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Original Research Article

Drug Release Kinetics of Gastroretentive Rantidine Hydrochloride (RHCL)

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Abstract

Synthetic polymer shows various disadvantages like higher in cost, non-biocompatible and toxicity. The design of effective and safe new natural polymer used as a matrix in drug delivery systems has become an integral part for the development and formulation of new medicines. So, research continuously keeps on searching for new ways to deliver drugs for a well-controlled release profile, to minimizing the loss of drug and to reduce the side effect. Therefore, the present study was conducted to determine drug release kinetics of gastrotentive Rantidine hydrochloride by using a natural polymer sodium alginate matrix which is in low cost, simplicity, and biocompatibility and easily biodegradability. A new emulsion gelation technique was used to prepare emulsion gel beads using sodium alginate and xanthan as the polymer. The gel beads containing oil was prepared gently by mixing oil and water phase containing sodium alginate which was then extruded into calcium chloride solution. Drug release kinetic profile was studied by different model like Zero order, First order, Higuchi equations, Korsmeyer–Peppas and Hixson-Crowell model. Among all 9 formulations, F4 containing drug and polymer at a drug-polymer ratio of 1:1 released the highest percentage of Ranitidine Hydrochloride at 12 hrs with 99.70%. The release exponent *n* of all the formulations are between 0.840~0.988. F2, F5 and F8 have n value of 0.873, 0.840 and 0.866 respectively. The diffusion exponent of F2, F5 and F8 meet $0.45 < n < 0.89$. F1~F8 were best fitted into first order kinetic model while F9 was into Higuchi matrix model. The cumulative percentage drug release significantly decreased with the increase in polymer concentration. The overall curve fitting into various mathematical models was found to be on first order release kinetics.

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Introduction

Despite tremendous advancement in drug delivery, oral route remains the preferred route for the administration of therapeutic agents and oral drug delivery is the most preferable route of drug delivery because of low cost of

therapy and ease of administration leads to high levels of patient compliance (Singh and Kim, 2000; Chawla et al., 2003).

The gastrointestinal physiology offers more flexibility in dosage form design than most other routes. Historically, the most convenient route for drug delivery has been considered as oral ingestion (Vyas and Khar, 2002). An oral controlled release formulation is an attempt to release the drug slowly into the gastro-intestinal tract and retain a constant drug concentration in the serum for longer period of time (Manjanna et al., 2009). The de novo design of an oral controlled drug delivery system (DDS) is primarily aimed at achieving more predictable and increased bioavailability of drugs (Chawla et al., 2003).

Rapid gastrointestinal transit can result in incomplete drug release from a device above the absorption zone, leading to diminished efficacy of the administered dose (Singh and Kim, 2000). Therefore, different approaches have been proposed to retain the dosage form in the stomach. These include bioadhesive systems, swelling and expanding systems and floating. Floating systems or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time (Mathur et al., 2010). While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration (Mayavanshi and Gajjar, 2008).

Ranitidine HCl (RHCl) is a histamine H_2-receptor antagonist with a furan ring structure that increases its potency to inhibit gastric acid secretion induced by various stimuli, while lacking the anti androgenic and hepatic microsomal enzyme inhibiting effects (Peden et al., 1979). It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis. The short biological half-life of the drug (~2.5-3 hours) also favors development of a sustained release formulation. It undergoes protonation in aqueous solutions with generation of different ionic forms depending on the pH of the solution (Singh and Kim, 2000). A traditional oral sustained-release formulation releases most of the drug at the colon; thus, the drug should have an absorption window either in the colon or throughout the gastrointestinal tract. Ranitidine is absorbed in only the initial part of the small intestine and has 50% absolute bioavailability (Lauritsen, 1990; Grant, 1989). Moreover, colonic metabolism of ranitidine is partly responsible for the poor bioavailability of ranitidine from the colon (Basit and Lacey, 2001).

