion of the drug due to a chemical potential gradient indicating diffusional controlled drug release. However, release of Ciprofloxacin from F2 in phosphate buffer was attributed mainly to polymer relaxation followed by diffusion of the drug, while the release of the drug from F1 was probably controlled by the swelling and relaxation of the polymers indicating super case II transport.

Keywords: Ciprofloxacin, C934, C940, Acidic buffer, Phosphate buffer.

INTRODUCTION

Ciprofloxacin (Cipro) is a second generation fluoroquinolone antibacterial (Fig 1). It shows low solubility in aqueous solution and a high rate of absorption from the stomach. It is likely to be precipitated out of solution upon entry into the small intestine where the pH is alkaline. The desire is for a controlled release system to maintain drug concentration in the blood as long as possible which is able to exert a control on the drug release rate and duration. Generally, a controlled release system initially releases part of the dose rapidly in order to attain the effective therapeutic concentration of the drug. Subsequently, the drug release kinetics follow a well defined behavior in order to supply the maintenance dose, enabling the attainment of the desired drug concentration [1, 2].

The benefits of administering Ciprofloxacin in controlled release system have been established and demonstrated by different workers. Larger dose of Ciprofloxacin is to be administered to overcome poor bioavailability which leads to systemic side effects. Controlled release formulations of Ciprofloxacin would be effective in overcoming the dissolution limitation by slowing the drug supply from the intact matrix base during its sojourn in the gastrointestinal tract and is thus expected to increase bioavailability and improve patient compliance with fewer side effects [3-6].

Taking into consideration of above factors, polymeric suspensions of Ciprofloxacin were prepared by using two grades of mucoadhesive biodegradable environmentally responsive carbopol polymers i.e., Carbopol934 (C934) and Carbopol940 (C940) which are considered as smart gels [7, 8]. Both C934 and C940 consist of chains of polyacrylic acid differing by the cross linking agents like allyl ethers of sucrose and pentaerythritol, respectively [9, 10]. They have recently attracted considerable interest in the field of drug delivery as a means of providing an on-off release by shrinking and swelling in response to the change in pH [11, 12]. The polymer can protect the drug from the physiological environment by improving its stability *in vivo* [13]. Carbopol polymers, being both gel forming materials as well as acidic in nature, have the advantage of acting as good matrix formers and also enhancing release of poorly soluble, weakly basic drugs in neutral or basic buffers. Generally, weakly basic drugs show a sharp drop in aqueous solubility with an increase in pH, thus resulting in high release in acidic media and low release in neutral or basic media. The gel properties of Carbopol polymers, which are largely defined by their crosslinker levels, are very important to drug release kinetics. The differences in the hydrated macromolecular structure of Carbopol polymers influence the macro- and microviscosities of the gel layer and, therefore, the drug release characteristics [14].

Since the qualitative and quantitative changes in a formulation may alter drug release and *in vivo* performance, several bio-studies are usually carried out. In this regard, the use of *In vitro* drug dissolution data to predict *in vivo* bio-performance can be considered as the rational development of controlled release formulations. There are several kinetic models, which describe the overall release of drug from the dosage forms. For this purpose, the use of mathematical modeling turns out to be very useful as this approach enables, in the best case, the prediction of release kinetics [15, 16]. Considering the importance, Model dependent methods (zero order, first order, Higuchi, Korsmeyer-Peppas model, etc.) and Model independent methods [disimilarity factor (f_1), similarity factor (f_2)] have been used, in the present study, for comparison of dissolution profiles of both the formulations. The objective of this study was to design and compare the release characteristics of controlled release oral formulations of Cipro containing polymers like C934 and C940.

EXPERIMENTAL SECTION

Materials:

The following materials were used: Ciprofloxacin was obtained from Dr. Reddy's Lab, Hyderabad, India, as a gift sample. C934, C940, Pluronic F 68 and Soya lecithin were purchased from Himedia Laboratories Pvt. Ltd., India. Glycerol, Methyl praraben sodium, Propyl paraben sodium, Sorbitol solution I.P. and Sucrose were supplied by Cosmo Chem. Laboratory, Pune, India. Ultra pure water was obtained from a Millipore Milli-Q UV water filtration system.

Methods:

Preparation of Formulation-

1. Preparation of Bulk A

In a beaker, 6 ml water was heated up to 80° C. Sucrose (10 gm) was added under continuous stirring. The temperature was monitored in such a way so that it should not fall below 70° C, till the sucrose was completely dissolved. The prepared syrup was cooled properly at room temperature and kept overnight. Syrup was filtered using 120 mesh nylon cloth.

2. Preparation of Bulk B

Five millilitre of Ultra pure water was taken in a beaker to which 1.8 ml of sorbitol solution and 0.2 ml glycerin were added. The mixture was stirred properly. To this solution, pluronic F 68 (5%), soya lecithin (1%) and C934 / C940 (5%) in w/w of drug were added with continuous stirring.

3. Preparation of Mucoadhesive Suspension and Ultrasonication

Five millilitre of water was taken in another beaker to which 1.25 gm of Cipro was added. To the drug suspension, the bulk B and bulk A were added with continuous stirring. Methyl paraben sodium (0.015%w/v) and Propyl paraben sodium (0.08%w/v) were added as preservatives. The volume was made up to 25 ml by Ultra pure water. The pH was adjusted to 5.5. Homogenization was carried out for at least 20 min by ULTRASONIC HOMOZENIZER LABSONIC^R M (SARTORIUS), having operating frequency 30 KHZ and line voltage 230 V/50 HZ, using the probe made up of Titanium of diameter 7 mm and length 80 mm. The setting knob "cycle" was adjusted to 0.8, indicating sound was emitted for 0.8 s and paused for 0.2 s. In this manner, we could expose our sample with 100% amplitude, while reducing the heating effect to 80%. This LABSONIC^{R}M generates longitudinal mechanical vibrations with a frequency of 30,000 oscillations / s (30 KHZ). The probes bolted to the sound

transducer were made of high-strength Titanium alloys, built as λ /2 oscillators. It amplified the vertical oscillation, and transferred the ultrasonic energy via its front surface with extremely high power density into the sample that was to be subjected to ultrasonic waves. In our study, stress applied was sound wave and in addition, mild rise in temperature of the sample occurred during ultrasonication which helped in the homogenization of the suspension.

Dissolution studies [17]

In vitro Drug release profile was evaluated using dissolution test apparatus (Harrison six stage dissolution rate test apparatus). The USP paddle method was selected to perform the dissolution profiles of Ciprofloxacin from mucoadhesive suspension. The same test for all the formulations was carried out in 900ml 0.1M HCl and phosphate buffer, 7.2 maintained at 37 ± 0.5 ^{0}C at a paddle rotation speed of 50 rpm. The samples were withdrawn at regular time intervals and the same volume was replaced with fresh dissolution medium. Samples were filtered (0.45 Millipore filter) and then drug concentrations were determined using ELICO BL-198 UV-Visible Biospectrophotometer at 276 nm.

Release Kinetics [16, 18, 19]

The dissolution data for each sample (suspension) were treated by converting observed drug concentration at each sampling time (30 minutes interval) and, in turn, to percentage drug dissolved, based on the amount incorporated as 100%.

