FORMULATION AND INVITRO EVALUATION OF FDDS TABLETS OF ZIDOVUDINE

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ABSTRACT:
Zidovudine inhibits the replication of HIV in human cells. The Zidovudine tablets were prepared by wet granulation technique by using different ratios of HPMC K4M, K15M, K100M using PVP K30, Magnesium state, talc, sodium bicarbonate, citric acid, lactose, Carbopol 934 & Microcrystalline Cellulose. The prepared tablets were subjected to post compressional parameters such as thickness, weight variation, hardness, drug content, diameter, buoyancy time, lag time, & invitro dissolution studies. The stability studies were conducted as per ICH guidelines. In all the formulations, hardness test indicated good mechanical resistance. Sodium bicarbonate was added as a gas generating agent, induced carbon dioxide generating in presence of dissolution medium 0.1 N HCl. The combination of sodium bicarbonate & citric acid provided desired floating ability and therefore this combination was selected for the formulation.
The present research work concludes that the formulation ZF13 consisting of HPMC K4M showed highest drug release in short duration of time.

Keywords: Zidovudine, HPMC, in vitro drug release, floating drug delivery system.

I. Introduction:

Oral controlled dosage form which is retained in the stomach for prolonged duration of time showing interest in researchers in current scenario. By controlling gastric residence time (GRT) one can achieve prolonged, predictable drug delivery system [1]. The main advantage of prolonged gastric retention is the drugs which are absorbed in proximal part & which are less soluble get benefited by this system. Prolonged gastric retention has many advantages like improvement in bioavailability, dose size reduction. Prolonged retention of drug in the stomach improves GI transit time. 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 [2,3].

Oral route of delivery is the most preferred route of administration of drug because of its ease in administration, patient compliance and ease in handling [4]. When the drug is released in the stomach the residual system will be emptied by which gastric resident time is increased, by this better control over the fluctuation of plasma drug concentration is achieved [5,6]. The main disadvantage of oral route is short residence time in GIT, drug degradation & gastric emptying due to which it becomes uncertain drug delivery system. By formulating Floating drug delivery system (FDDS) will help in increasing the gastric retention time of system [7].

Mechanism of Floating System: FDDS has a bulk density less than gastric fluids so that they remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time [8].

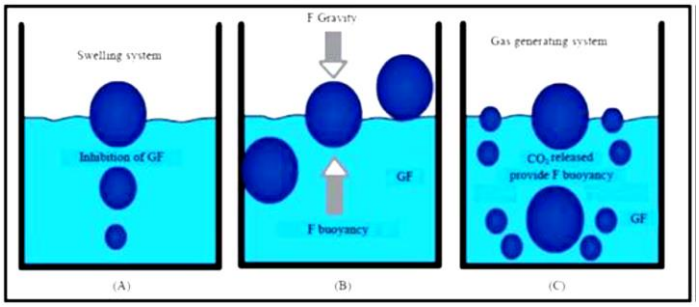

Fig. 1: Mechanism of floating.

The floating systems are further classified as effervescent or noneffervescent depending upon the inclusion or exclusion of gas forming mechanism. The slower drug release rates are achieved by water penetration or diffusion of drug from the floating system. For the reason a minimum floating force is required to keep the dosage form buoyant at the surface of physiologic fluid [9]. Floating systems utilize highly swellable and gelforming hydrocolloids. A variety of materials such as hydroxyl propyl methyl cellulose (HPMC), carboxy methyl cellulose and carbopol are used to achieve desired swelling and drug release

properties. HPMC takes up water after exposure to aqueous medium and form a gel that control the drug release [10]. Zidovudine the first U.S. approved a antiretroviral drug used in the treatment of HIV/AIDS, is a nucleoside analog reverse transcriptase inhibitor (NRTI) [11]. It significantly reduces the replication of the virus in patients and leading to clinical and immunologic improvements [12,13]. It can also be used to prevent HIV transmission, such as from mother to child during the period of birth or after a needle stick injury. Used by itself in HIV-infected patients, it slows HIV replication in patients, but does not stop it entirely [14]. Floating Zidovudine tablets were prepared by using different concentrations of hydroxy propyl methyl cellulose (HPMC K4M, K15M & K100M), carbopol, sodium bicarbonate and citric acid. Other excipients used were sodium bicarbonate a gas generating agent, sodium alginate as a gel forming agent. 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 [3,15,16,17]. Hence present research work on Floating tablets of Zidovudine was planned for prolong release and increased gastric retention time. The Floating tablets of Zidovudine were prepared by wet granulation technique.

II. MATERIALS AND METHODS:

Zidovudine was obtained as a gift sample from Emcure Pharma Pvt Ltd. Pune, HPMC was gifted by AstraZeneca Pvt. Ltd. Bangalore and other chemicals & reagents were of SD fine chemicals provided by college.

Preparation of Floating tablets of Zidovudine: According to the present invention, the FDDS includes a swelling agent PVP, gas generating component generated by sodium bicarbonate. The gas generating component sodium bicarbonate contacts with gastric fluid to generate carbon dioxide that gets entrapped within the hydrated gel matrix of the swelling composition. Sodium bicarbonate ($NaHCO_3$) was incorporated in the formulation in such a way that when in contact with the acidic gastric contents, CO_2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage form. Magnesium stearate and talc as lubricant and glidant, all the composition of different formulations are shown in table 1.