Formulation of RHCl as a sustained release dosage form can also minimize the loss of drug in comparison of conventional tablets. Out of the available category of drugs for the treatment of ulcer, H_2 antagonists class of drugs like Famotidine, Ranitidine are considered to be the safest drugs available and hence this drug has promising future if controlled release formulations are made (Goel and Shah, 2008).

Due to its pharmaceutical importance and a common use, several methods have been proposed for Ranitidine HCl determination in bulk, pharmaceuticals and in clinical samples. Therefore, the present study was focused to design the formulating floating beads of Ranitidine HCl using combination of polymers sodium alginate and xanthan gum to determine drug release kinetics.

Materials and methods

Study design

The experimental research based study was conducted in 2014 AD at the Department of Pharmacy, State University of Bangladesh, Dhaka. The gift sample of RHCL was obtained from Incepta Pharmaceuticals Ltd., Dhaka, Bangladesh.

Study sample

Nine batches of the light liquid paraffin entrapped emulsion gel beads were prepared by a new emulsion gelation technique using sodium alginate and xanthan gum as polymers.

Sample selection and processing

Altogether 10 dried beads were randomly selected from each batch for the present study.

Preparation of RHCl beads

Dispensing
API and all other ingredients were weighed properly.
↓
Preparation of polymeric solution
Polymers were dissolved gradually in required amount of distilled water with vigorous stirring.
↓
Addition of drug and oil
Ranitidine hydrochloride and Light Liquid Paraffin were added into the polymeric solution.
↓
Homogenization of the mixture
The mixture of Drug, Polymers and Oil were homogenized for 15 minutes at 1000 rpm.
↓
Extrusion
The mixture was extruded through 21G specially modified needles into 5% $CaCl_2$ solution from 5cm distance at a rate of 2ml/min.
↓
Filtration and Separation
The formed beads were separated from solution by filtration through mesh 100 and washed using distilled water.
↓
Drying
Formed beads were dried at 40-45ºC until constant weight was achieved.

Flowcart 1. Preparation of RHCl beads.

200 mg RHCL was loaded with sodium alginate beads from each formulation
↓
Placed in vessel of USP Type II dissolution apparatus containing 900 ml of 0.1 N HCl (pH 1.2)
↓
Maintained at 37±0.5ºC and stirred at 50 rpm
↓
10 ml of samples were collected at interval of 60 minutes
↓
Replaced with a fresh dissolution solution i.e. 0.1N HCl
↓
Samples were filtered with filter paper
↓
Analyzed with help of UV spectrophotometer at 313.5nm

Flowchart 2. Determination of drug release.

Drug release study

Only those batches were selected for drug release study, which have good drug content and drug entrapment efficiency more than 50%.

Drug release kinetics study

Study of drug release kinetics of Ranitidine HCl emulsion gel beads was done by using linear regression analysis. Zero order, first order, Higuchi equations, Korsmeyer–Peppas model and Hixson-Crowell model were fitted to dissolution data of optimized batch.

Zero-order model

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$$Q_0 - Q_t = k_0 t$$

Rearrangement of above equation yields:

$$Qt = Q0 + k0t$$

Where, Q_t = amount of drug dissolved in time *t*, Q_0 = initial amount of drug in the solution and k_0 = zero order release constant expressed in unit of concentration/time.

First order model

The release of the drug which followed first order kinetics can be expressed by the equation:

$$\frac{dd}{dd} = -kk$$

Where, *K* = first order rate constant expressed in units of time^{-1}.

The equation can be expressed as:

$$\log C = \log C_0 - kt / 2.303$$

Higuchi matrix model

To study Higuchi release model the release data were fitted to following equation:

$$Q_t = Q_0 - k_H t^{1/2}$$

Where, Q_t = amount of drug dissolved in time *t*, Q_0 = initial amount of drug in the solution and k_H = Higuchi release constant.

Korsmeyer-Peppas model

To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer Peppas model.

$$M_t / M_\infty = kt^n$$

Where, M_t/M_∞ = fraction of drug released at time t, k = release rate constant, n = release exponent.