In order to understand the kinetic and mechanism of drug release, the result of *In vitro* drug release study of formulations was fitted with various kinetic equations like zero order (cumulative% release vs. time), first order (log% drug remaining vs. time), Higuchi's model (cumulative% drug release vs. square root of time), Peppas plot (log of cumulative% drug release vs. log time). Moreover, R^2 (coefficient of correlation) values were calculated for the linear curve obtained by regression analysis of the above plots.

The equations of different release kinetics are as follows:

Zero order equation: $Q = Q_0 – K_0t$; First order equation: $\ln Q = \ln Q_0 – K_1t$;

Higuchi equation: $Q = K_2t^{1/2}$; Korsmeyer – Peppas equation: $Q/Q_0 = Kt^n$.

In the equations, K_0 to K_2 were release rate constants, Q/Q_0 was fraction of drug released at time t, K was constant and n was diffusion constant that indicates general operating release mechanism.

It is known that the Peppas model is widely used to confirm whether the release mechanism is Fickian diffusion and non-Fickian diffusion. The 'n' (release exponent of Korsmeyer-Peppas model) value could be used to characterize different release mechanisms. The interpretation of n values was done in the following manner:

- n<0.5 (0.45) - quasi-Fickian Diffusion
- n=0.5 (0.45) - Diffusion mechanism
- 0.5<n<1 - Anomalous (non-Fickian) Diffusion - both diffusion and relaxation (erosion)
- n=1 (0.89) - Case 2 transport (zero order release)
- n>1 (0.89) - Super Case 2 transport (relaxation)

Comparison of Dissolution Profiles [15, 16, 20]

To compare the dissolution data of the formulations, a statistical method was used which was independent of the dissolution process. This method established two comparison factors: the dissimilarity factor (f1) and the similarity factor (f2). These factors are easily calculated and provide a simple measure of similarity between pairs of dissolution profile but do not provide information on individual batches.

The dissimilarity factor (f1) and the similarity factor (f2) are calculated using the following equations:

$$f_1 = \{[\Sigma_{t=1}^{r} | R_t - T_t |] / [\Sigma_{t=1}^{n} R_t]\} * 100$$

$$f_2 = 50 * \log \{[1 + (1/n)\Sigma_{t=1}^{n} (R_t - T_t)^2]^{-0.5} * 100\}$$

Where R_t = amount of drug released from the reference formulation
T_t = amount of drug released from the tested formulation
n = number of experimental data

Generally, f1 values up to 15 (0-15) and f2 values greater than 50 (50-100) ensure similarity or equivalence of the two dissolution profiles.

RESULTS

The formulations F1 and F2 were subjected to *In vitro* dissolution studies both in acidic buffer of pH 1.2 and phosphate buffer of pH 7.2. The results indicated that dissolution of Ciprofloxacin was faster in acidic buffer of pH 1.2. In the first and second hour, drug release was found to be 82.46% and 90.17%, respectively, from formulation F1, and 90.17% and 91.12%, respectively, from formulation F2 in acidic buffer. From the dissolution study, it is clear that the formulations had faster dissolution in that buffer. (Table 1, Figs. 1 and 2)

Table 1: *In vitro* drug release profile of Ciprofloxacin containing formulations

Time (h)	Cumulative percentage of drug released			
	Acidic Buffer of pH 1.2		Phosphate Buffer of pH 7.2	
	F1	F2	F1	F2
0.5	64.44	50.56	38.25	9.05
1	82.46	85.12	48.82	20.45
1.5	85.66	89.17	54.34	31.26
2	90.17	91.12	58.48	42.01
2.5	92.84	93.16	64.82	47.06
3	93.12	93.82	67.85	52.89
5	93.75	94.25	72.84	63.08
7	93.82	94.74	78.14	72.56
9	94.10	94.82	82.79	81.01
12	94.71	95.25	86.21	90.25

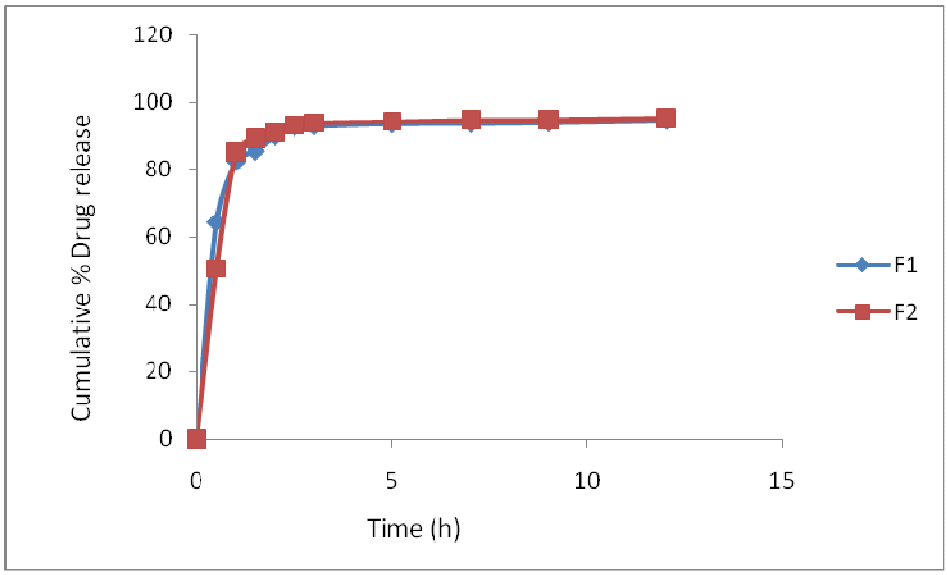

Fig. 1: *In vitro* drug release profile of both the formulations (F1 and F2) in acidic buffer

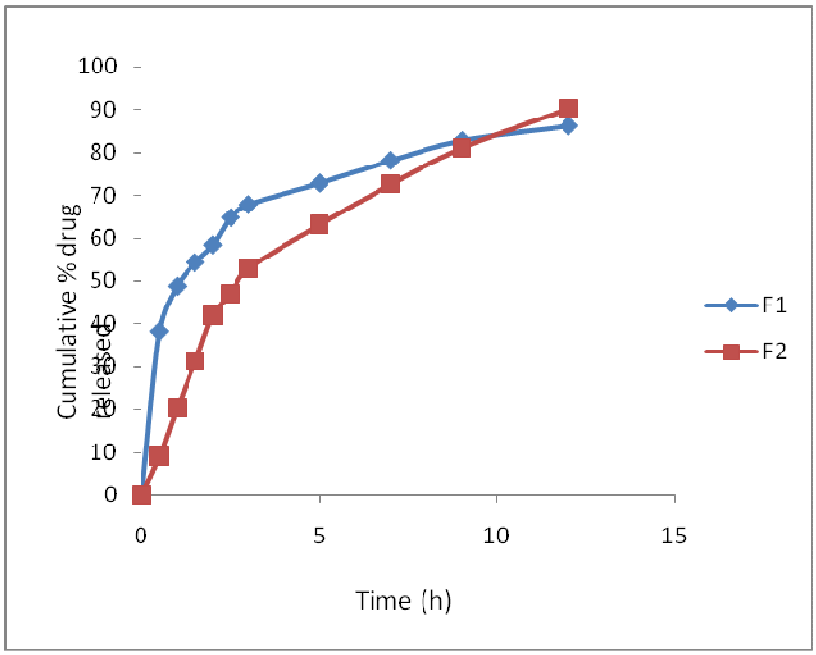

Fig. 2: *In vitro* drug release profile of both the formulations (F1 and F2) in phosphate buffer

