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FORMULATION AND EVALUATION OF GASTRORETENTIVE EFFERVESCENT FLOATING DRUG DELIVERY SYSTEM OF ZIDOVUDINE

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ABSTRACT

The objective of the present study was to prepare and evaluate gastroretentive effervescent floating drug delivery system containing Zidovudine as a model drug. Zidovudine is the first approved compound for the treatment of AIDS; however the main limitation to therapeutic effectiveness of zidovudine is its dose-dependent toxicity, short biological half-life and poor bioavailability. Zidovudine gastroretentive effervescent floating tablets were prepared by direct compression method**.** Sodium bicarbonate and citric acid were incorporated as gas-generating agents. Drug compatibility with excipients was checked by DSC and FTIR studies revealed that, there was no incompatibility of the drug with the excipients used. The results of *in-vitro* buoyancy time and lag time study, the values of *in-vitro* buoyancy time ranges from 180 to 870 min where as floating lag time ranges from 2.11 to 51.36 min. The formulations prepared with carbopol have longer floating lag times. The formulation GREFT-6 shows the lag time 2.11 min and buoyancy time 870 min. The release of Zidovudine from all the formulations ranges from 45.05 - 64.96 % drug released at the end of 6 hrs. The formulations GREFT-1 and GREFT-2 shows 90 % of drug release within 10 hrs. The formulations GREFT-3 to GREFT-7 shows drug release ranges from 86.17 - 96.65 % at the end of 12 hrs. The results were revealed that as the concentration of carbopol increases, there is decrease in the drug release and floating time has been increased. The formulation GREFT-6 containing Carbopol 934P 100 mg showed the controlled drug release when compare to other formulations. The stability study conducted as per the ICH guidelines and the formulations were found to be stable. From the above studies, it has been observed that effervescent based floating drug delivery system is a promising approach to achieve controlled release behavior.

Key wards: Zidovudine, HPMC K4M, carbopol, floating tablets, effervescent.

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INTRODUCTION:

Oral drug delivery remains the most popular route of administration. However, limitations in the physical–chemical properties of the drug sometimes prevent a successful therapeutic outcome[1]. Dosage form with prolonged gastric residence time or gastro-retentive dosage form (GRDF) provides an important option[2]. Under certain circumstances prolonging the gastro-retentive of a delivery system is desirable for achieving greater therapeutic benefit of the drug substance. For example, drugs that are absorbed in the proximal part of the gastrointestinal tract and drugs that are less soluble may benefit from prolonged gastric retention. In addition, for local and sustained drug delivery to the stomach and proximal small intestine to treat certain conditions, prolonged gastric retention of the therapeutic moiety may offer numerous advantages including improved bioavailability and therapeutic efficacy, and possible reduction of dose size. Retention of drug delivery systems in the stomach prolongs the overall gastrointestinal transit time, thereby resulting in improved bioavailability. Scintigraphic studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically two complications, which of short gastric residence time and unpredictable gastric emptying rate[3]. Depending on the mechanism of buoyancy, two distinctly different methods viz., effervescent and non effervescent systems have been used in the development of floating drug delivery systems (FDDS)[4]. Effervescent drug delivery systems utilize matrices prepared with swellable polymers such as methocel[5] or polysaccharides and effervescent components are like sodium bicarbonate and citric acid. A controlled drug delivery system is usually designed to deliver the drug in order to maintain blood levels above its minimum effective concentration and below its maximum safe concentration. These are matrix type of systems prepared with the help of swellable polymers such as HPMC, Carbopol, Methylcellulose and chitosan and various effervescent compounds, e.g. sodium bicarbonate, tartaric acid and citric acid. They are formulated in such a way that when in contact with the gastric contents, CO2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms. The common approach for preparing these systems involves resin beads loaded with bicarbonate and coated with ethylcellulose. The coating, which is insoluble but permeable, allows permeation of water. Thus, carbon dioxide is released, causing the beads to float in the stomach[6]. The gastroretentive tablets results in release of the drug in to the more absorptive regions of the GIT, is in to the stomach and the small intestine rather than into the large intestine where drug absorption is poor or erratic. This is achieved by adjusting the time period of release for the drug

so that it is about the same as or less than the retention time of the tablets at the site of absorption. Thus the system is not transported past the "absorption window" prior to releasing the entire drug, and the maximum bioavailability is attained [7-9].

AIDS is considered to be an epidemic, and according to estimates from the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) AIDS Epidemic Update 2005, 38 million adults and 2.3 million children were living with the human immunodeficiency virus (HIV) at the end of 2005[10-12]. The annual number of AIDS deaths can be expected to increase for many years to come, unless more effective and patient-compliant antiretroviral medications are available at affordable prices. The major drawbacks of antiretroviral drugs for the treatment of AIDS are their adverse side effects during long-term therapy, poor patient compliance, and their huge cost[13]. In present research work Zidovudine is used, is a dideoxynucleoside compound in which 3- hydroxy group on the sugar moiety can be replaced by group and this modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chain. Zidovudine appears most promising because it crosses the blood brain barrier and be taken orally[14-16]. Zidovudine (AZT) is the first approved compound for the treatment of AIDS; however the main limitation to therapeutic effectiveness of AZT is its dose-dependent toxicity, short biological half-life and poor bioavailability[17]. It is crucial for the success of AIDS therapy to maintain the systemic drug concentration consistently above its target antiretroviral concentration throughout the course of the treatment. There are a number of drugs that have been considered as to be anti HIV[18, 19].