The n value was used to characterize different release for cylindrical shaped matrices and mechanism of drug as described in Table 1.

Table 1. Diffusion exponent and drug transport mechanism for cylindrical shape.

Diffusion exponent (n)	Drug transport mechanism	Rate as a function of time
0.45	Fickian diffusion	$t^{-0.5}$
0.45 < n < 0.89	Non-fickian diffusion	t^{n-1}
0.89	Case-II transport	Zero order release
n > 0.89	Super case-II transport	t^{n-1}

To find out the exponent of *n* the portion of the release curve, where, M_t/M_∞ <0.6 should only be used.

Hixson-Crowell cube root model

To find out the mechanism of drug release, first 60% drug release data were fitted in the following equation:

$$W_0^{1/3} - W_t^{1/3} = \kappa t$$

Where, W_0 = initial amount of drug in the pharmaceutical dosage form, Wt = remaining amount of drug in the pharmaceutical dosage form at time t, κ (kappa) = constant incorporating the surface volume relation.

Data analysis

Data obtained from in vitro drug release studies were plotted as cumulative amount of drug released vs. time for zero-order, log cumulative percentage of drug remaining vs. time for first order, cumulative percentage drug release vs. square root of time for Higuchi matrix, log cumulative percentage drug release vs. log time for Korsmeyer-Peppas, cube root of drug percentage remaining in matrix vs. time for Hixson-Crowell cube root model.

Results and discussion

It is evident from the recent scientific and patent literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged

and predictable period of time exists today in academic and industrial research groups. One of the most feasible approaches for achieving a prolonged and predictable drug delivery profile in the GI tract is to control the gastric residence time (Vyas and Khar, 2002; Babu, 1995). These considerations have led to the development of oral controlled release (CR) dosage forms possessing gastric retention capabilities.

The design of gastroretentive drug delivery system depends upon physicochemical properties, dose and purpose of controlling the drug release, constraining gastrointestinal factors (Crèmer, 1997).

Various approaches have been pursued including low density dosage form that remains buoyant above gastric fluid or high density dosage form that is retained at the bottom of the stomach, imparting bioadhesion to the stomach mucosa, utilizing ion-exchange resin which adheres to mucosa, expanding the dosage form by swelling or unfolding to a large size which limits emptying of dosage form through pyloric sphincter, using modified shape system, or other effervescent systems using a gas generating material like sodium bicarbonate and calcium carbonate or the same with citric acid (Jimenez et al., 1993; Caldwell et al., 1998; Yang et al., 1999).

Ranitidine competes with histamine for binding at H2 receptors on gastric parietal cells which results in reduced basal and nocturnal gastric acid secretion. It also decreases the amount of gastric acid released in response to stimuli such as food, caffeine, insulin, betazole, or pentagastrin and an increase in gastric bacterial flora such as nitrate-reducing organisms (Korteja et al., 2005).

The present study highlights that formulations F1, F2 and F3 containing drug and polymer at a drug-polymer ratio of 1:0.99, 1:1.09, 1:1.19 released 98.86%, 94.97% and 92.29% of RHCL in 10, 12 and 12 hrs respectively. Formulations F4, F5 and F6 containing drug and polymer at a drug-polymer ratio of 1:1, 1:1.1 and 1:12 released 99.70%, 92.99% and 88.25% of RHCL at 12 hrs. Formulations F7, F8 and F9 containing drug and polymer at a drug-polymer ratio of 1:1.01, 1:1.11 and 1:1.21 released 95.45%, 93.70%, and 85.78 of RHCL in 11, 12 and12 hrs respectively. The drug release profiles of formulation F1-F9 at different time interval are shown in Tables 2-10.