Table 1. Different Formulations of Zidovudine

Ingredients	**ZF 1**	**ZF 2**	**ZF 3**	**ZF 4**	**ZF 5**	**ZF 6**	**ZF 7**	**ZF 8**	**ZF 9**	**ZF10**	**ZF11**	**ZF12**	**ZF13**	**ZF14**	**ZF15**
Zidovudine	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg
HPMC K100m	50 Mg	75 Mg	100 mg	125 mg	150 mg	-	-	-	-	-	-	-	-	-	-
HPMC K15m						50 mg	75 mg	100 mg	125 mg	150 Mg	-	-	-	-	-
HPMC K4m	-	-	-	-	-	-	-	-	-	-	50 mg	75 mg	100 mg	125 mg	150 mg
Carbopol 934	20 Mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
PVP K30	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Magnesium Stearate	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Talc	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Sodium Bicarbonate	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg
Citric acid	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Lactose	10 mg	60 mg	110 mg	160 mg	10 mg	60 mg	110 mg	160 mg	10 mg	60 mg	110 mg	160 mg	85 mg	135 mg	185 mg
Microcrystalline Cellulose	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Total weight	**540 mg**	**565 mg**	**590 mg**	**615 mg**	**640 mg**	**540 mg**	**565 mg**	**590 mg**	**615 mg**	**640 mg**	**540 mg**	**565 mg**	**590 mg**	**615 mg**	**640 mg**

III. RESULTS AND DISCUSSION:

Pre-Compressional Parameters:

The properties/characteristics of powder blend plays an important in formulations. Table 2 shows the powder blend properties of prepared granules. Bulk density depends on particle size, shape and tendency of particles to adhere together, may influence compressibility, porosity, dissolution and other properties.

The bulk density and tapped density of powder blend was found between 0.610 ± 0.01 to 0.750 ± 0.02 gm/cm3 and 0.670 ± 0.03 to 0.910 ± 0.01 gm/cm^3, which indicates good packing capacity of powder blend. For inter particulate cohesive property, Carr's index was evaluated with angle of repose measurements and studied for the effects of geometry of packing solids with bulk and tapped density.

The measurements of bulk density and tapped density found that density of a powder depends on particles packing and density changes as the powder consolidates. The degree of consolidation is unique to the powder and ratio of these densities is related to inter particulate friction. This ratio, percent compressibility, was used as an index of flow. Adhesive/cohesive forces of particles are related to flow behaviors. Values of Carr's index below 15% usually show good flow characteristics and above 25% indicate poor flow ability. Carr's index was found to be between 21.11 ± 0.10 to 28.22 ± 0.05 Hausner's ratio method used to evaluate stability of powder column and to estimate the flow properties, it was found between 1.10 ± 0.03 to 1.28 ± 0.09. Low range observed of Hausner's ratio which indicates good flow ability. Other different types of angular properties have been employed to assess flow ability. The angle of repose indicates the flow ability of the powder/granules. Angle of repose is suited for particles >150 m. Values ≤300 generally indicate the free flowing material and angle of ≥400 indicates a poor flowing. The angle of repose of all the formulations were found to be within the range of 22.10 ± 0.08 to 30.41 ± 0.09 which showed that, granules were of good flow properties.

Table 2: Precompressional parameters of all the Formulations

Formulations	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index	Hausner Ratio	Angle of repose (θ)
ZF1	0.740 ±0.02	0.680 ± 0.04	21.11 ± 0.10	1.22 ± 0.05	30.41 ± 0.09
ZF2	0.720 ±0.03	0.730 ± 0.02	25.96 ± 0.04	1.20 ± 0.03	26.23 ± 0.10
ZF3	0.650 ± 0.01	0.745 ± 0.01	20.14 ± 0.06	1.15 ± 0.02	27.15 ± 0.17
ZF4	0.700 ± 0.01	0.720 ± 0.04	24.63 ± 0.07	1.20 ± 0.05	25.06 ± 0.09
ZF5	0.746 ± 0.01	0.812 ± 0.04	23.19 ± 0.08	1.19 ± 0.02	22.15 ± 0.09
ZF6	0.624 ± 0.03	0.670 ± 0.03	26.50 ± 0.05	1.10 ± 0.03	24.18 ± 0.12
ZF7	0.680 ± 0.01	0.881 ± 0.05	24.10 ± 0.10	1.14 ± 0.02	22.10 ± 0.08
ZF8	0.710 ± 0.08	0.743 ± 0.02	28.22 ± 0.05	1.21 ± 0.04	30.21 ± 0.07
ZF9	0.630 ± 0.01	0.800 ± 0.06	26.16 ± 0.12	1.15 ± 0.05	22.16 ± 0.08
ZF10	0.620 ± 0.04	0.910 ± 0.01	20.50 ± 0.10	1.25 ± 0.04	28.40 ± 0.10
ZF11	0.610 ± 0.01	0.875 ± 0.02	26.44 ± 0.09	1.18± 0.02	30.19 ± 0.09
ZF12	0.750 ± 0.02	0.690± 0.02	21.17 ± 0.12	1.22 ± 0.04	25.12 ± 0.10
ZF13	0.650 ± 0.07	0.850 ± 0.07	24.14 ± 0.09	1.17 ± 0.02	23.40 ± 0.18
ZF14	0.640 ± 0.04	0.710 ± 0.04	26.80 ± 0.10	1.13 ± 0.04	30.11 ± 0.13
ZF15	0.668 ± 0.01	0.900 ± 0.07	22.77 ± 0.27	1.28 ± 0.09	28.13 ± 0.19