Zidovudine gastroretentive effervescent floating tablets were prepared by using different concentrations of hydroxy propyl methyl cellulose (HPMC K4M), carbopol, sodium bicarbonate, sodium CMC, Sodium alginate and citric acid. So, in order to improve the therapeutic effect of the drug by increasing its bioavailability, safe and effective levels are maintained for a long period time[20-22]. The Zidovudine gastroretentive effervescent floating tablets were prepared by direct compression method. Main advantages of direct compression are low manufacturing cost and high mechanical integrity of the tablets. Therefore, direct compression appears to be a better option for manufacturing of tablets[23]. The compositions of gastroretentive effervescent floating tablets are given in Table 1.

Table 1: Composition of Zidovudine gastroretentive effervescent floating tablets.

Ingredients /FC	GREFT-1	GREFT-2	GREFT-3	GREFT-4	GREFT-5	GREFT-6	GREFT-7
Zidovudine	300	300	300	300	300	300	300
HPMC K4M	75	100	--	--	50	100	75
C-934 P	--	--	75	100	50	100	75
Sod CMC	20	20	20	20	20	20	20
SB	50	50	50	50	50	50	50
CA	20	20	20	20	20	20	20
C- PVP	20	20	20	20	20	20	20
XG	20	20	20	20	20	20	20
SA	20	20	20	20	20	20	20
Lactose	155	130	55	130	130	30	80
M S	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10
Total weight	**700**	**700**	**700**	**700**	**700**	**700**	**700**

*FC – Formulation code, Magnesium Stearate - M S, Sodium Bicarbonate – SB, Carbopol 934 P- C-934 P, Sodium carboxy methyl cellulose – Sod CMC, Cross linked PVP – C- PVP, Xanthan Gum- XG, Sodium Alginate-SA

MATERIALS AND METHODS

Zidovudine is obtaining gift sample from Emcure Pvt Ltd. HPMC K4M was procured as gift samples from AstraZeneca Pharma India Ltd, Bangalore. Carbopol 934, magnesium stearate and citric acid are purchased from Hi media laboratories Pvt. Ltd, Mumbai. India, Sodium bicarbonate, cross linked CMC, lactose, and talc were purchased from SD. Fine Chemicals, Mumbai. All other materials used were of pharmaceutical grade.

Preparation of Zidovudine gastroretentive effervescent floating tablets:

Zidovudine gastroretentive effervescent floating ***tablets*** were prepared by mixing the Zidovudine 300 mg with the gas generating component, and the selling agent, the gas entrapping viscolyzing agent and including gel forming polymer, citric acid as acid source and lactose by geometric mixing in mortar and pestle for 10 min. The above powder was lubricated with magnesium stearate in mortar and pestle for 2 min. The lubricated blend was compressed into tablets using 11.9 mm flat-force round tooling on Rimek Press rotary tablet machine. Compression force was adjusted to obtain tablet of hardness 6-8 kg/cm^2 with 4.4 mm tablet thickness [24].

Compatibility studies:

FTIR Studies:

IR spectra for pure drug Zidovudine, Zidovudine gastroretentive effervescent floating tablets were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR 1615, Perkin Elmer, USA) with KBr pellets.

DSC Studies:

5 mg of pure Zidovudine and Zidovudine gastroretentive effervescent floating tablets were sealed in perforated aluminium pans for DSC scanning using an automatic thermal analyzer system (Mettler Toledo, USA). Temperature calibrations were performed using indium as standard. An empty pan sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 10^0 C/min from 50-300^{0}C.

Evaluation of Zidovudine gastroretentive effervescent floating tablets:

The powder blend was subjected for pre-compressional parameters. The prepared gastroretentive tablets were evaluated for post-compressional parameters as weight variation, hardness, friability, thickness, drug content, lag time subsequently buoyancy time, in-vitro dissolution studies, and stability studies. For weight variation ten tablets were selected randomly from each formulation and weighed individually using a Shimadzu digital balance (BL-220H). The individual weights were compared with the average weight for the weight variation. Pfizer [25- 28] hardness tester was used for the determination of the hardness of tablets. Tablet was placed in contact between the plungers, and the handle was pressed, the force of the fracture was recorded. The thickness and diameter of 4 tablets (3 tablets from each batch) were recorded during the process of compression using vernier calipers (Mitotoyo; Japan). The friability of tablets was determined using Roche friabilator (Cambel Electronics, Mumbai, India). Two tablets were accurately weighed and placed in the friabilator and operated for 100 revolutions. The tablets were de-dusted and reweighed. Percentage friability was calculated using the following formula.

$$F = (1- W_0 / W) \times 100$$

Where, W_0 is the weight of the tablets before the test and W is the weight of the tablet after the test.

Drug content was performed to check dose uniformity in the formulation. Randomly ten tablets were weighed and powdered. A quantity equivalent to 300 mg of Zidovudine was added in to a 100 ml volumetric flask and dissolved in 0.1N HCL, shaken for 10 min and made up the volume up to the mark and filtered. After suitable dilutions the drug content was determined by UV spectrophotometer at 266 nm against blank.

Floating or Buoyancy Test [24]:

The time taken for tablet to emerge on the surface of the medium is called the floating lag time (FLT) or buoyancy lag time (BLT) and duration of time the dosage form constantly remains on the surface of the medium is called the total floating time (TFT).The buoyancy of the tablets was

studied in USP type II dissolution apparatus at 37 ± 0.5^0 C in 900ml of simulated gastric fluid at 0.1N HCl. The time of duration of floatation was observed visually.