Table 2. Drug release profile of formulation F1 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0.000	0.00	0.000	2.000	4.642
1	0.000	1.000	28.30	1.452	1.856	4.642
2	0.301	1.414	54.58	1.737	1.657	3.568
3	0.477	1.732	74.01	1.869	1.415	2.962
4	0.602	2.000	84.60	1.927	1.187	2.488
5	0.699	2.236	89.18	1.950	1.034	2.212
6	0.778	2.449	91.23	1.960	0.943	2.062
7	0.845	2.646	93.64	1.971	0.804	1.853
8	0.903	2.828	94.97	1.978	0.702	1.714
9	0.954	3.000	97.28	1.988	0.435	1.396
10	1.000	3.162	98.86	1.995	0.058	1.045
11	1.041	3.317	100.50	2.002	-	-0.794
12	1.079	3.464	101.29	2.006	-	-1.09

Table 3. Drug release profile of formulation F2 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0.000	0.00	0.000	2.000	4.642
1	0.000	1.000	26.36	1.421	1.867	4.192
2	0.301	1.414	48.28	1.684	1.714	3.726
3	0.477	1.732	65.52	1.816	1.538	3.255
4	0.602	2.000	76.08	1.881	1.379	2.881
5	0.699	2.236	80.28	1.905	1.295	2.702
6	0.778	2.449	83.25	1.920	1.224	2.559
7	0.845	2.646	85.47	1.932	1.162	2.440
8	0.903	2.828	86.04	1.935	1.145	2.408
9	0.954	3.000	89.98	1.954	1.001	2.156
10	1.000	3.162	91.91	1.963	0.908	2.008
11	1.041	3.317	93.30	1.970	0.826	1.885
12	1.079	3.464	94.97	1.9776	0.702	1.714

Table 4. Drug release profile of formulation F3 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0.00	0.000	2.000	4.642
1	0.000	1.000	20.39	1.309	1.908	4.325
2	0.301	1.414	44.29	1.646	1.767	3.881
3	0.477	1.732	61.59	1.790	1.626	3.483
4	0.602	2.000	70.62	1.849	1.529	3.233
5	0.699	2.236	76.97	1.886	1.444	3.030
6	0.778	2.449	81.68	1.912	1.369	2.861
7	0.845	2.646	83.88	1.924	1.329	2.774
8	0.903	2.828	85.04	1.930	1.306	2.726
9	0.954	3.000	87.43	1.942	1.256	2.621
10	1.000	3.162	89.61	1.952	1.203	2.518
11	1.041	3.317	90.92	1.959	1.168	2.452
12	1.079	3.464	92.29	1.9652	1.129	2.378

Table 5. Drug release profile of formulation F4 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0.00	0.000	2.000	4.642
1	0.000	1.000	26.10	1.417	1.869	4.197
2	0.301	1.414	50.38	1.702	1.696	3.675
3	0.477	1.732	71.18	1.852	1.460	3.066
4	0.602	2.000	83.09	1.920	1.228	2.567
5	0.699	2.236	86.85	1.939	1.119	2.360
6	0.778	2.449	89.80	1.953	1.009	2.169
7	0.845	2.646	92.55	1.966	0.872	1.953
8	0.903	2.828	94.20	1.974	0.763	1.797
9	0.954	3.000	96.42	1.984	0.554	1.530
10	1.000	3.162	97.64	1.990	0.373	1.331
11	1.041	3.317	98.70	1.994	0.114	1.091
12	1.079	3.464	99.70	1.999	-0.528	0.667

Table 6. Drug release profile of formulation F5 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0.00	0.000	2.000	4.642
1	0.000	1.000	19.84	1.298	1.904	4.312
2	0.301	1.414	45.27	1.656	1.738	3.797
3	0.477	1.732	63.76	1.805	1.559	3.309
4	0.602	2.000	72.65	1.861	1.437	3.013
5	0.699	2.236	77.89	1.891	1.345	2.807
6	0.778	2.449	80.49	1.906	1.290	2.692
7	0.845	2.646	82.64	1.917	1.240	2.589
8	0.903	2.828	85.98	1.934	1.147	2.411
9	0.954	3.000	88.54	1.947	1.059	2.255
10	1.000	3.162	90.69	1.958	0.969	2.104
11	1.041	3.317	91.79	1.963	0.915	2.018
12	1.079	3.464	92.99	1.968	0.846	1.914