Post-compressional parameters:

Tablet Thickness, Diameter & Hardness:

All the formulations were evaluated for various parameters like thickness; diameter and hardness. All the prepared tablets formulations F1 to F15 shown in Table 3, it was found that there was no much variation in thickness of tablets; it showed that powder blends was consistent in particle size and uniform behavior during tablet compression. Thickness and diameter of tablets of all formulations were measured by vernier caliper and there will be no any change in thickness and diameter of tablets respectively. Thickness was in range of 4.0 ± 0.06 to 4.5 ± 0.06. The hardness of tablets was measured by Pfizer hardness tester. The hardness was in range of 6.5 ± 0.01 to 8.0 ± 0.04 Kg/cm^2. Tablet hardness reflects differences in tablet density and porosity, which showed results in difference release patterns of the drug by affecting the rate of penetration in the dissolution medium at the surface of the tablet.

Weight Variation: The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation. The results are showed in table 3.

Friability: The present study of tablets is within the limit and the slight variation in seen in friability because of the variation in compression force applied and its total weight. The friability of tablets also depends on type of filler and moisture contents present in it. The friability was found to be in the range of 0.25 ± 0.041 to 0.65 ± 0.010 shown in Table 3.

Table 3: Post-Compressional properties of Zidovudine tablets

Formulations	Average weight (mg)	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)
ZF1	537 ± 0.02	4.1 ± 0.04	11.9 ± 0.03	6.5 ± 0.01	0.25 ± 0.041
ZF2	560 ± 0.04	4.3 ± 0.02	12.0 ± 0.02	6.8± 0.02	0.60 ± 0.056
ZF3	592 ± 0.03	4.3 ± 0.06	11.9 ± 0.04	6.9 ± 0.04	0.50 ± 0.047
ZF4	610 ± 0.02	4.4 ± 0.03	11.8 ± 0.02	7.9 ± 0.06	0.39 ± 0.080
ZF5	642 ± 0.01	4.5 ± 0.02	12.1 ± 0.01	7.8 ± 0.02	0.46 ± 0.054
ZF6	538 ± 0.02	4.2 ± 0.04	11.8 ± 0.04	7.1 ± 0.04	0.30 ±0.010
ZF7	560 ± 0.01	4.2 ± 0.02	11.8 ± 0.06	7.4 ± 0.02	0.45 ± 0.016
ZF8	600 ± 0.02	4.4 ± 0.02	11.9 ± 0.08	6.9 ± 0.05	0.50 ± 0.020
ZF9	608 ± 0.03	4.5 ± 0.02	12.0 ± 0.05	7.3 ± 0.04	0.35 ± 0.025
ZF10	638 ± 0.02	4.4 ± 0.04	11.9 ± 0.05	7.0 ± 0.04	0.65 ± 0.010
ZF11	540 ± 0.02	4.0 ± 0.06	11.8 ± 0.04	7.2 ± 0.04	0.40 ± 0.048
ZF12	560 ± 0.02	4.1 ± 0.03	12.1 ± 0.06	7.9 ± 0.09	0.32 ± 0.080
ZF13	595 ± 0.01	4.3 ± 0.01	11.8 ± 0.09	8.0 ± 0.04	0.40 ± 0.054
ZF14	612 ± 0.02	4.4 ± 0.05	12.2 ± 0.04	7.5 ± 0.05	0.62 ± 0.020
ZF15	650 ± 0.05	4.5 ± 0.06	12.2 ± 0.06	7.6 ± 0.04	0.56 ± 0.019

Drug Content & Swelling Index (WATER UP TAKE) Study: The drug content and swelling index (water up take) studies were carried out for all the prepared formulations, the results are shown in Table 4.

Drug Content: Drug content was in range of 97.11 ± 0.32 to 99.89 ± 0.69, which reflects good drug content uniformity in all the prepared formulations. The reading complies as per I P. which indicates drug was uniformly distributed throughout the tablet compressed.

Swelling Index Study: Swelling of tablet is also a vital & important factor to ensure floating. To obtain floating balance between swelling and water acceptance must be restored. Tablets composed of polymeric matrices, when they come in contact with water, build a layer of gel around the tablets core. This gel layer governs the release of drug. Swelling is important because the gel barrier is formed by water permeation. Swelling index results study showed that, the order of swelling in these polymers indicate the rates at which the preparations are able to absorb water and swell. Maximum liquid uptake and swelling of polymer was achieved up to 24 hrs and then gradually decreased due to erosion. The swelling of polymers used in these tablets (HPMC, sodium alginate) could be determined by water uptake of the tablets. The complete swelling was achieved by the end of 24 hrs. The swelling index was in range 59.74 ± 0.21 to 70.19 ± 0.27. ZF15 formulation has higher swelling index. The reason for higher swelling index values are due channelling agent, allows more permeation of water into the gel layer and it enhances the water retention property also. This could be the reason for more moisture uptake by formulations of ZF14, values are given in Table 4.