Swelling index[29]: The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of all the formulation was studied. One tablet from each formulation was kept in a Petridish containing 0.1N HCL. At the end of 1 hr, the tablet was withdrawn, soaked with tissue paper, and weighed. Then for every 2 hrs, weights of the tablet were noted, and the process was continued till the end of 12 hrs. % weight gain by the tablet was calculated by formula;

$$S.I = \{(Mt-Mo) / Mo\} X 100,$$

Where, S.I = Swelling index, Mt = Weight of tablet at time't' and Mo = weight of tablet at time t = 0.

In-vitro release studies for gastroretentive effervescent floating tablets[27]:

The in-vitro dissolution studied was carried out using USP XXIV Dissolution apparatus No 2 (type) at 50 rpm. The dissolution medium consisted of 0.1N HCL for 2 hrs and for subsequent 10 hrs in Phosphate buffer pH 7.4 (900ml) maintained at 37± 0.5^0. The release studies were conducted triplet. Aliquots of sample 5ml were withdrawn at specific time interval and drug content was determined spectrophotometrically at 266 nm.

Kinetic study:

To analyze the mechanism of drug release form the tablets the in-vitro dissolution data were fitted to zero order (K=kt), Korsmeyer and Peppas model ($F=kt^n$), Higuchi ($F=k\sqrt{t}$) release models. Where F is the fraction of drug release, k is the release constant and t is time[30-33].

Stability study:

The fabricated Zidovudine gastroretentive effervescent floating tablets formulations were subjected for stability study[34, 35]. To assess the stability of the optimized formulation, stability studies were conducted as per the ICH and WHO guidelines. Formulations were packed in HDPE bottles and were kept in the humidity chamber (Thermo lab, India) maintained at 25^0 C/60%RH and 40^0 C/75% RH for 3 months. At the end of studies, samples were analyzed for the hardness, drug content, in-vitro dissolution, floating behavior.

RESULT AND DISCUSSION:

IR spectra of Zidovudine and Zidovudine gastroretentive effervescent floating tablets formulations GREFT-6 and GREFT-7 are shown in Figure 1. The IR Spectra of Zidovudine was recorded and it has showed short absorption peak due to -OH group present in the drug

molecules. In this case -NH absorption peak present in the form of amine because of its weak characters exhibits a weak absorption at 3313 cm^{-1}. The aliphatic -CH absorption peak are seen from 3212-2800 cm^{-1}. The amide C=o present in the molecules given a short absorption peak at 1683 cm^{-1}.