Table 2: Release Kinetics Profiles of Formulation containing C934 in acidic buffer

Time (h)	Square Root of time	Log time	CDR	%CDR	Log of %CDR	Log Cu % of drug remaining
0.5	0.707	- 0.301	178.95	64.44	1.8091	1.5510
1	1	0	228.99	82.46	1.9162	1.2440
1.5	1.224	0.176	237.88	85.66	1.9328	1.1565
2	1.414	0.301	250.40	90.17	1.9551	0.9926
2.5	1.581	0.397	257.82	92.84	1.9677	0.8548
3	1.732	0.477	258.59	93.12	1.9690	0.8377
5	2.236	0.698	260.34	93.75	1.9720	0.7956
7	2.645	0.845	260.54	93.82	1.9723	0.7909
9	3	0.954	261.32	94.10	1.9736	0.7707
12	3.464	1.079	263.01	94.71	1.9764	0.7235

Table 3: Release Kinetics Profiles of Formulation containing C940 in acidic buffer

Time (h)	Square Root of time	Log time	CDR	%CDR	Log of %CDR	Log Cu % of drug remaining
0.5	0.707	- 0.301	140.56	50.56	1.7038	1.6936
1	1	0	236.63	85.12	1.9300	1.1699
1.5	1.224	0.176	247.90	89.17	1.9502	1.0306
2	1.414	0.301	253.31	91.12	1.9596	0.9436
2.5	1.581	0.397	258.98	93.16	1.9692	0.8287
3	1.732	0.477	260.82	93.82	1.9723	0.7838
5	2.236	0.698	262.02	94.25	1.9743	0.7518
7	2.645	0.845	163.38	94.74	1.9765	0.7124
9	3	0.954	263.60	94.82	1.9769	0.7056
12	3.464	1.079	264.80	95.25	1.9789	0.6670

Table 4: Release Kinetics Profiles of Formulation containing C934 in phosphate buffer

Time (h)	Square Root of time	Log time	CDR	%CDR	Log of %CDR	Log Cu % of drug remaining
0.5	0.707	- 0.301	106.22	38.25	1.5826	1.7906
1	1	0	135.57	48.82	1.6886	1.7091
1.5	1.224	0.176	150.9	54.34	1.7351	1.6595
2	1.414	0.301	162.4	58.48	1.7670	1.6183
2.5	1.581	0.397	180.01	64.82	1.8117	1.5463
3	1.732	0.477	188.42	67.85	1.8315	1.5072
5	2.236	0.698	202.28	72.84	1.8624	1.4339
7	2.645	0.845	216.99	78.14	1.8929	1.3397
9	3	0.954	229.9	82.79	1.9180	1.2359
12	3.464	1.079	239.41	86.21	1.9356	1.1395

Table 5: Release Kinetics Profiles of Formulation containing C940 in phosphate buffer

Time (h)	Square Root of time	Log time	CDR	%CDR	Log of %CDR	Log Cu % of drug remaining
0.5	0.707	- 0.301	25.16	9.05	0.9557	1.9588
1	1	0	56.85	20.45	1.3107	1.9005
1.5	1.224	0.176	86.90	31.26	1.4950	1.8370
2	1.414	0.301	116.79	42.01	1.6234	1.7630
2.5	1.581	0.397	130.83	47.06	1.6727	1.7234
3	1.732	0.477	147.03	52.89	1.7234	1.6726
5	2.236	0.698	175.36	63.08	1.7999	1.5665
7	2.645	0.845	201.72	72.56	1.8607	1.4371
9	3	0.954	225.21	81.01	1.9085	1.2765
12	3.464	1.079	250.90	90.25	1.9554	0.9846

Table 6: Mathematical Model used to describe the drug release

Formulations	Zero order kinetics	First order kinetics	Higuchi model	Korsmeyer – Peppas model		Type of Transport
	Regression co-efficient (R^2)				n	
F1 in Acidic Buffer	0.249	0.535	0.501	0.677	0.3306	Fickian diffusion
F2 in Acidic Buffer	0.249	0.472	0.516	0.525	0.1508	Fickian diffusion
F1 in Phosphate Buffer	0.826	0.952	0.928	0.973	3.9459	Super case II transport
F2 in Phosphate Buffer	0.876	0.988	0.960	0.920	-0.1856	Fickian diffusion

Table 7: Comparison of dissolution Profiles of both formulations in acidic buffer

Obs	Time (h)	% released R of F1	% released T of F2	R-T	$(R-T)^2$
1	0.5	64.44	50.56	0.66	0.4356
2	1	82.46	85.12	-2.66	7.0756
3	1.5	85.66	89.17	-3.51	12.3201
4	2	90.17	91.12	-0.95	0.9025
5	2.5	92.84	93.16	-0.32	0.1024
6	3	93.12	93.82	-0.70	0.49
7	5	93.75	94.25	-0.50	0.25
8	7	93.82	94.74	-0.92	0.8464
9	9	94.10	94.82	-0.72	0.5184
10	12	94.71	95.25	-0.540	0.2916
		$\sum R = 885.07$		$\sum(R-T) = -10.16$	$\sum(R-T)^2 = 23.2326$
f1 (Disimilarity factor) = 1.15 f2 (Similarity factor) = 88.30					

The release kinetics of both the formulations in acidic and phosphate buffers have been indicated in Tables 2, 3, and 4, 5, respectively. The highest values of regression coefficient suggested that both formulations, in the acidic buffer, followed Korsmeyer Peppas model release kinetics. The values of regression coefficient were found to be 0.667 and 0.525 for F1

and F2, respectively. Moreover, the n values for Korsmeyer Peppas model were 0.3306 and 0.1508 for F1 and F2, respectively, indicating Fickian release (Tables 2, 3, 6 and Figs. 3-10). The release patterns of both the formulations in acidic buffer were compared according to the dissimilarity factor (f1) and the similarity factor (f2). The value f1 (1.15) was less than 15 and f2 (88.30) was more than 50, ensured the release profile of the formulation containing C934 (F1) was similar to the formulation containing C940 (F2) (Table 7).