Table 4: Physico-chemical properties of Zidovudine tablets

Formulations	Drug content (%)	Swelling index
ZF1	97.50 ± 0.26	60.13 ± 0.87
ZF2	97.11 ± 0.32	59.74 ± 0.21
ZF3	99.62 ± 0.74	61.88 ± 0.47
ZF4	99.89 ± 0.69	63.41 ± 0.59
ZF5	99.19 ± 0.29	63.60 ± 0.20
ZF6	98.20 ± 0.25	65.10 ± 0.80
ZF7	97.70 ± 0.47	60.90 ± 0.40
ZF8	98.12 ± 0.80	64.23 ± 0.80
ZF9	97.14 ± 0.70	62.87 ± 0.21
ZF10	99.40 ± 0.90	61.50 ± 0.19
ZF11	98.67 ±0.20	60.00 ± 0.83
ZF12	99.10 ± 0.90	63.58 ± 0.55
ZF13	98.78 ± 0.36	65.50 ± 0.87
ZF14	97.90 ± 0.82	68.47 ± 0.12
ZF15	99.70 ± 0.50	70.19 ± 0.27

***In-Vitro* Buoyancy & Lag Time Study:** The floating lag time for all the formulations were found to be less than 90 minutes, the floating time duration was found to up to 24 hrs in all the formulations. Results are in table 5 and in figure 2. The tablet floated with less lag time due to high concentration of gas generating agent. Some results revealed that, as the concentration HPMC K4M increased, total floating time also increased; this is because of increased gel strength of matrices, which prevents escape of evolved carbon dioxide from matrices, leading to decreased density of the formulations. The outermost hydrophilic polymer hydrates and swells and a gel barrier were formed at the outer surface. As the gelatinous layer progressively dissolves and/or is dispersed, the hydration swelling release process is repeated towards new exposed surfaces, thus maintaining the integrity of the dosage form. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity, as well as floating capability, hence from the above results concluded that linear relationship exists between swelling process and viscosity of polymer. So the presence of optimum amount of HPMC K4, $NaHCO_3$, and citric acid is important in achieving good floating time and minimum floating lag time. Incorporation of sodium bicarbonate helps to produce carbon dioxide gas which entrapped inside the hydrophilic matrices leads to increase in volume of dosage form resulting in lowering of density and dosage form starts to float. As the amount of polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent ($NaHCO_3$) increases the drug release increases and at the same time floating lags time decreases.

Side view **Top view**

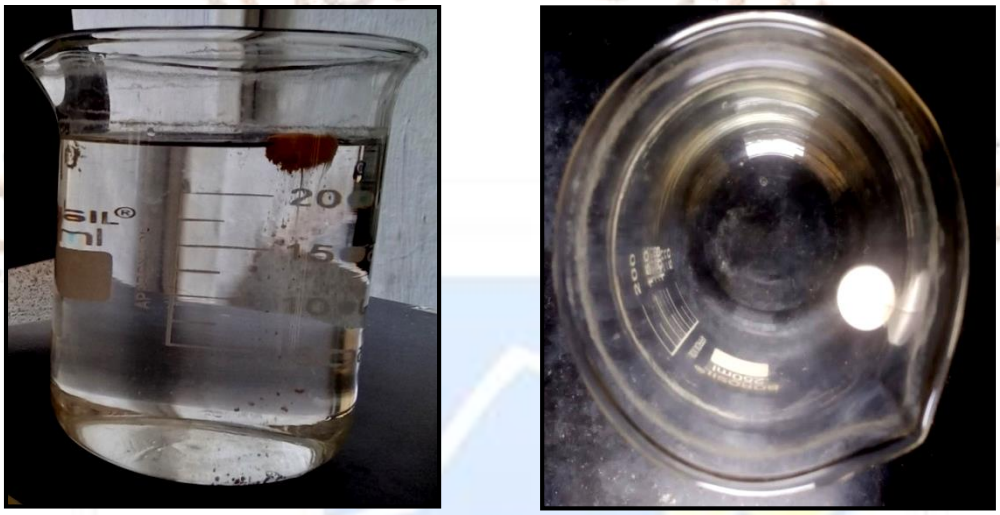

Fig. 2: *In-vitro* Buoyancy Study

Table 5: Floating ability of various Zidovudine tablets

Formulation codes	Floating lag time (sec/min /hrs)	Floating time (hrs)
ZF1	2.3 min	24
ZF2	3 min	24
ZF3	4.3 min	24
ZF4	2.3 min	24
ZF5	3.3 min	24
ZF6	2.3 min	24
ZF7	2.3 min	24
ZF8	3 min	24
ZF9	3 min	24
ZF10	2.3 min	24
ZF11	3 min	24
ZF12	2.3 min	24
ZF13	3 min	24
ZF14	4 min	24
ZF15	3 min	24

In-Vitro Release Study:

Table 6: *In vitro* release data of FDDS of Zidovudine ZF1, ZF2, ZF3, ZF4 & ZF5

Timings	ZF1	ZF2	ZF3	ZF4	ZF5
1 hr	11.56±0.47	12.26±0.85	14.23±0.87	14.00±0.56	10.14±0.45
2 hr	27.23±0.18	18.96±0.55	29.23±0.14	19.20±0.78	23.35±0.70
3 hr	45.66±0.32	32.54±0.12	38.63±0.36	25.84±0.36	31.77±0.13
4 hr	51.45±0.14	41.36±0.54	47.55±0.15	35.23±0.87	42.19±0.89
5 hr	59.23±0.45	50.21±0.92	58.88±0.63	40.55±0.31	47.33±0.67
6 hr	65.12±0.34	61.29±0.36	67.46±0.74	54.10±0.48	62.81±0.55
7 hr	69.87±0.60	68.41±0.84	70.85±0.96	66.77±0.29	69.41±0.36
8 hr	76.22±0.49	74.28±0.23	77.22±0.54	73.14±0.50	74.15±0.18
9 hr	87.74±0.22	86.11±0.95	86.88±0.33	78.12±0.74	77.22±0.11
10 hr	98.63±0.18	93.23±0.87	94.77±0.57	85.32±0.41	81.96±0.17
11 hr	99.00±0.77	95.89±0.51	96.15±0.20	89.44±0.69	87.35±0.60
12 hr	-	98.11±0.57	97.47±0.99	94.37±0.74	92.16±0.61
13 hr	-	-	-	98.21±0.40	93.47±0.29
14 hr	-	-	-	-	94.56±071
15 hr	-	-	-	-	96.99±0.18
16 hr	-	-	-	-	98.17±0.84