Table 7. Drug release profile of formulation F6 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0.00	0.000	2.000	4.642
1	0.000	1.000	18.31	1.263	1.912	4.339
2	0.301	1.414	39.21	1.593	1.784	3.932
3	0.477	1.732	56.88	1.755	1.635	3.507
4	0.602	2.000	66.67	1.824	1.523	3.218
5	0.699	2.236	71.95	1.857	1.448	3.038
6	0.778	2.449	74.77	1.874	1.402	2.933
7	0.845	2.646	78.35	1.894	1.335	2.787
8	0.903	2.828	81.54	1.911	1.266	2.643
9	0.954	3.000	84.33	1.926	1.195	2.502
10	1.000	3.162	85.94	1.934	1.148	2.413
11	1.041	3.317	87.25	1.941	1.106	2.336
12	1.079	3.464	88.25	1.946	1.070	2.274

Table 8. Drug release profile of formulation F7 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0.00	0.000	2	4.642
1	0.000	1.000	24.13	1.383	1.880	4.233
2	0.301	1.414	49.85	1.698	1.700	3.688
3	0.477	1.732	70.93	1.851	1.463	3.075
4	0.602	2.000	82.23	1.915	1.250	2.609
5	0.699	2.236	85.50	1.932	1.161	2.438
6	0.778	2.449	87.44	1.942	1.099	2.324
7	0.845	2.646	89.40	1.951	1.026	2.197
8	0.903	2.828	91.36	1.961	0.937	2.052
9	0.954	3.000	93.50	1.971	0.813	1.866
10	1.000	3.162	94.98	1.978	0.701	1.712
11	1.041	3.317	95.45	1.980	0.658	1.657
12	1.079	3.464	100.32	2.001	-	-0.683

Table 9. Drug release profile of formulation F8 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0.00	0.000	2	4.642
1	0.000	1.000	19.74	1.295	1.905	4.314
2	0.301	1.414	43.95	1.643	1.749	3.827
3	0.477	1.732	60.80	1.784	1.593	3.397
4	0.602	2.000	72.91	1.863	1.433	3.003
5	0.699	2.236	75.61	1.879	1.387	2.900
6	0.778	2.449	77.54	1.890	1.351	2.821
7	0.845	2.646	81.86	1.913	1.259	2.627
8	0.903	2.828	90.36	1.956	0.984	2.128
9	0.954	3.000	91.94	1.964	0.906	2.005
10	1.000	3.162	92.59	1.967	0.870	1.950
11	1.041	3.317	93.06	1.969	0.841	1.907
12	1.079	3.464	93.70	1.972	0.800	1.847

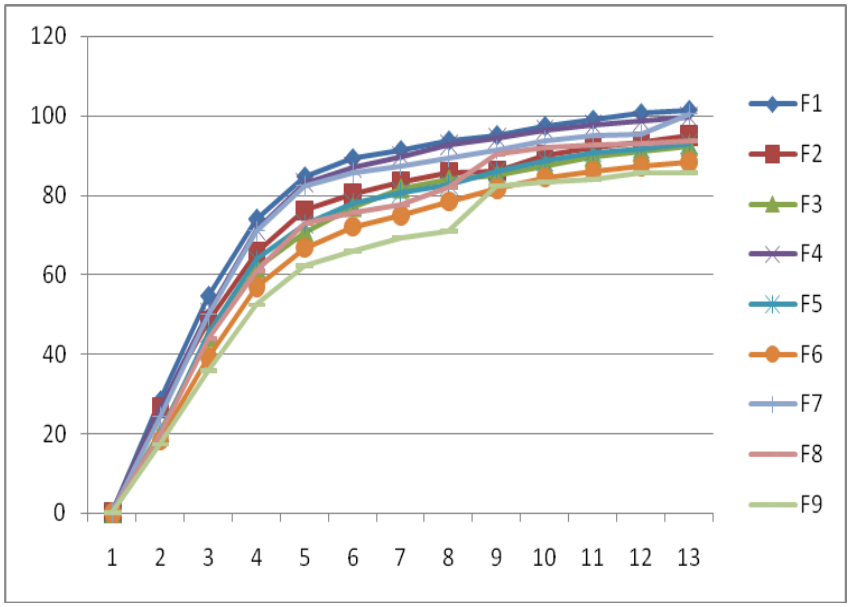
Table 10. Drug release profile of formulation F9 at different time interval.