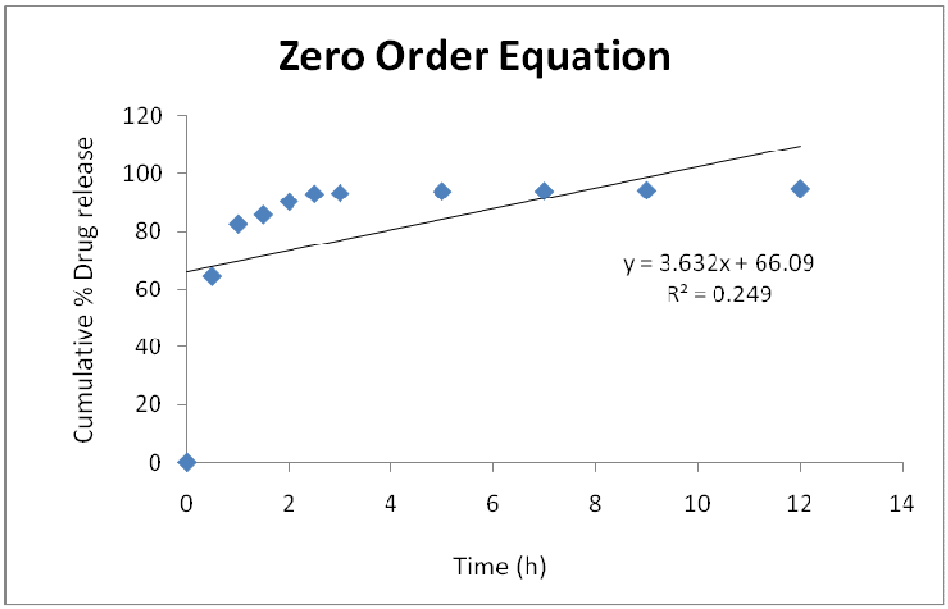

Fig. 3: Zero Order Release Kinetics of Formulation F1 in acidic buffer

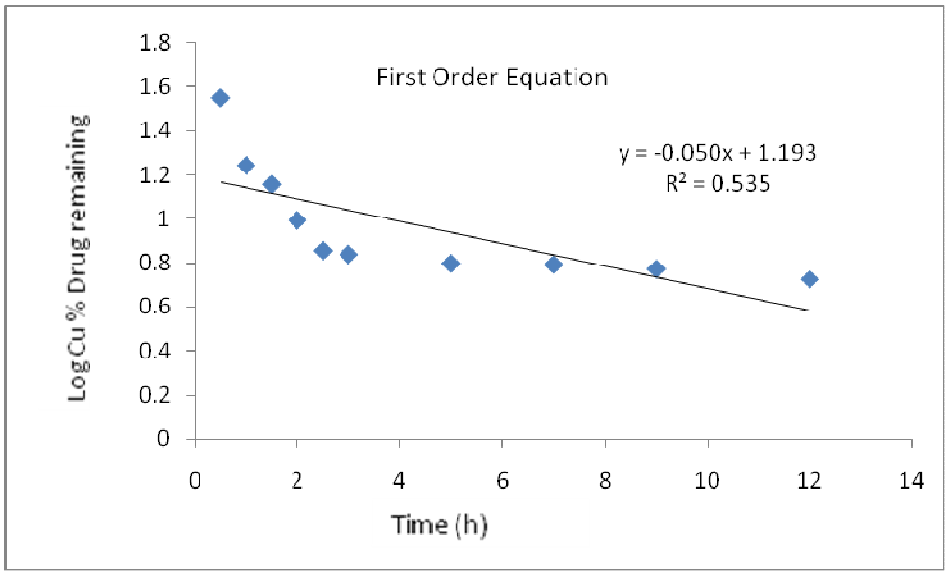

Fig. 4: First Order Release Kinetics of Formulation F1 in acidic buffer

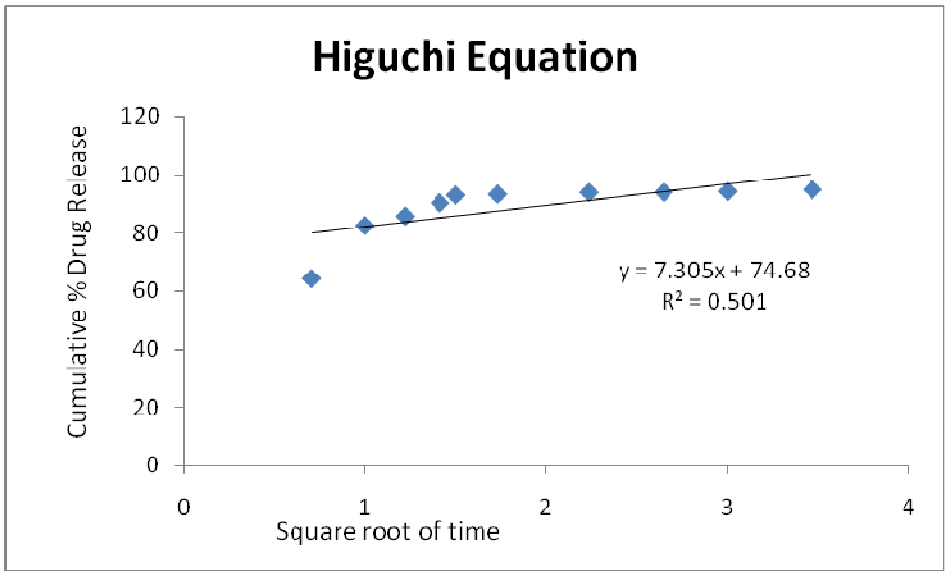

Fig. 5: Higuchi Model Release Kinetics of Formulation F1 in acidic buffer

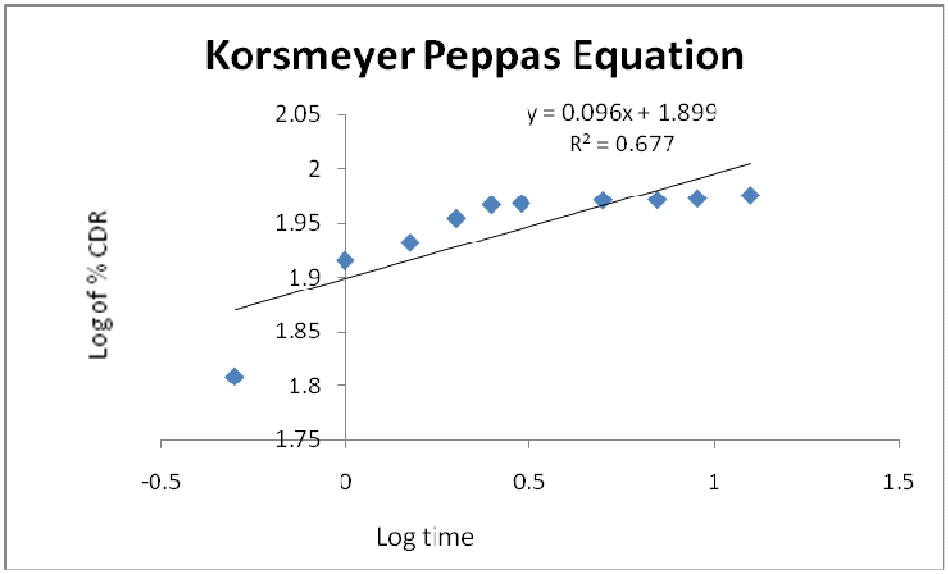

Fig. 6: Korsmeyer Peppas Model Release Kinetics of Formulation F1 in acidic buffer