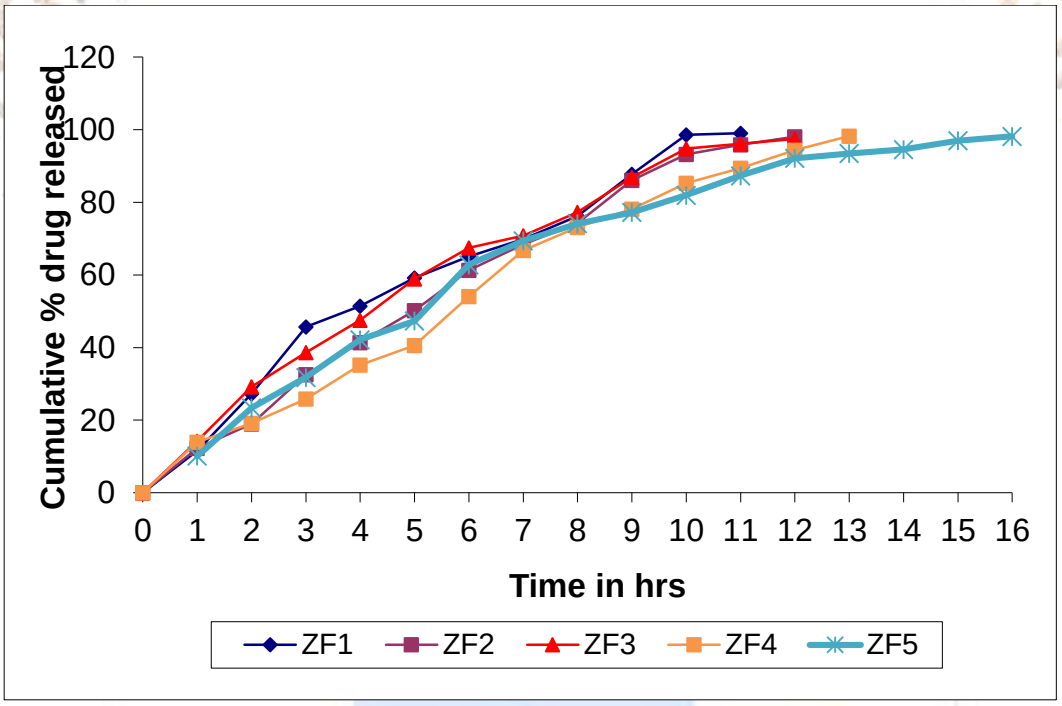

Fig.3 *In vitro* release data of FDDS of Zidovudine ZF1, ZF2, ZF3, ZF4 & ZF5

Table 7: *In vitro* release data of FDDS of Zidovudine ZF6, ZF7, ZF8, ZF9 & ZF10

Timings	ZF6	ZF7	ZF8	ZF9	ZF10
1 hr	16.16±0.21	14.00±0.51	15.13±0.45	12.80±0.71	13.54±0.17
2 hr	20.89±0.51	19.23±0.84	23.89±0.14	19.84±0.26	20.80±0.23
3 hr	26.54±0.88	27.78±0.16	31.54±0.71	21.97±0.22	22.50±0.12
4 hr	35.47±0.60	39.11±0.90	39.66±0.23	27.15±0.84	28.89±0.54
5 hr	44.11±0.39	43.25±0.89	47.23±0.19	36.35±0.88	42.18±0.89
6 hr	47.22±0.41	46.21±0.20	54.25±0.20	47.26±0.70	50.13±0.45
7 hr	56.94±0.12	53.22±0.54	59.67±0.48	52.19±0.20	57.26±0.79
8 hr	66.13±0.87	60.77±0.52	68.99±0.88	61.16±0.81	62.89±0.10
9 hr	78.10±0.45	76.58±0.13	87.55±0.87	70.11±0.14	67.19±0.40
10 hr	87.19±0.89	85.26±0.10	94.16±0.33	81.92±0.82	73.15±0.22
11 hr	96.94±0.37	94.17±0.53	96.97±0.13	91.44±0.90	82.35±0.75
12 hr	-	98.13±0.74	99.45±0.14	96.67±0.22	89.21±0.78
13 hr	-	-	-	99.23±0.10	94.16±0.38
14 hr	-	-	-	-	95.88±0.27
15 hr	-	-	-	-	98.19±0.14