Time (hr)	Log time (hr)	SQRT time (hr)	Cum. % rel.	Log Cum. % rel.	Log drug % rem.	Cube root % rem.
0	-	0	0	0.000	1.918	4.358
1	0.000	1.000	17.26	1.237	1.807	4.002
2	0.301	1.414	35.89	1.555	1.677	3.623
3	0.477	1.732	52.45	1.720	1.578	3.357
4	0.602	2.000	62.17	1.794	1.531	3.238
5	0.699	2.236	66.05	1.820	1.484	3.124
6	0.778	2.449	69.51	1.842	1.460	3.066
7	0.845	2.646	71.17	1.852	1.241	2.592
8	0.903	2.828	82.59	1.917	1.222	2.556
9	0.954	3.000	83.31	1.921	1.199	2.510
10	1.000	3.162	84.18	1.925	1.156	2.429
11	1.041	3.317	85.66	1.933	1.153	2.423
12	1.079	3.464	85.78	1.933	1.918	4.358

To analyze the mechanism of drug release and release rate kinetic from the RHCl loaded sodium alginate beads, the data obtained were fitted in Zero order, First order, Higuchi equations, Korsmeyer–Peppas model and Hixson-Crowell cube root model after linear transformation of dissolution curve.

Zero-order kinetics is often referred as pseudo-zero-order reactions which is always an artifact of the conditions under which the reaction is carried out. The rates of these zero-order reactions do not vary with increasing nor decreasing reactants concentrations which means that the rate of the reaction is equal to the rate constant i.e. kk, of that reaction and zero-order process cannot continue after a reactant has been exhausted. First order model had been used to describe absorption and/or elimination of some drugs, although it is difficult to conceptualize this mechanism on a theoretical basis (Tipnis and Bajaj, 2002).

Huguchi matrix model is based on the hypotheses that initial drug concentration in the matrix is much higher than drug solubility; drug diffusion takes place only in one dimension; drug particles are much smaller than system thickness; matrix swelling and dissolution are negligible; drug diffusivity is constant; and perfect sink conditions are always attained in the release environment. Korsmeyer–Peppas model describes simple relationship of drug release from a polymeric system equation. Hixson-Crowell cube root model recognized that the particle's regular area is proportional to the cube root of its volume (Dixit, 2011).



[Y-axis = cumulative % drug released & x-axis = time (hr)]

Fig. 1: Plots of cumulative % drug released vs. time (hour) for F1 – F9 of Ranitidine HCl emulsion gel beads [Zero order kinetics].

The present study revealed that the release of F1 and F7 upto 12 hrs was not extended because the amount of polymer was lowest in F1 but F7 deviated where it had higher polymer amount than F1 and F4. In all other formulations except F1, F7 and F8 drug release at 12 hrs according to zero order kinetics were directly proportional to their respective polymer concentration. The release characteristics of different formulations varied due to changes in the concentration of polymer. This means that the drugs were entrapped more complexly in the formulations due to higher viscosity where polymer concentration was more. The results are shown in Fig. 1.

This study represents the *in vitro* drug release of formulation F1-F8 was best fitted by first order release kinetics, as the plots showed the highest linearity and F9 showed highest linearity at Higuchi matrix equation plot (Figs. 2 and 3). The release kinetics constants and correlation-coefficients for Zero order, first order, Higuchi matrix, Korsmeyer-Peppas and Hixson-Crowell cube root model are shown in Table 11.