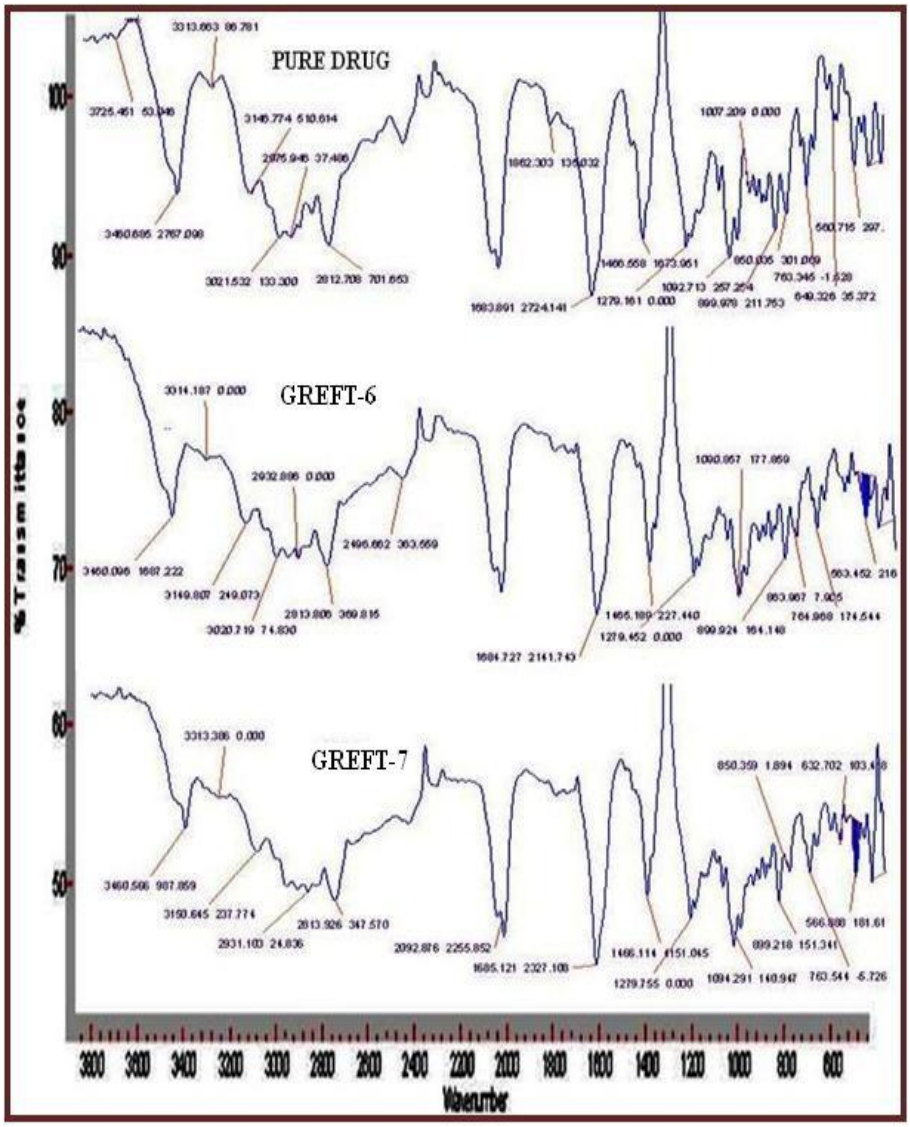

Figure 1: IR spectrum of pure drug Zidovudine and spectrums Zidovudine gastroretentive effervescent floating tablets GREFT-6 and GREFT-7.

In formulations IR all the characteristics absorption peak of the drug and HPMC and carbopol are observed and found that no chemical reaction taken place. Hence drug present in free state not in the form of reaction product. These peaks can be considered as characteristic peaks of zolmitriptan and were not affected and prominently observed in IR spectra of Zidovudine along with polymers, indicated no interaction between Zidovudine and polymers.

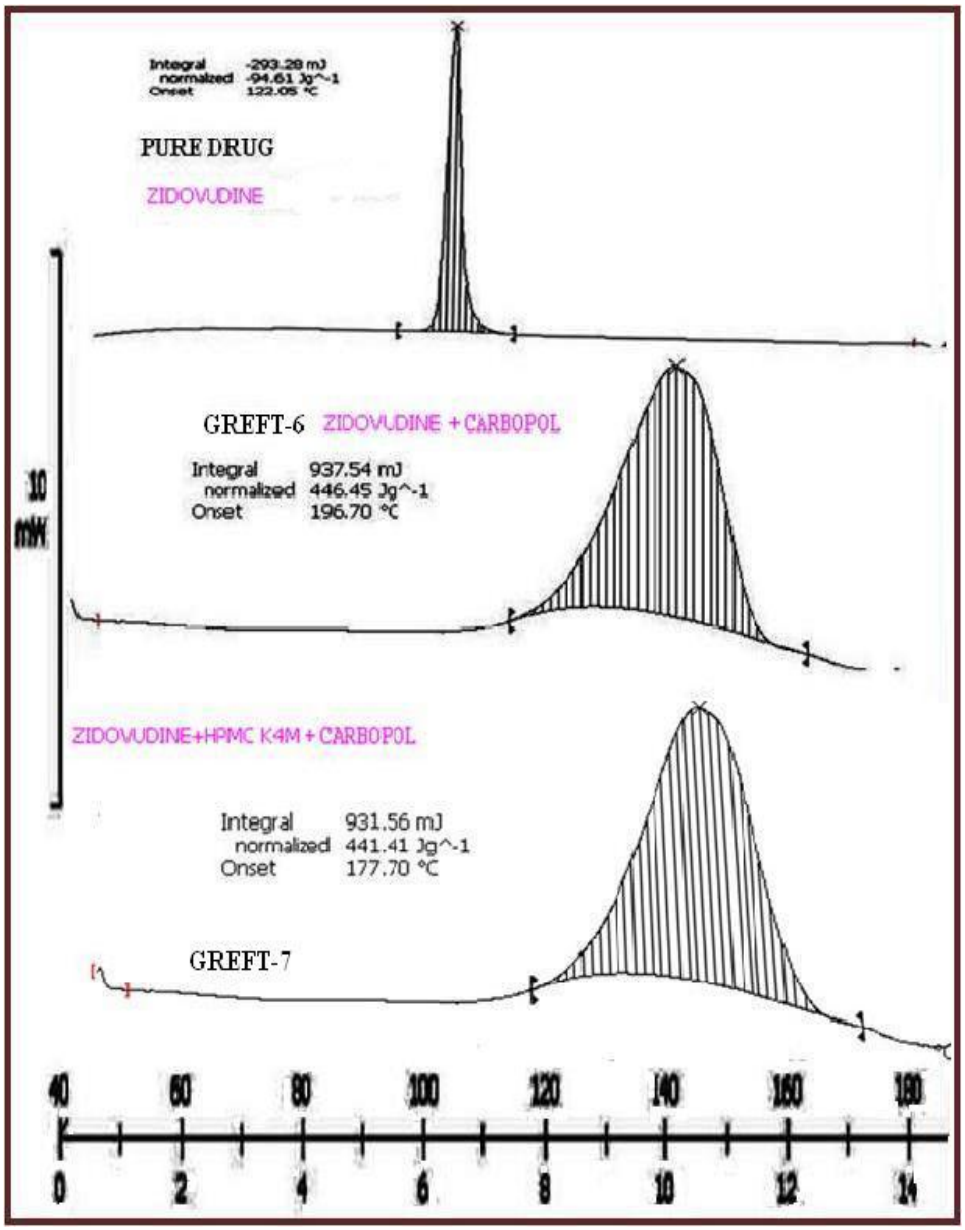

Figure 2: DSC Thermograms of pure drug Zidovudine and Thermograms Zidovudine Gastroretentive effervescent floating tablets GREFT-6 and GREFT-7.