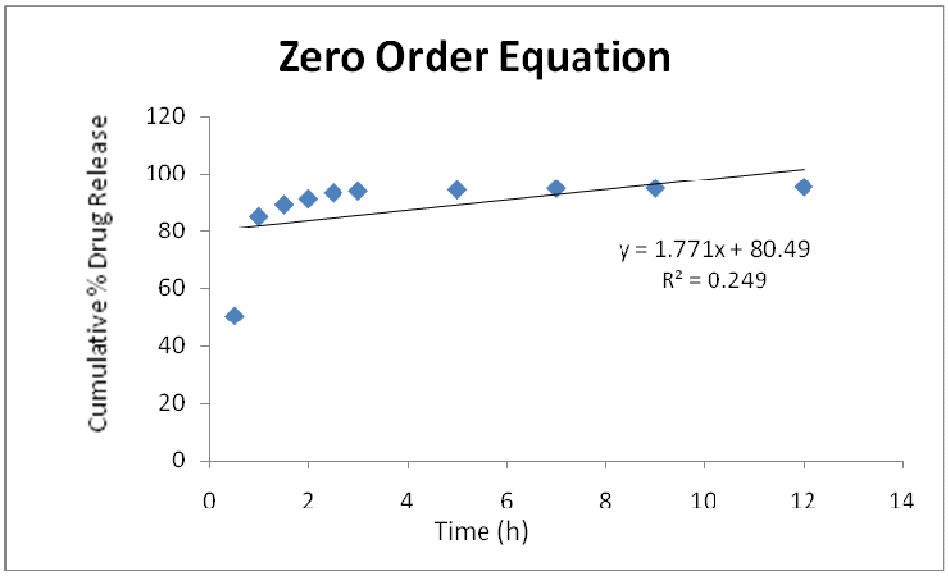

Fig. 7: Zero Order Release Kinetics of Formulation F2 in acidic buffer

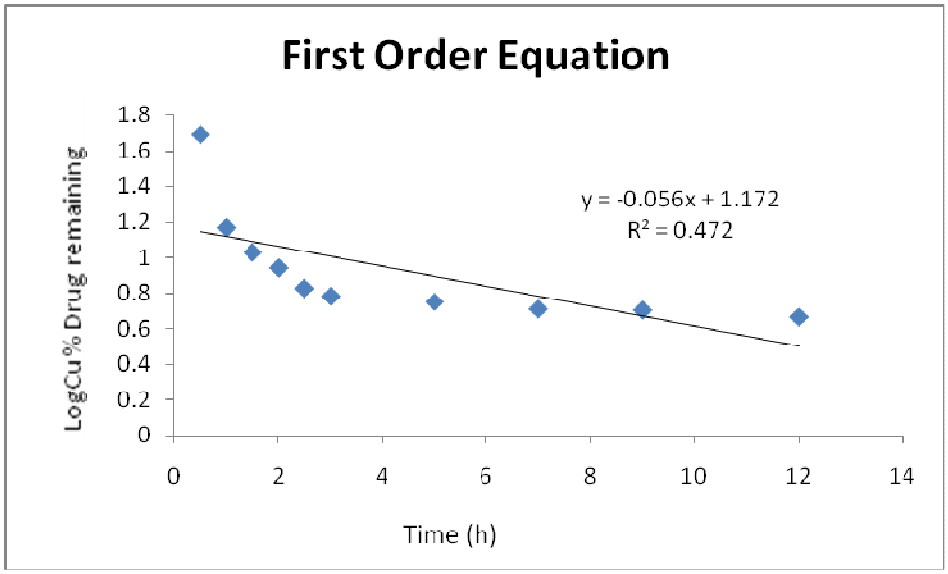

Fig. 8: First Order Release Kinetics of Formulation F2 in acidic buffer

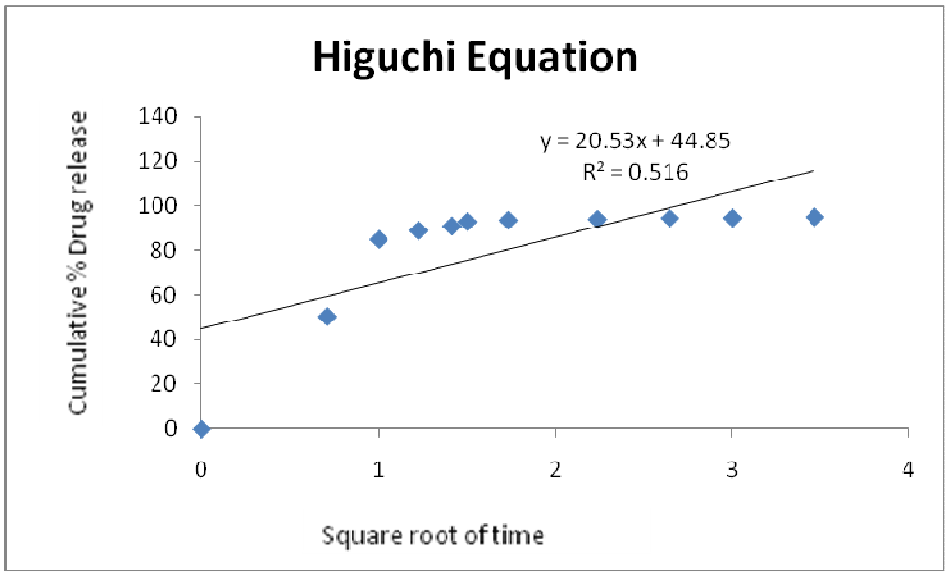

Fig. 9: Higuchi Model Release Kinetics of Formulation F2 in acidic buffer

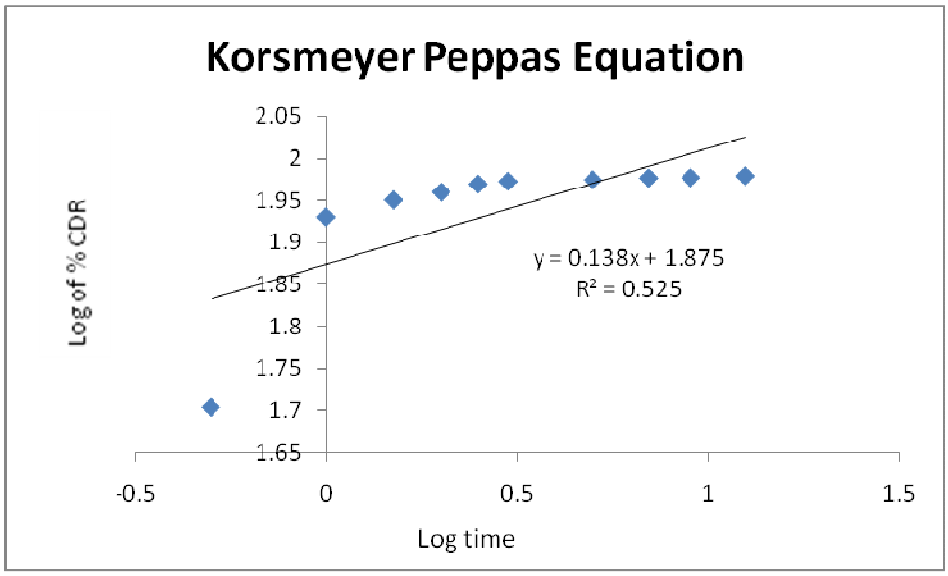

Fig. 10: Korsmeyer Peppas Model Release Kinetics of Formulation F2 in acidic buffer

In the first and second hour, the drug release was found to be 48.82% and 20.45%, respectively, from formulation F1 and 58.48% and 42.01%, respectively, from formulation F2 when phosphate buffer of pH 7.2 was used (Table 1 and Fig. 2). The release kinetics of both the formulations has been indicated in Tables 4 and 5. The highest values of regression coefficient suggested that formulation F1 followed Korsmeyer Peppas model release kinetics whereas F2 showed first order release kinetics. The values of regression coefficient were found to be 0.973 and 0.988 for F1 and F2, respectively. Moreover, the n values for Korsmeyer Peppas model were 3.9459 and -0.1856 for F1 and F2, respectively, indicating swelling-controlled super case II transport, and Fickian release, respectively (Table 6 and Figs. 11-18) [21]. The release patterns of both the formulations in phosphate buffer were compared according to the dissimilarity factor (f1) and the similarity factor (f2). The value f1 (33.56) was more than 15, while f2 (27.85) value was less than 50, ensured that the release profile of the formulation containing C934 (F1) was different from that of formulation containing C940 (F2) (Table 8).