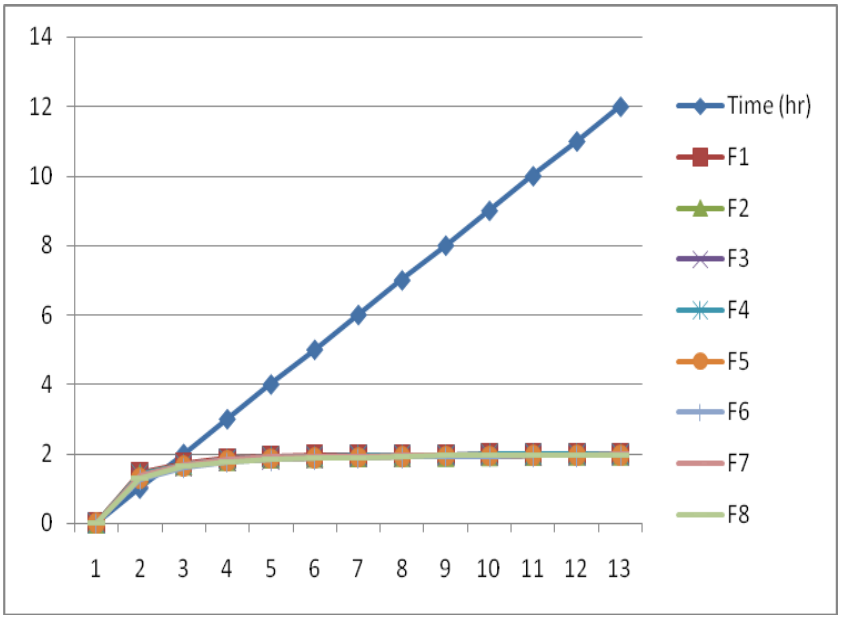


Fig. 2: Plots of log drug % remaining vs. time (hour) of F1- F8 of Ranitidine HCl emulsion gel beads [First order kinetics].

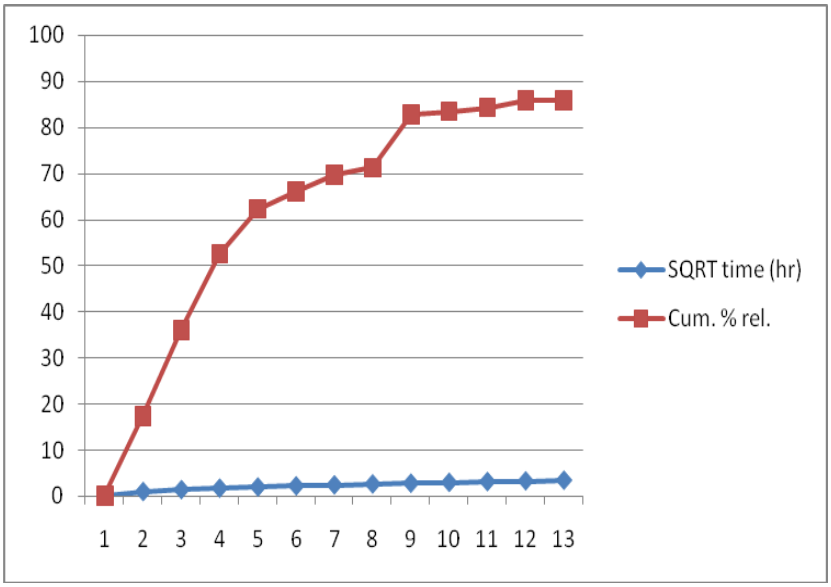


Fig. 3: Plots of cumulative drug % released vs. square root time (hour) for F9 of Ranitidine HCl emulsion gel beads [Higuchi matrix].