In Figure 2 shows the thermograms obtained by the thermal analysis of the pure drug Zidovudine and Zidovudine gastroretentive tablets formulations GREFT-6 and GREFT-7. The formulation was prepared using the drug Zidovudine and HPMC the all respective data obtained from this formulation indicated that drug has not undergoes any chemical reaction or any type of interaction with other constituents present in formulation. To as set in this formulated product was subjected that the DSC measurement of the drug Zidovudine indicated in the graph it melts at sharp at 120.05^0 C subjecting that sharp melting point indicates the purity of the drug molecules taken for the formulation. When the formulated product GREFT-6 was taken it has

started at 180^0 C and prolonged up to 260^0 C subjecting that it is a mixture of drug Zidovudine and carbopol but not the reaction single product this is supporting evidence to show that drug is freely available in its original form whenever it is administered. In the DSC Measurements indicated that formulated product similar observation during next formulation where HPMC and Carbopol the formulated product starts its melting process at 186 ^{0}C and completes 266 ^{0}C supporting the ideas that this formulation is also a mixture all the three constituents i.e. drug + HPMC+ Carbopol.

Evaluation of Zidovudine gastroretentive effervescent floating tablets:

The values of pre-compression parameters of prepared Zidovudine gastroretentive tablets evaluated were within prescribed limits and indicated good free flowing property. The results of pre-compression parameters were given in Table 2.

Table 2: Pre-compressional parameters for Zidovudine gastroretentive effervescent floating tablets.

FC	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio	Angle of Repose
GREFT-1	0.662 ± 0.03	0.856 ± 0.01	13.64 ± 0.05	1.16 ± 0.06	27.05 ± 0.12
GREFT-2	0.746 ± 0.01	0.766 ± 0.02	20.62 ± 0.06	1.25 ± 0.04	26.24 ± 0.11
GREFT-3	0.648 ± 0.02	0.754 ± 0.04	19.36 ± 0.05	1.24 ± 0.06	27.84 ± 0.12
GREFT-4	0.658 ± 0.04	0.844 ± 0.03	24.36 ± 0.04	1.36 ± 0.04	29.24 ± 0.15
GREFT-5	0.628 ± 0.02	0.874 ± 0.04	23.24 ± 0.05	1.28 ± 0.08	27.36 ± 0.14
GREFT-6	0.638 ± 0.06	0.736 ± 0.05	12.64 ± 0.04	1.12 ± 0.06	28.22 ± 0.12
GREFT-7	0.654 ± 0.04	0.769 ± 0.06	12.46 ± 0.02	1.13 ± 0.02	28.34 ± 0.12

***The values represent mean ± S.D; n=3, FC = Formulation Code.**

In all the formulations, thickness of the tablets was ranges from 3.99 to 4.18 mm. Hardness test indicated good mechanical strength, the hardness and percentage friability of the tablets of all the batches remained in the range of 6.6 to 7.9 kg/cm^2 and 0.28 to 0.72% respectively. Friability is less than 1%, indicated that tablets had a good mechanical resistance. The evaluation parameters were within acceptable range for all the formulations. The weight variation of Zidovudine gastroretentive effervescent floating tablets was ranges between 599 to 614 mg. Weight variation test revealed that the tablets were within the range of pharmacopoeial limit. The drug content of the tablets was ranges from 97.24 % to 99.92 % which is within acceptable limits. The swelling index of the tablets was in the range 45.36 to 78.68 %. The results of quality control tests reveal that all the Zidovudine gastroretentive tablets are meeting the official pharmacopoeia requirements Table 3.

Table 3: Post-compressional and Floating ability parameters for Zidovudine Gastroretentive effervescent floating tablets.

FC	Thickness Mm	Hardness Kg/cm^2	Friability (%)	Average weight mg	Drug Content (%)	Swelling Index (%)	Floating lag time(min)	Floating duration (min)
GREFT-1	4.12 ± 0.05	6.6 ± 0.04	0.28	599	97.24	45.36	42 min 24 sec	180
GREFT-2	4.16 ± 0.07	7.3 ± 0.02	0.44	601	98.22	58.26	51 min 36 sec	248
GREFT-3	4.18± 0.06	7.5 ± 0.04	0.42	603	99.44	68.64	04 min 48 sec	460
GREFT-4	4.12± 0.04	7.7 ± 0.06	0.56	605	97.66	70.66	39 min 53 sec	480
GREFT-5	3.99 ± 0.02	7.9 ± 0.05	0.52	602	99.92	48.48	21 min 31 sec	560
GREFT-6	4.16 ± 0.05	7.2 ± 0.02	0.62	608	98.58	78.68	2 min 11 sec	870
GREFT-7	4.14 ± 0.03	7.6 ± 0.06	0.72	614	97.44	73.82	03 min 46 sec	715

***The values represent mean ±S.D; n=3. FC = Formulation Code.**

Sodium bicarbonate was added as a gas-generating agent. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N hydrochloric acid). The combination of Sodium bicarbonate and citric acid provided desired floating ability and therefore this combination was selected for the formulation of the Zidovudine gastroretentive tablets. It was observed that the gas generated is trapped and protected within the gel, formed by hydration of polymer (methocel), thus decreasing the density of the tablet below 1 and tablet becomes buoyant. The tablet swelled readily and axially during *in-vitro* buoyancy studies. The pH of the stomach is elevated under fed condition (~3.5), therefore citric acid was incorporated in the formulation to provide an acidic medium for Sodium bicarbonate; more over citric acid has an stabilizing effect on Zidovudine formulation.