Table 8: Comparison of dissolution Profiles of both formulations in phosphate buffer

Obs	Time (h)	% released R of F1	% released T of F2	R-T	$(R-T)^2$
1	0.5	60.80	40.16	20.64	426.01
2	1	90.34	46.93	43.41	1884.4281
3	1.5	90.40	53.85	36.55	1335.9025
4	2	90.59	56.14	34.45	1186.8025
5	2.5	90.71	57.26	33.45	1118.9025
6	3	90.85	60.20	30.65	939.4225
7	5	91.20	64.90	26.3	691.69
8	7	91.30	66.90	24.4	595.36
9	9	91.40	68.00	23.4	547.56
10	12	91.58	69.80	21.78	474.3684
		$\sum R$ = 879.17		$\sum(R-T)$ = 295.03	$\sum(R-T)^2$ = 9200.4465
f1 (Disimilarity factor) = 33.56 f2 (Similarity factor) = 27.85					

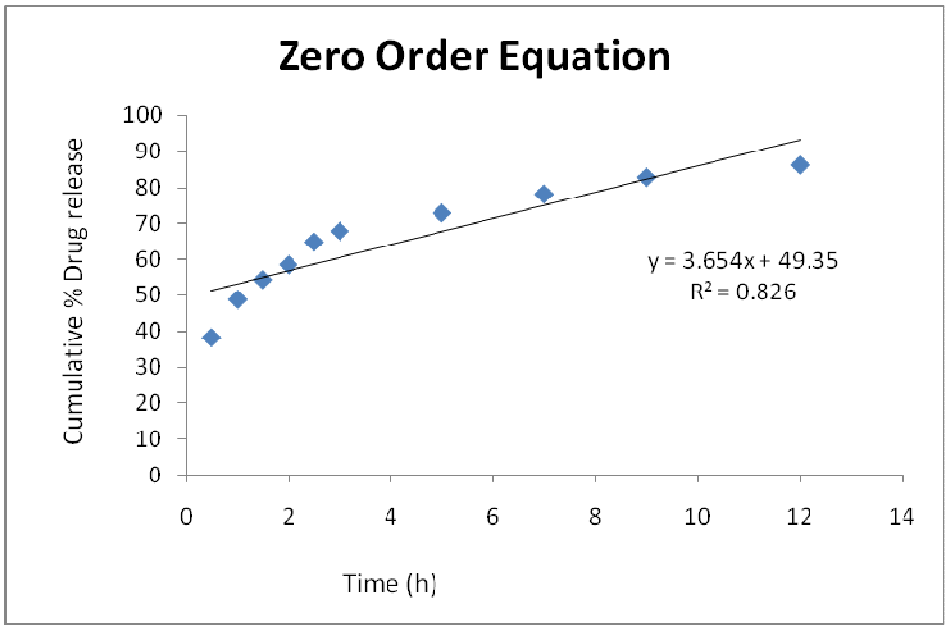

Fig. 11: Zero Order Kinetics of Formulation F1 in phosphate buffer

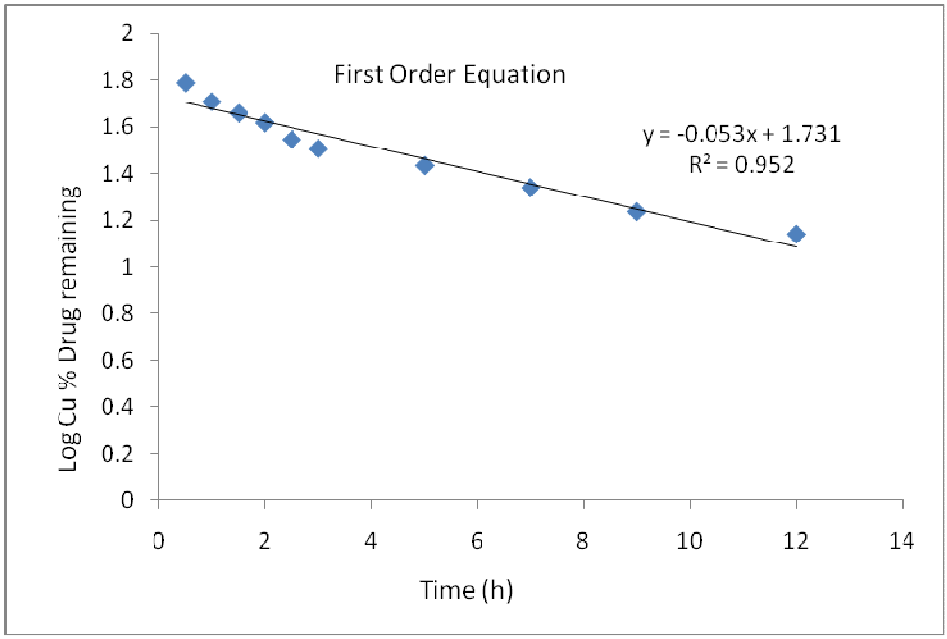

Fig. 12: First Order Kinetics of Formulation F1 in phosphate buffer

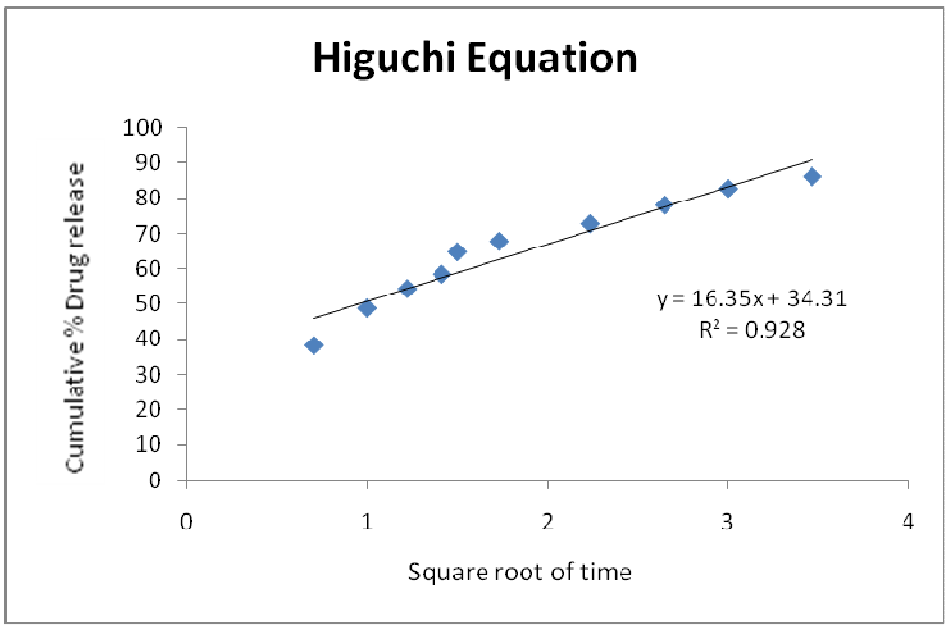

Fig. 13: Higuchi Model Release Kinetics of Formulation F1 in phosphate buffer

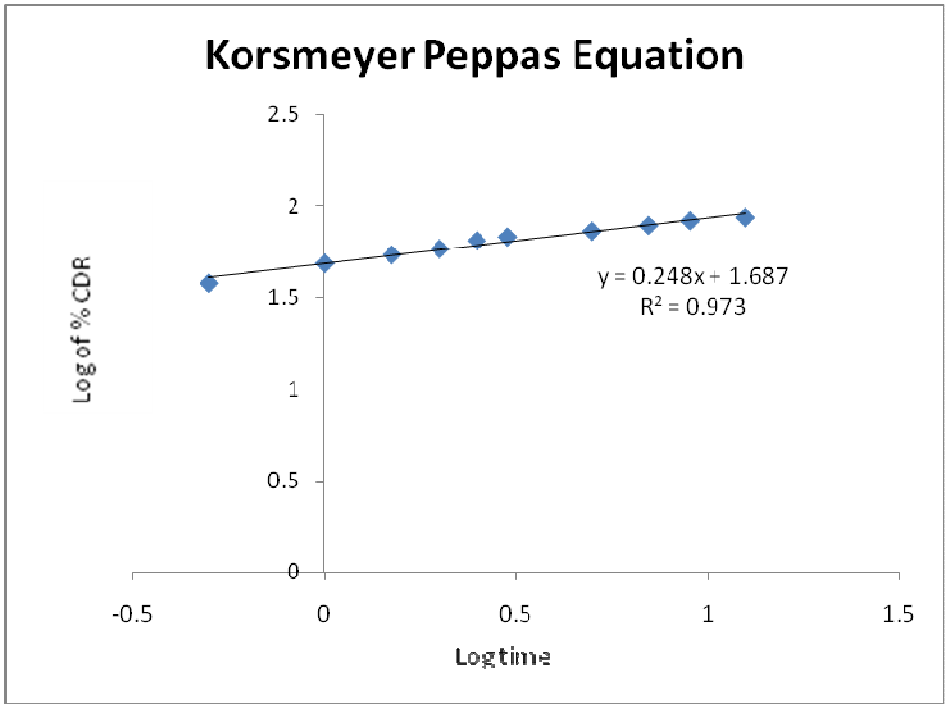

Fig. 14: Korsmeyer Peppas Model Release Kinetics of Formulation F1 in phosphate buffer