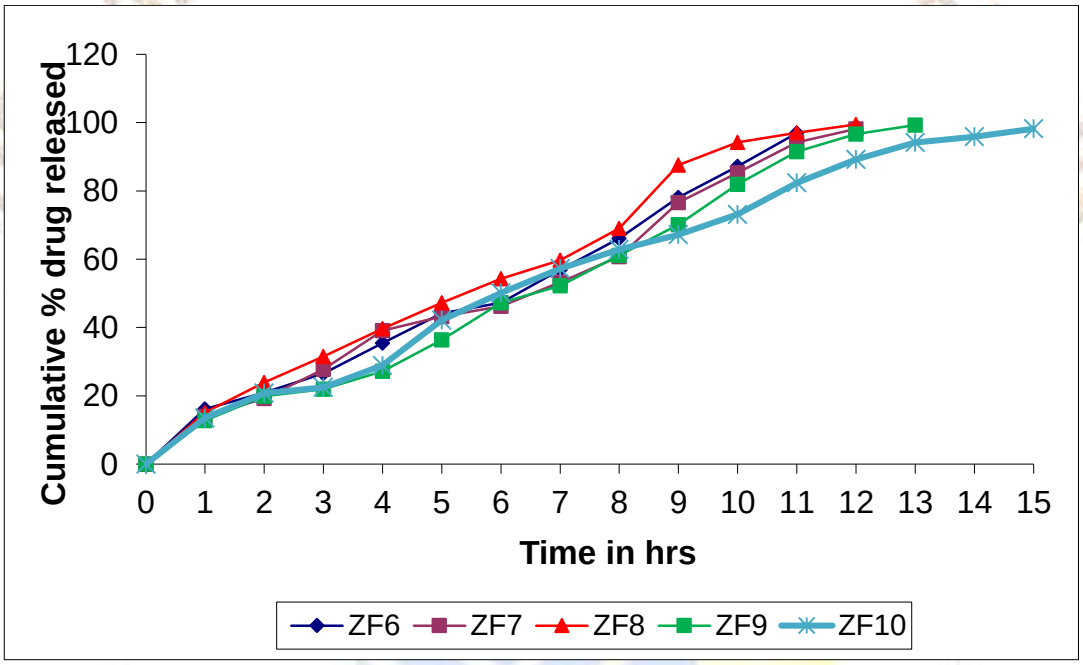

Fig.4 *In vitro* release data of FDDS of Zidovudine ZF6, ZF7, ZF8, ZF9 & ZF10

Table 8: *In vitro* release data of FDDS of Zidovudine ZF11, ZF12, ZF13, ZF14 & ZF15

Timings	ZF11	ZF12	ZF13	ZF14	ZF15
1 hr	10.23±0.11	12.23±0.89	15.12±0.52	12.12±0.40	12.87±0.23
2 hr	12.87±0.55	14.76±0.44	22.16±0.41	15.80±0.22	15.51±0.99
3 hr	16.77±0.41	17.52±0.14	29.27±0.59	20.59±0.30	21.69±0.78
4 hr	19.32±0.89	19.88±0.99	37.18±0.15	24.98±0.14	27.44±0.19
5 hr	21.63±0.34	22.41±0.13	44.90±0.13	31.50±0.62	34.12±0.63
6 hr	36.99±0.71	34.26±0.58	51.67±0.47	42.13±0.60	45.77±0.31
7 hr	44.45±0.12	47.88±0.15	57.87±0.88	52.99±0.31	55.21±0.77
8 hr	57.61±0.33	59.11±0.90	63.14±0.63	61.29±0.52	62.74±0.24
9 hr	67.43±0.56	66.96±0.52	69.54±0.14	64.63±0.25	65.38±0.96
10 hr	77.94±0.36	78.00±0.10	77.21±0.13	77.38±0.12	74.56±0.38
11 hr	89.23±0.51	91.55±0.20	84.98±0.47	80.10±0.74	78.24±0.50
12 hr	95.23±0.58	93.47±0.11	90.30±0.17	83.89±0.15	83.78±0.26
13 hr	99.35±0.44	97.29±0.70	98.90±0.98	87.25±0.90	87.29±0.37
14 hr	-	-	-	92.47±0.23	90.99±0.74
15 hr	-	-	-	96.87±0.68	93.36±0.41
16 hr	-	-	-		95.96±0.71

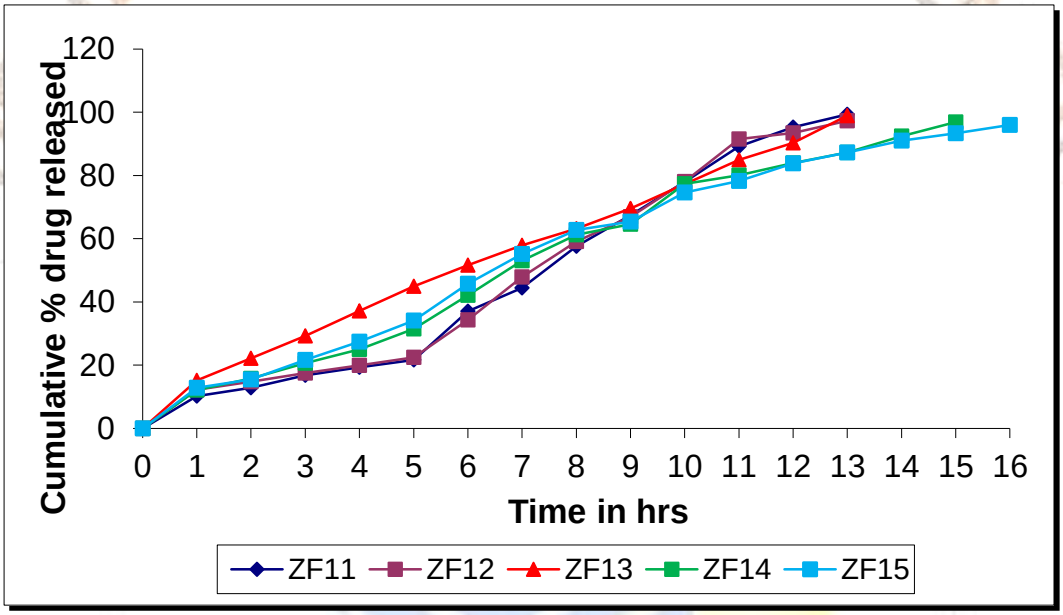

Fig.5 *In vitro* release data of FDDS of Zidovudine ZF11, ZF12, ZF13, ZF14 & ZF15

Table 9: Linear regression analysis data of FDDS of Zidovudine tablets.