The results of *in-vitro* buoyancy time and lag time study, the values of *in-vitro* buoyancy time ranges from 180 to 870 min where as floating lag time ranges from 2.11 to 51.36 min. Zidovudine gastroretentive effervescent floating tablets formulations prepared with effervescent have shown good floating lag time and good floating characters. The formulations prepared with carbopol have longer floating lag times when compare to formulations prepared with HPMC. Carbopol slowly swells and attains the density < 1 for floating. Increased floating time was observed with formulations containing carbopol and HPMC. The formulation GREFT-6 shows the lag time 2.11 min and buoyancy time 870 min. The results are shown in Table 3. The results of *in-vitro* buoyancy time and lag time study revealed that as the concentration of carbopol and d HPMC increases and also in presence of sodium CMC and sodium alginate there is increase in total buoyancy time and decrease in lag time as shown in Figure 3.

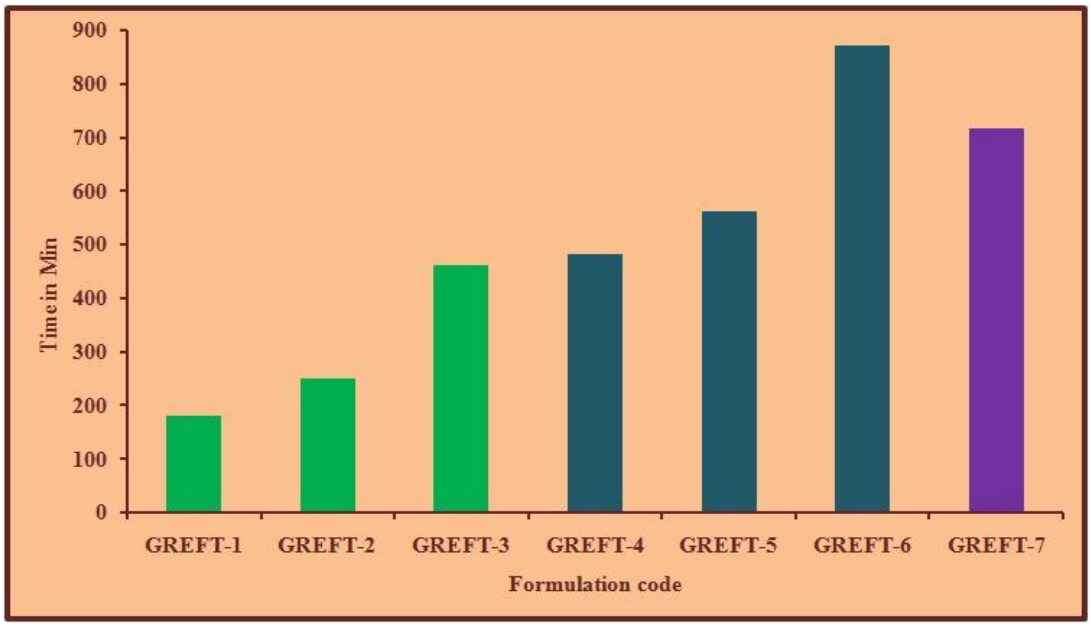

Figure 3: Comparative floating duration time of formulations GREFT-1 to GREFT-7.

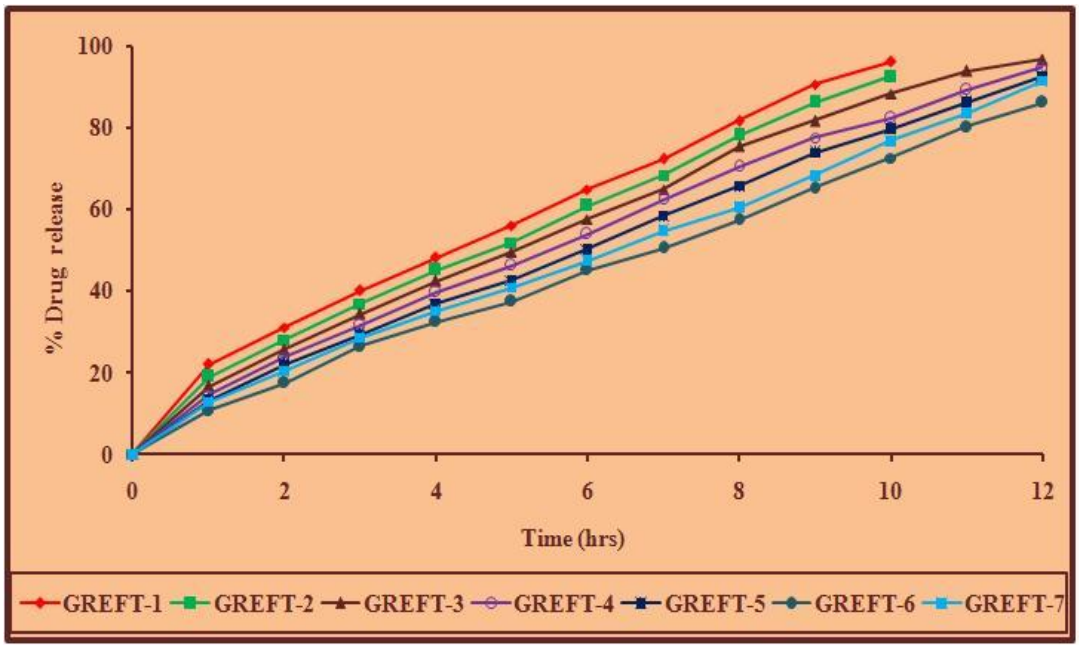

Figure 4: Comparative release profile of Zidovudine gastroretentive effervescent floating tablets formulations GREFT-1 to GREFT-7.

