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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF ZIDOVUDINE

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ABSTRACT

The present investigation an attempt has been made to increase therapeutic efficacy, reduce frequency of administration and improve patient compliance, by developing sustained release matrix tablets of Zidovudine. Sustained release matrix tablets of Zidovudine, were developed by using different drug: polymer ratio. Kollidon SR, Hydroxypropyl methylcellulose K15M, K100M as matrix former. All lubricated formulations were compressed by direct compression and by wet granulation method. Compressed tablets were evaluated for uniformity of weight, content of active ingredient, friability, hardness, thickness, *in-vitro* dissolution, and swelling index. All the formulation showed compliance with pharmacopoeial standards. Among the different formulation, B8 showed sustained release of drug for 12 hours with 86.55% release. The regression coefficient value of Higuchi plot was found to be 0.9925 that showed that drug was released by diffusion mechanism. The slope value of korsmeyer - peppas equation was found to be 0.5062 which indicating that drug was released by non-fickian release mechanism. The R^2 value for Hixson Crowell plot was found to be 0.9919 which indicates that drug release was limited by drug particle dissolution rate and erosion of the polymer matrix. Thus, drug in combination with Hydroxypropyl methylcellulose K100M were found to be effective in retarding the release of Zidovudine.

Key words: Zidovudine, sustained release, matrix tablet, HPMC K100M.

INTRODUCTION

The basic rationale for sustained and controlled drug delivery is to alter the pharmacokinetics and pharmacodynamics of pharmacological active moieties by using novel drug delivery system or by modifying the molecular structure and physiological parameters inherent in the selected route of administration. It is desirable that the duration of drug action becomes more a design property of a rate controlled dosage form and less or not at all a property of the drug molecules inherent kinetics properties. Thus optional design of controlled release systems necessitates a thorough understanding of the pharmacokinetics and pharmacodynamics of the drugs. Acquired Immuno Deficiency Syndrome (AIDS), which threatens to cause a great plague in the present generation. It is very crucial for the success of AIDS therapy to maintain the therapeutic drug concentration consistently above its target antiretroviral concentration throughout the course of the treatment. Zidovudine/Azidothymidine (AZT), the first anti-HIV compound approved for the clinical use is widely used for treatment of AIDS either alone or in combination with other antiviral agents and Zidovudine is water soluble and soluble at all pH ranges and absorbs throughout the gastrointestinal tract and so sustained release tablet is better approach then the conventional dosage form. Since Zidovudine acts as a metabolic antagonist of thymidine and its antiviral effect is time dependant so a sustained release delivery of AZT is desired to maintain anti-AIDS effect and avoiding severe side effects. By considering above facts, the present study was aim to formulate and evaluate the sustained release matrix tablets of Zidovudine to prolong the release of drug for extended period of time in order to; Improve patient compliance, Reduce dosing frequency,

Reduce side effects, Minimum plasma fluctuation,Increase bioavailability of the drug.

MATERIALS AND METHODS

Zidovudine – IP is procured by Aurobindo Pharma ltd. Hyderabad, Polyvinyl acetate-Polyvinyl pyrrolidone (Kollidon SR) , Hydroxypropyl methyl cellulose (HPMC K15 M), Hydroxypropyl methyl cellulose (HPMC K100 M) , Dicalcium phosphate anhydrous (A-Tab) were gifted by Colorcon Asia Pvt. Ltd., Goa , Directly Compressible Lactose , Polyvinyl pyrrolidone (PVP K30) were procured by DMV International, Netherlands, Talc, Magnesium Stearate, Colloidal Silicon dioxide (Aerosil) were procured by Loba chemie,cochin.

Formulation of Sustained Release Matrix Tablets

Preparation of matrix tablets by direct compression method

Different tablet formulation were prepared by direct compression method. Formulation B1, B2 and B3 shown in Table No.10 were prepared by direct compression method. The formulation are composed of Drug Zidovudine, polymer Polyvinyl acetate – polyvinyl pyrrolidone (Kollidon SR), and Dicalcium phosphate anhydrous granular (A-Tab), talc, magnesium stearate, and silicon dioxide (aerosil). Firstly Zidovudine and polymer Kollidon SR was mixed in a polybag and passed through sieve no. 30# then followed by sieve no. 40#. Then passed A-Tab from sieve no. 40# and mixed with the above blend then passed talc and magnesium stearate separately from sieve no. 40# and added to the above blend and mixed in a polybag for 3 mins. and silicon dioxide was passed through sieve no. 40# and added to the above blend for formulation IInd and IIIrd. The lubricated blend was evaluated for precompression parameters and then compressed using 11mm punch into tablets. Compression pressure was adjusted during tableting of each formula to get the tablet hardness in the range of 130 – 170 N. The total weight of tablet was kept at 500 mg.