The present study revealed that the release exponent *n* of all the formulations are between 0.840~0.988. F2, F5 and F8 have n value of 0.873, 0.840 and 0.866 respectively. The diffusion exponent of F2, F5 and F8 meet 0.45 < n < 0.89 which means they released drug by non-fickian diffusion mechanism. Formulation F1, F3, F4, F6, F7 and F9 had diffusion exponent n value n > 0.89 which means they followed super case-II transport mechanism to release drugs from beads. Barhate et al. (2009) reported in vitro dissolution study of factorial batches of RHCL showed zero-order drug release. Battu et al. (2010) reported that the co-relation coefficient value (r) indicates the kinetic of drug release was zero order and the mechanism of drug release was found to be super case II transport which is in accordance with this study.

Table 11. Model fitting release profile of Ranitidine hydrochloride emulsion gel beads.

Formulation	0 order		1st order		Higuchi matrix		Korsmeyer-Peppas			Hixson-Crowell		Best fitted
	k_0	r^2	k_1	r^2	k_H	r^2	*n*	k_{KP}	r^2	k_{HC}	r^2	
F1	0.165	0.714	0.333	0.982	28.295	0.906	0.947	0.283	0.869	0.055	0.947	**1st order**
F2	0.159	0.740	0.306	0.972	26.361	0.923	0.873	0.264	0.898	0.053	0.917	**1st order**
F3	0.123	0.771	0.212	0.935	20.387	0.933	0.893	0.191	0.887	0.041	0.887	**1st order**
F4	0.156	0.727	0.302	0.959	26.096	0.911	0.948	0.261	0.865	0.052	0.955	**1st order**
F5	0.124	0.766	0.221	0.971	19.839	0.929	0.840	0.198	0.864	0.041	0.917	**1st order**
F6	0.117	0.798	0.202	0.962	18.313	0.945	0.967	0.183	0.894	0.039	0.918	**1st order**
F7	0.142	0.724	0.275	0.961	24.072	0.907	0.955	0.241	0.862	0.047	0.897	**1st order**
F8	0.124	0.797	0.220	0.970	19.735	0.944	0.866	0.197	0.887	0.041	0.935	**1st order**
F9	0.113	0.837	0.189	0.960	17.256	0.961	0.988	0.172	0.916	0.038	0.932	**Higuchi**

Kumar et al. (2011) reported drug release kinetics indicated that all the formulation showed linearity with respect to zero order (R2 = 0.90 – 0.99) as compared to first order (R2 = 0.78 – 0.96). According to Korsemeyer Peppas model, the exact release mechanism was found to be diffusion and non fickian anamolous transport. Pandey et al. (2010) revealed that kinetic modeling of dissolution profiles revealed that the drug release mechanism was Fickian diffusion (n<0.5) which was found to be governed by the concentration of polymer and gas generating agent. The study conducted by Satheeshbabu and Sarvaiya (2016) reported that formulation F followed first order release and formulations F1 to F9 followed Higuchi model. As the n values of the Korsemeyer and Peppas model for all formulations was found to be less than 0.5 which suggested that drug release from the bead matrices was Fickian diffusion which is not concurred with this study.

Conclusion

Gastro retentive drug delivery system provide new and

important therapeutic options depending upon physicochemical properties, dose and purpose of controlling the drug release, constraining pathophysiological factors (Cremer, 1997; Jimenez et al., 1993; Yang et al., 1999). Such retention systems are important for drugs that are degraded in the intestine or for drugs like antacids or certain antibiotics, enzymes that should act locally in the stomach. Retention of drug delivery system in stomach prolongs over all gastro-intestinal transit time resulting in improved bioavailability for some drugs (Shivkumar et al., 2003).

The present study concluded that cumulative percentage drug release significantly decreased with the increase in polymer concentration. Overall curve fitting into various mathematical models was found to be on first order release kinetics. F1~F8 were best fitted into first order kinetic model while F9 was best fitted into Higuchi matrix model. The formulating floating beads of Ranitidine HCl using combination of polymers sodium alginate and xanthan gum to control release rate was achieved with success.

Conflict of interest statement

Authors declare that they have no conflict of interest.

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