The dissolution profiles of the formulations from GREFT-1 to GREFT-7 are represented graphically in Figure 4 and the results are shown in Table 4. The release of Zidovudine from all the formulations ranges from 45.05 - 64.96 % drug released at the end of 6 hrs. The formulations GREFT-1 and GREFT-2 shows 90 % of drug release within 10 hrs. The formulations GREFT-3 to GREFT-7 shows drug release ranges from 86.17 – 96.65 % at the end of 12 hrs. The results were revealed that as the concentration of carbopol increases, there is decrease in the drug

release and floating time has been increased. The formulation containing large concentration of high viscosity polymers induced formation of strong viscous gel layer that leads to decreased water diffusion into the tablet matrix which results in decrease drug release.

Table 4: *In- vitro* release study of Zidovudine gastroretentive effervescent floating tablets.

FC	% drug release after 2 hrs	% drug release after 4hrs	% drug release after 6 hrs	% drug release after 8 hrs	% drug release after 10 hrs	% drug release after 12hrs
GREFT-1	31.17 ± 1.24	48.20 ± 0.12	64.96 ± 1.24	81.72 ± 0.14	96.13 ± 0.18	--
GREFT-2	28.02 ± 0.16	45.05 ± 0.42	60.77 ± 0.34	78.05 ± 0.62	92.46 ± 0.46	--
GREFT-3	25.68 ± 0.36	42.43 ± 0.24	57.62 ± 0.42	75.44 ± 0.18	88.27 ± 0.28	96.65 ± 0.42
GREFT-4	23.83 ± 1.14	39.81 ± 0.32	53.96 ± 1.14	70.46 ± 0.36	82.25 ± 0.62	94.82 ± 0.68
GREFT-5	22.00 ± 0.64	36.93 ± 0.42	50.29 ± 0.66	65.74 ± 0.34	79.63 ± 0.38	92.46 ± 0.72
GREFT-6	17.55 ± 1.02	32.48 ± 0.46	45.05 ± 0.68	57.36 ± 0.42	72.55 ± 0.46	86.17 ± 0.38
GREFT-7	20.43 ± 1.08	35.10 ± 0.86	47.41 ± 0.84	60.51 ± 0.48	76.75 ± 0.36	91.41 ± 0.94

All values are expressed as mean ± SD, n=3, FC = Formulation code

The formulation GREFT-6 containing Carbopol 934P 100 mg and HPMC 100 mg showed the controlled drug release when compare to other formulations. A retarded drug release is seen in formulation GREFT-6 at the end of 12 hrs 86.17 % drug released. The preliminary studies revealed the HPMC K4M alone matrix could not sustained the drug release for a period of 12 hrs, and this may due the fact that HPMC upon contact with water forms a hydrogel layer which acts as a gel boundary for the delivery system, but it failed to retard the release of drug through the matrix because of the high solubility of drug in the stomach pH. The Carbopol 934 and HPMC both containing formulation not only retarded the release but also sustain the release for a period for 12 hrs.

The data obtained from *in-vitro* dissolution studies Zidovudine gastroretentive effervescent floating tablet formulations were fitted in different models viz. zero order, first order and Korsemeyer's equation represented graphically in Figure 5 to 7. Kinetics drug release result reveals that all Zidovudine gastroretentive effervescent floating tablet formulations follow zero-order release kinetics. The zero-order kinetics as correlation coefficient (R values 0.9478 to 0.9932) values is higher than that of first order release kinetics. To ascertain, the drug release mechanism the *in-vitro* release data were also subjected to Higuchi's diffusion equation the r-values of all the formulations were 0.87942 to 0.9571. It suggests that the drug released by diffusion mechanism. To confirm the exact mechanism of drug release from these tablets, the data were fitted according to Korsemeyer's equation[27-28]. Regression analysis was performed and regression values 'R' were 0.9915 to 0.9982 for different formulations. Slope values were in the

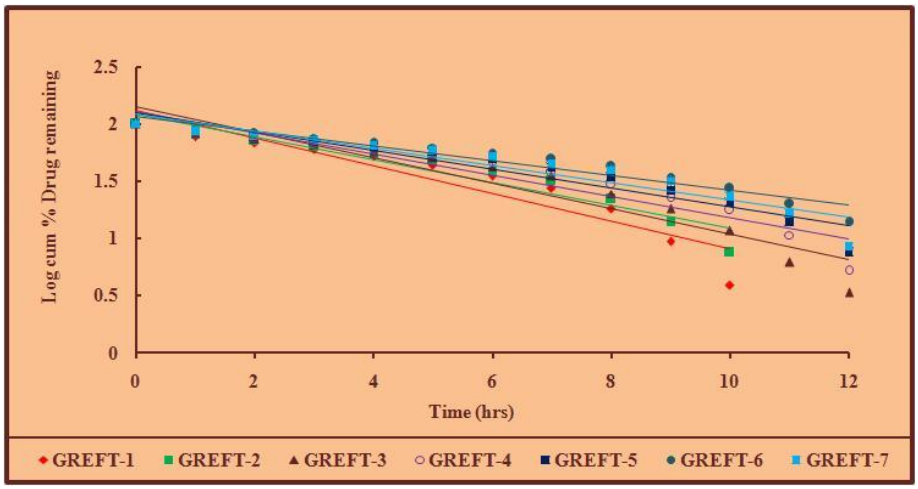

Figure 5: First order release plots of Zidovudine gastroretentive effervescent floating tablet formulations GREFT-1 to GREFT-7.