Preparation of matrix tablets by wet granulation method

Different tablet formulations were prepared by Wet granulation method. Formulation B4 – B8 shown in Table No. 10 were prepared by Wet granulation method. The formulation are composed of Drug Zidovudine, polymer Hydroxypropyl methyl cellulose (HPMC K15M, HPMC K100M), and Dicalcium phosphate anhydrous granular (A-Tab), Lactose, Polyvinyl pyrrolidone (PVP K30), isopropyl alcohol, magnesium stearate. Firstly Zidovudine and polymer HPMC K15 M or HPMC K100M was mixed in a polybag and passed through sieve no. 30# then followed by sieve no. 40#. Then passed A-Tab or Lactose DCL15 from sieve no. 40# and mixed with the above blend then PVP K30 was dissolved in sufficient quantity of IPA to get clear solution and added this solution to above blend to make granules. Then dried the granules in rapid dryer and passed through the sieve no. 18# and passed magnesium stearate separately from sieve no. 40# and added to the above blend and mixed in a polybag for 3 mins. The lubricated granules were evaluated for precompression parameters and then compressed using 11mm punch into tablets. Compression pressure was adjusted during tableting of each formula to get the tablet hardness in the range of 230 – 250 N. The total weight of tablet was kept at 500 mg.

Coating of Tablets

Coating of the tablets was done in conventional coating pan with 10%w/w aqueous Opadry AMB solution having pH of 5.05. Firstly tablets were put in to the pan and maintained the bed temperature at 35 – 40°C with inlet air temperature of 60°C and speed of coating pan was set at 8 rpm, peristaltic pump speed at 1 rpm, then spray was done with nozzle at atomizing air pressure 2 kg/cm^2, with spray rate of 2ml/min. and after achieving the coating layer and buildup, the spray of solution was stopped and slowly temperature of the tablets were decreased to room temperature while continuing the pan rotation and tablets were taken out and analyzed.

Table 1: Coating solution

S. No.	Ingredients	Quantity/tab (in mg)	Quantity (in g)
1	Opadry AMB	7.5	5.0
2	Purified Water	-	45.0

Sustained release matrix tablets of Zidovudine were prepared and evaluated. In the present study eight formulations with variable concentration of polymer were prepared and evaluated for physico-chemical parameters, in-vitro release studies and stability studies. The formulated batches were shown in Table No. 2.

Table 2: Formulated batches sustained release matrix tablets of zidovudine

S. No.	Ingredients	B1	B2	B3	B4	B5	B6	B7	B8
1	Zidovudine	300	300	300	300	300	300	300	300
2	Kollidon SR	60	60	75	-	-	-	-	-
3	HPMC K15 M	-	-	-	60	60	90	-	-
4	HPMC K100 M	-	-	-	-	-	-	60	75
5	DCP (A-Tab)	125	120	105	110	-	-	-	-
6	Lactose	-	-	-	-	110	80	110	95
7	PVP K30	-	-	-	25	25	25	25	25
8	IPA				Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
9	Talc	10	10	10	-	-	-	-	-
10	Mg Stearate	5	5	5	5	5	5	5	5
11	Aerosil	-	5	5	-	-	-	-	-

All quantities are in mg and wt. of tablet 500 mg

RESULTS AND DISCUSSION

Preformulation Studies

Determination of melting point

Melting point of Zidovudine was found in the range of 123 - 125^{0}C, which complied with the standard, indicating purity of the drug sample.

Solubility

Zidovudine was found soluble in water, phosphate buffer pH 1.2, 5.8, 6.8 and 7.4, ethanol and methanol and slightly soluble in isopropyl alcohol.

Powder Characteristics

Powder characteristics of Zidovudine were performed for Bulk density, Tapped density, % Compressibility, Porosity. These were found as 0.26g/ml, 0.37g/ml, 29.27% and 29% respectively.

pH of the solution

pH of the 1% solution of Zidovudine was determined by μpH Cal_{10} pH analyzer. It was found to be 6.2.

EVALUATION STUDIES

Evaluation of Granules

Bulk Density

The bulk density for the formulated blend was carried out for all formulations and found in the range of 0.37 – 0.50 g/ml. Results were shown in Table No. 3

Tapped density

The tapped densities for the formulated blend was carried out for all formulations and found in the range of 0.45 – 0.62 g/ml. Results were shown in Table No.3.

Angle of repose

The angles of repose for the formulated blends were carried out and the results were shown in Table No.3. It concluded that the entire formulations blend was found in the range of $27^0.70'$ to $39^0.8'$.

Compressibility index

Compressibility index was carried out and the results were shown in Table No.3. It were found between 11.1% to 21.2 % indicating the powder blend have the required flow property for compression except for batch B1 that is having %compressibility 27.2%.

Porosity

Porosity was carried out and the results were shown in Table No.3. It were found between 12% to 23 % indicating the powder blend have the required flow property for compression except for batch B1 that is having % porosity 28%.