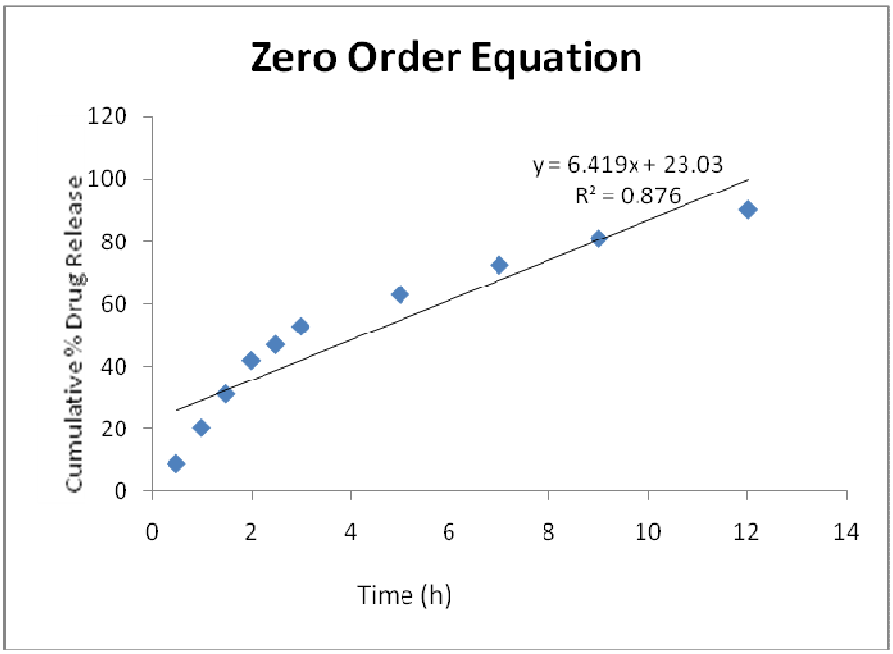

Fig. 15: Zero Order Release Kinetics of Formulation F2 in phosphate buffer

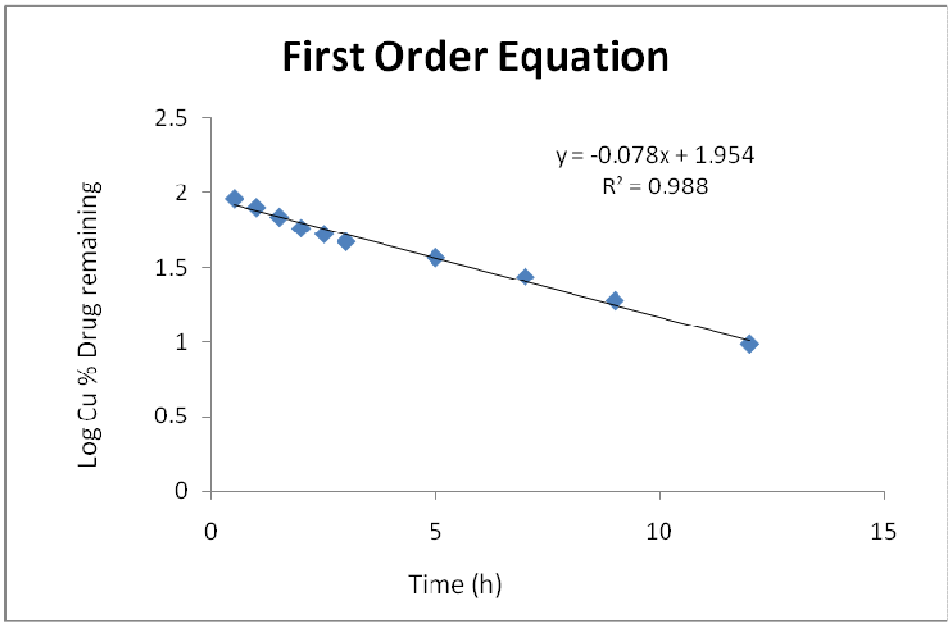

Fig. 16: First Order Release Kinetics of Formulation F2 in phosphate buffer

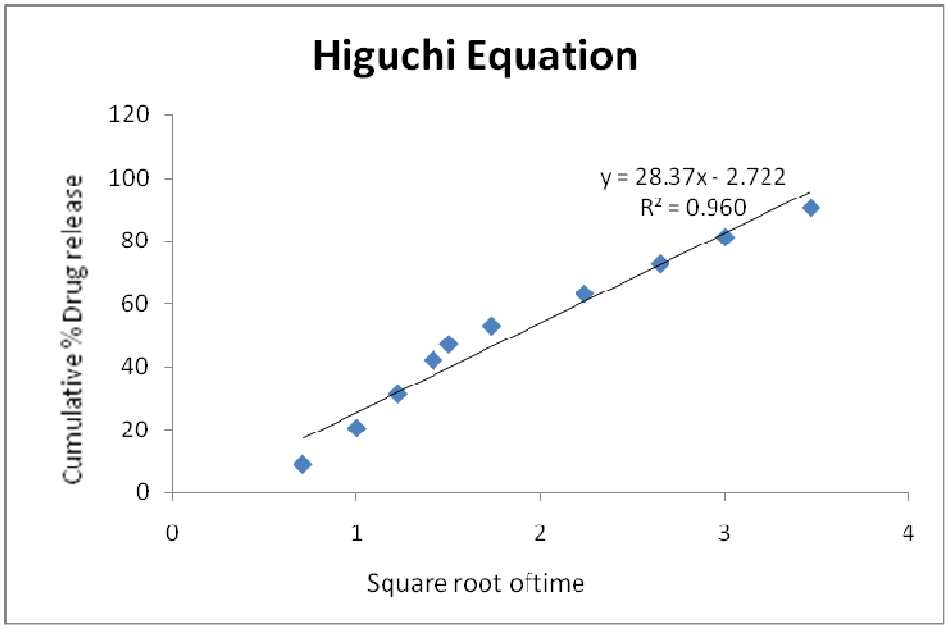

Fig. 17: Higuchi Model Release Kinetics of Formulation F2 in phosphate buffer

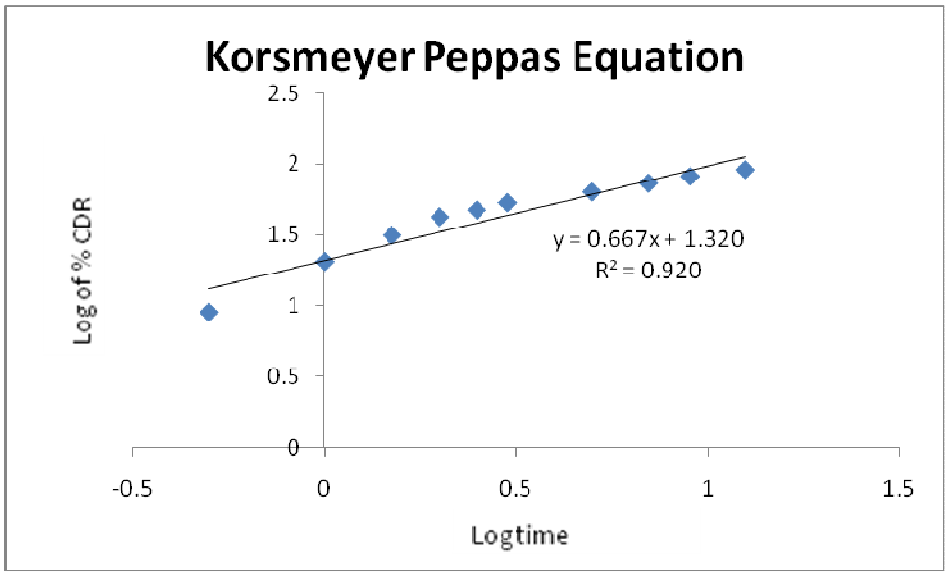

Fig. 18: Korsmeyer Peppas Model Release Kinetics of Formulation F2 in phosphate buffer

DISCUSSION

From the study it was found that both F1 and F2 in acidic buffer showed faster dissolution rate than that of phosphate buffer. Since Carbopol polymers have a pKa of 6, at pH 1.2 they are virtually un-ionised and they will start to ionize at pH 4.5. At lower pH values the polymer is not fully swollen, and there are larger regions of microviscosity. The solvent can penetrate first and deep into the glassy core and the drug is released faster before complete swelling. As the pH increases, the ionization of carboxylic acid groups causes maximum swelling, resulting in fewer and smaller regions of microviscosity. The rapid gel formation acts as a barrier for the release of drug prolonging the release. The release tends to be more diffusion controlled at lower pH region (stomach), while at higher pH (intestine), the drug release mechanism is more polymer relaxation controlled. This is due to reduction in regions of low microviscosity and the closing of micropores in the swollen polymers at higher pH [14].

As has been mentioned earlier, the highest values of regression coefficient indicated that both formulations in acidic buffer followed Korsmeyer Peppas model release kinetics. Moreover, it was found that the drug release from both the formulations in that buffer showed Fickian diffusional release. Such release occurs by the usual molecular diffusion of the drug due to a chemical potential gradient indicating diffusional controlled drug release.

On the other hand, the highest values of regression coefficient indicated that formulation F1 in the phosphate buffer followed Korsmeyer Peppas model release kinetics, while F2 showed first order release kinetics. Considering the n values for the Peppas model, swelling-controlled super case II transport was found in case of F1, suggesting swelling and relaxation of the polymers whereas Fickian release was possible in F2, indicating polymer relaxation followed by diffusion of the drug. This may lead to reduction in frequency of dosing and minimize the blood level oscillations, dose related adverse effects, cost, ultimately improve the patient compliance and drug efficiency.