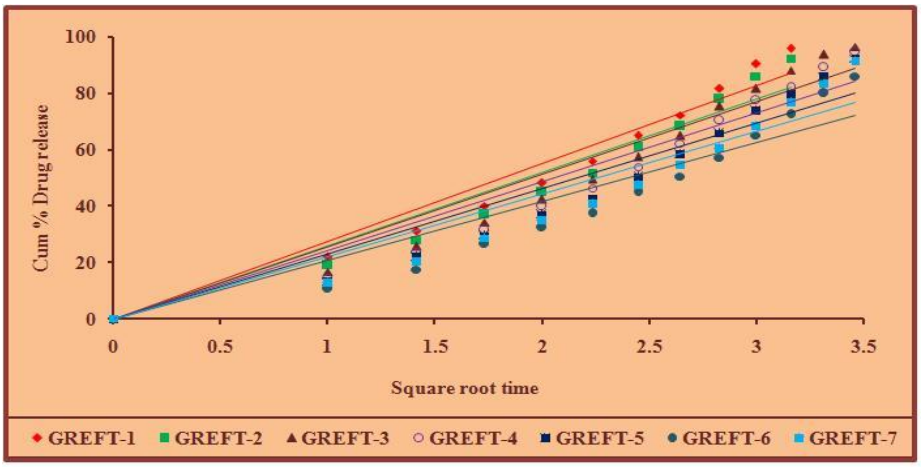

Figure 6: Higuchi diffusion plots of Zidovudine gastroretentive effervescent floating tablet formulations GREFT-1 to GREFT-7.

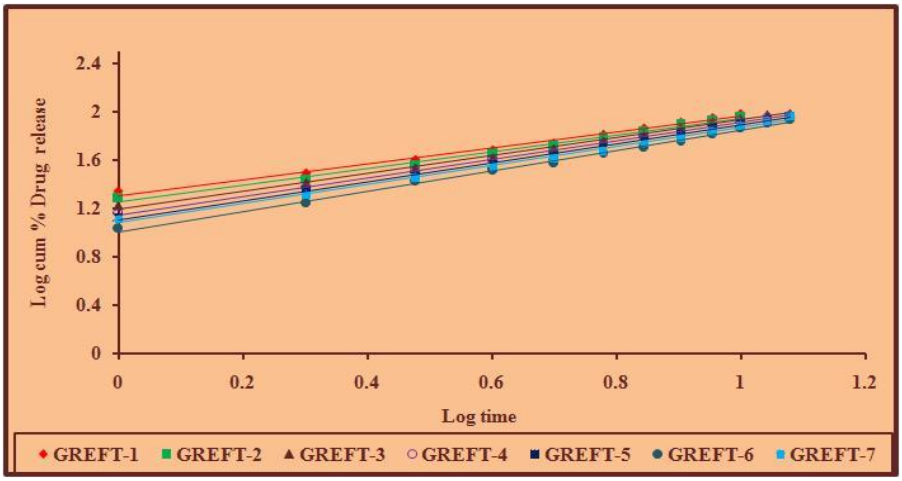

Figure 7: Peppas log-log plots of Zidovudine gastroretentive effervescent floating tablet formulations GREFT-1 to GREFT-7.

range of 0.65 to 0.84. For tablets of a known geometry (in this case a slab) $n = 0.5$ means Fickian diffusion, $0.5 < n < 1.0$ non-Fickian diffusion, and $n = 1.0$ case II diffusion[29]. Slope values (0.5>n<1.0) suggest that the release of Zidovudine from gastroretentive tablets followed non-Fickian and first order with swelling.

The stability study conducted as per the ICH guidelines for 3 months and the optimized formulation GREFT-6 were selected for stability study. After storage, the formulation GREFT-6 was subjected to drug content, hardness, floating behavior and *in-vitro* dissolution studies. The statistical analysis of the parameters drug content, hardness and floating behavior (Table 5) after storage at 25 ^{0}C/60 % RH and 40 ^{0}C/75 % RH for three months showed no significant change in hardness, drug content and floating behavior was observed even after the evaluation for 3 months.

Table 5: Characteristics of Zidovudine gastroretentive effervescent floating tablets GREFT-6 formulation.

Characteristics	Hardness [Kg/Cm^2]	Drug Content [%]	Floating behavior	
			Floating lag time (min)	Floating duration(min)
Before storage	7.2 ± 0.02	98.58	2 min 11 sec	870
3 Months at 25 ^{0}C/60 % RH	7.2 ± 0.08	98.24	2 min 28 sec	871
3 Months at 40 ^{0}C/75 % RH	7.3 ± 0.06	98.04	2 min 42 sec	873

CONCLUSION:

Release of Zidovudine from the effervescent floating tablets formulated with HPMC and /carbopol was slow and spread over 12 hrs and depended on % of polymer in the tablet. Effervescent is essential for the formulations to have well floating property and Carbopol and HPMC both containing formulations retards the drug release in the floating formulations. The concentration of carbopol-940, HPMC, SCMC and sodium alginate significantly affects the drug release rate, buoyancy lag-time. The formulation retained for longer periods of time in the stomach and provides controlled release of the drug.

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