Formulation code		Zero order	1st order	Higuchi	Korsemeyer
ZF1	**r**	0.9830	-0.8838	0.9931	0.9828
	A	13.289	2.370	-24.210	1.156
	B	8.266	-0.1759	37.159	0.8417
ZF2	**r**	0.9912	-0.9496	0.9945	0.9961
	A	7.313	2.306	-32.303	1.072
	B	8.268	-0.1434	38.306	0.8869
ZF3	**r**	0.9838	-0.9220	0.9969	0.9933
	A	15.717	2.241	-21.424	1.207
	B	7.573	-0.1349	35.438	0.7634
ZF4	**r**	0.9904	-0.9400	0.9880	0.9902
	A	6.485	2.276	-31.813	1.072
	B	7.582	-0.1225	36.159	0.8394
ZF5	**r**	0.9610	-0.9885	0.9901	0.9844
	A	18.849	2.133	-18.450	1.110
	B	5.746	-0.09607	30.997	0.7924
ZF6	**r**	0.9938	-0.8766	0.9684	0.9814
	A	3.357	2.237	-30.617	1.116
	B	8.163	-0.1145	35.392	0.7806
ZF7	**r**	0.9923	-0.8855	0.9722	0.9889
	A	3.692	2.302	-31.903	1.080
	B	7.864	-0.1259	35.579	0.8162
ZF8	**r**	0.9925	-0.9269	0.9803	0.9941
	A	6.835	2.342	-30.838	1.141
	B	8.160	-0.1486	37.220	0.7926
ZF9	**r**	0.9942	-0.8990	0.9721	0.9819
	A	0.3785	2.262	-37.332	1.012
	B	7.837	-0.1098	36.632	0.8600
ZF10	**r**	0.9928	-0.9393	0.9890	0.9892
	A	7.914	2.279	-28.958	1.063
	B	6.497	-0.1091	32.935	2.8000
ZF11	**r**	0.9845	-0.8986	0.9510	0.9586
	A	-8.705	2.273	-47.810	0.8189
	B	8.376	-0.1016	38.677	1.015
ZF12	**r**	0.9809	-0.9105	0.9471	0.9452
	A	-6.835	2.337	-44.970	0.8861
	B	8.178	-0.1167	37.744	0.9444
ZF13	**r**	0.9994	-0.8538	0.9895	0.9975
	A	9.132	2.259	-24.858	1.137
	B	6.852	-0.1126	32.431	0.7476
ZF14	**r**	0.9908	-0.9497	0.9832	0.9841
	A	3.405	2.224	-33.747	0.9662
	B	6.608	-0.9151	33.368	0.8705
ZF15	**r**	0.9873	-0.9740	0.9892	9868
	A	7.432	2.192	-29.489	1.003
	B	6.074	-0.08604	31.863	0.8337

'r'=Regression co-efficient
'A'= Intercept
'B'= Slope

Table.10: Dissolution of t_{50}, t_{70} and t_{90} values of various formulations

Formulations	t_{50} (hr)	t_{70} (hr)	t_{90} (hr)
ZF1	3.50	7	9.20
ZF2	5	7.10	9.40
ZF3	4.30	7	9.20
ZF4	5.30	7.20	11
ZF5	5.10	7	11.10
ZF6	6.20	8.30	10.30
ZF7	6.30	8.30	10.40
ZF8	5.30	8.10	9.30
ZF9	6.20	9	10.30
ZF10	6	9.20	12.10
ZF11	7.20	9.30	11.10
ZF12	7.30	9.40	10.50
ZF13	5.50	9.05	12
ZF14	6.30	9.40	13.50
ZF15	6.20	9.30	14