In the case of highly crosslinked Carbopol polymers (such as Carbopol 934), the release is faster as the drug diffuses out through the water-filled interstitial spaces between the microgels. In comparison, Carbopol 940 polymer is lightly crosslinked, thus the microgels form a more uniform and continuous structure resulting in a slower drug release (Table 1**)**. The possible explanation for such a release characteristics of C940 is probably due to high concentration of Carbopol upon exposure to moist surfaces and the pH of the microenvironment becomes acidic which causes an increase in mucoadhesion. Moreover, Carbopol forms secondary bioadhesion bonds with mucin and interpenetration of polymer chains occur in the interstitial region. The increase in viscosity of swollen polymer contributes more hindrance to drug diffusion and consequent reduction in the release rate. As

the carboxyl groups of Carbopol dissociate highly at pH above their pKa, electrostatic repulsions between the negatively charged carboxyl groups cause uncoiling and expansion of the molecules, resulting in swelling and consequent gel formation.

Earlier it has been mentioned that the release from Carbopol polymer gel is generally slower for drugs with low water solubility. Drugs exhibiting poor solubility tend to partition into the more hydrophobic domains of the system (such as the acrylic backbone of the Carbopol polymer) from where they would be released in a linear or almost linear fashion.

From our result it is clear that release profile of the formulation containing C934 was similar to the formulation containing C940 in the acidic buffer. On the other hand, the release profile of the formulation containing C934 was different from that of formulation containing C940 in the phosphate buffer. Since the degree of gel formation and characteristics of gel depends on the change in pH and respective crosslinkers present in both the polymers, the release pattern of both the polymers differs in phosphate buffer (at higher pH). However, in case of acidic buffer (at lower pH), no gellation occurs and the release is only controlled by molecular diffusion indicating a similarity in the release pattern.

CONCLUSION

The controlled release drug delivery systems developed as Ciprofloxacin mucoadhesive formulations offered gel forming matrix for poorly soluble drug, served as a depot in GIT for controlled drug release and provided a rate limiting gel forming barrier for modulation of drug release. From the results obtained in this work, it can be concluded that a significant variation exists in the *In vitro* release pattern of Ciprofloxacin from the tested formulations in relation to change in pH and polymer grades. In addition, the formulation containing C934 (in both the buffers) showed slower release profile with respect to time than the formulation containing C940. Further investigation using *ex vivo* models are being carried out to substantiate the *In vitro* results.

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