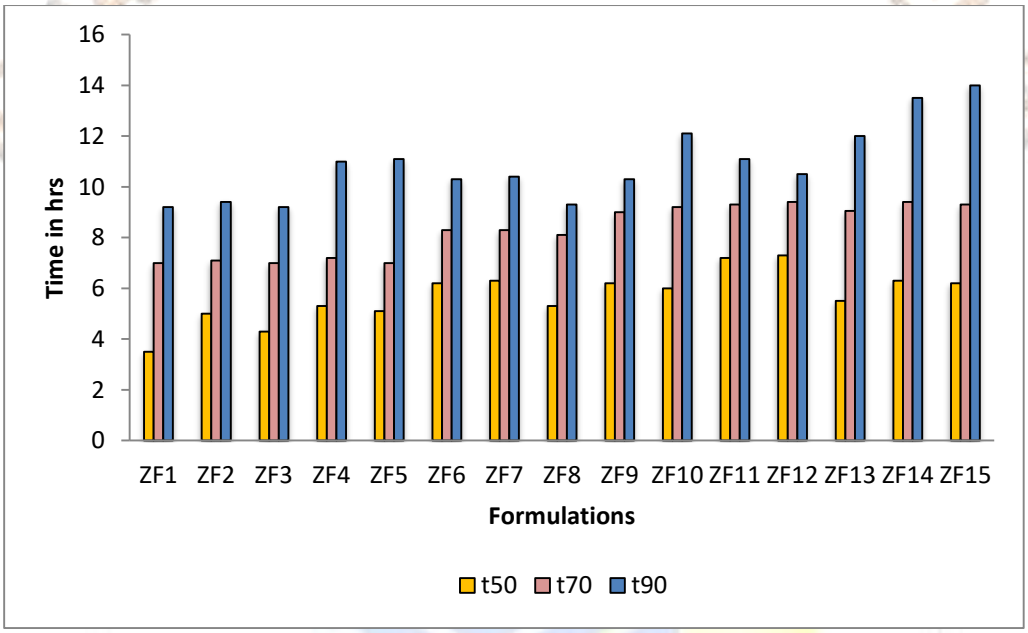

Fig.6 Dissolution of t_{50}, t_{70} and t_{90} values of various formulations

Stability Studies: The most promised formulations were selected stability studies. Three month stability studies were performed as per ICH guidelines at a temperature of 450 ± 10 C over a period of three month on the promising Floating tablet formulation ZF13 Sufficient number of tablets (10) were packed in aluminium packing and kept in stability chamber maintained at 450 ± 10 C / 75 ± 5 % RH for 3 months. Samples were taken at weekly intervals for drug content estimation. At the end of three weeks period, dissolution test and in-vitro floating studies were performed to determine the drug release profiles, the estimation of drug contents and data of dissolution and in-vitro floating studies are shown in tables 11 and 12.

Table-11: Stability studies of Formulation ZF13

Sl no	Time in days	Physical changes	Mean ± SD (45° C)
1.	01	--	99.10±0.12
2.	30	No Change	98.00±0.80
3.	60	No Change	98.80±0.19
4.	90	No Change	98.99±1.52

Table.12: InVitro release data of the stability formulation ZF13

Sl. No.	Time (Hrs)	Cumulative*percent drug released ± SD	
		45±1^0 C	45±1^0 C
		1st Day	90th Day
1.	01	16.29±0.90	15.17±0.27
2.	02	27.45±0.10	26.81±0.45
3.	03	33.43±1.45	29.02±1.19
4.	04	48.10±0.40	47.10±0.18
5.	05	59.42±0.55	58.90±0.53
6.	06	68.18±0.26	67.43±0.12
7.	07	77.16±0.91	75.80±0.90
8.	08	88.14±0.11	86.13±0.80
9.	09	97.88±1.90	96.90±1.90
10.	10	98.12±0.15	97.90±0.77

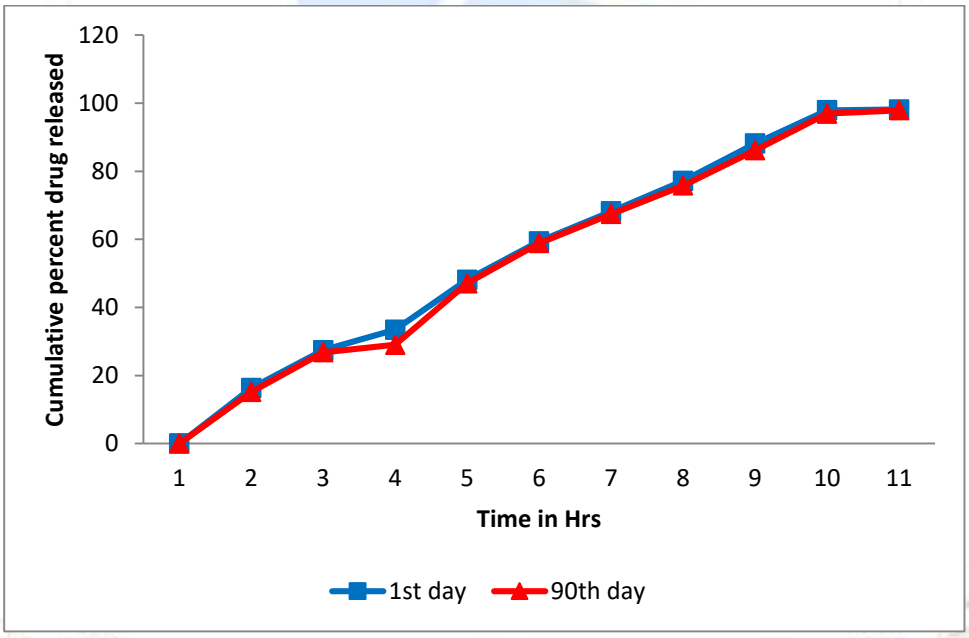

Fig.7 InVitro release data of the stability formulation ZF13

IV. CONCLUSION:

From study it is evident that, floating tablets of Zidovudine can be developed to increase gastric residence time and thereby increasing its bioavailability. All the prepared tablet formulations were found to be good without capping and chipping. Formulated FDDS tablets gave satisfactory results for various post-compressional parameters like hardness, friability, thickness, weight variation and content uniformity.

As the amount of polymer (HPMC) in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent (NaHCO3) increases the drugs releases increases and at the same time floating lag time decreases. Swelling index has a significant effect on the drug release. Short term stability studies of formulation ZF13 indicates there are no significant changes in the drug content and dissolution parameter value at stable at 45^0C and 75% RH for a period of 3 Months.

V. ACKNOLEDGEMENTS:

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