Hausner's Ratio

Hausner's Ratio was carried out and the results were shown in Table No.3. It were found between 11.1% to 21.2 % indicating the powder blend have the required flow property for compression except for batch B2 that is having Hausner's ratio 27.2%.

Table 3: Characterization of trial blends

B. NO	Bulk density (g/ml)	Tapped density (g/ml)	Compressibil-ity index (%)	Hausner's ratio	Porosity (%)	Angleof repose (θ)	Loss on drying (%)
B1	0.40	0.55	27.2	1.37	28	39°.8′	-
B2	0.47	0.55	14.5	1.17	15	32°.8′	-
B3	0.50	0.62	20.0	1.25	20	32°.4′	-
B4	0.37	0.47	21.2	1.27	23	28°.3′	2.26
B5	0.38	0.43	11.6	1.13	12	28°.7′	2.31
B6	0.40	0.45	11.11	1.12	12	29°.3′	2.08
B7	0.38	0.47	19.1	1.23	20	27°.7′	2.11
B8	0.38	0.45	15.5	1.18	16	27°.9′	2.17

Evaluation of Tablets

Weight Variation

The percentage weight variations for all formulations were tabulated in Table No. 4. All the formulated tablets passed weight variation test except formulation B1 as the % weight variation was within the pharmacopoeial limits of ±5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

Thickness Test

The thickness was determined for formulated tablets and tabulated in Table No. 4. Tablets mean thickness (n=3) were uniform in B1 to B8 formulations and were found to be in the range of 3.74mm to 3.90mm for batches B1 to Batch B3 and 4.14mm to 5.11mm for batches B4 to B8 and the coated tablets having thickness 5.13mm to 5.18 mm.

Hardness Test

The measured hardness of tablets of each batch ranged between 130 – 170N for formulation (B1-B3) and 230 - 250N for formulation (B4-B8) were tabulated in Table No.4. This ensures good handling characteristics of all batches.

Friability Test

The values of friability test were tabulated in Table No.4. The % friability was less than 1% in all the formulations except formulation B4 ensuring that the tablets were mechanically stable.

Content Uniformity

The percentage of drug content for B1 to B8 was found to be between 97.85% and 99.53% of Zidovudine, it complies with official specifications. The results were shown in Table No.4.

Table 4: Physical parameters of tablets from each batch

B. NO.	Weight variation Test (mg)*	Thickness Test (mm)*	Hardness Test (n)*	Friability Test (%)	Drug content (%)
B1	502.4±25.7	3.90±0.18	149.0±15.09	0.36	-
B2	495.2±3.11	3.82±0.06	151.3±8.96	0.33	99.53
B3	500.3±3.06	3.74±0.09	147.6±8.32	0.10	98.73
B4	501.3±2.7	4.15±0.10	236.6±4.16	1.26	-
B5	501.8±4.62	4.14±0.08	239.6±7.23	0.68	97.85
B6	502.8±2.67	4.14±0.10	235.3±6.11	0.30	99.23
B7	496.6±1.80	4.18±0.13	239.0±4.35	0.10	98.79
B8	500.4±1.9	5.13±0.02	236.3±3.51	0.11	98.72
B8c	510.2±1.15	5.18±0.03	241.6±4.50	-	97.84

* Each value represents the mean ± standard deviation (n = 3)

* B8 = Core Tablet

* B8c = Coated Tablet

In-vitro Dissolution Study and Kinetic modeling of drug release

All the eight formulation of prepared matrix tablets of Zidovudine were subjected to in-vitro release studies except batch B1 and B4 these studies were carried out using Electrolab TDT 08L dissolution apparatus (USP). The dissolution medium consisted of 900 ml of purified water for 12 hrs.

The results obtained in in-vitro release studies were plotted in different model of data treatment as follows:

1. Cumulative percent drug released vs. time (zero order rate kinetics)

2. Log cumulative percent drug retained vs. time (First Order rate Kinetics)

Log Cumulative percent drug released vs. square root of time (Higuchi's

Classical Diffusion Equation)

4. Log of cumulative % release Vs. log time (Peppas Exponential Equation)

5. (Percentage retained)$^{1/3}$ Vs. time (Hixson –Crowell Erosion Equation)

The release of Zidovudine from sustained release tablet of the various formulations varied according to the ratio of the different polymer. In case of tablets of formulation B1 containing drug to polymer (Kollidon SR) ratio 1:0.2 failed in weight variation, so for in the next formulation B2, 1% Aerosil has been added to improve the flow property, but the release was more. Formulation B3, the concentration of polymer Kollidon SR was increased and drug to polymer ratio was 1:0.25 and release was less at 4th and 12th hr. These all the formulation (B1-B3) were done with direct compression. Then the method of formulation was changed from direct compression to wet granulation method and polymer has changed from kollidon SR to HPMC.Formulation B4 was prepared with drug to polymer (HPMC K15M) ratio 1:0.2 using the same excipients; it failed in friability (i.e. 1.16%). So far in formulation B5 dicalcium phosphate anhydrous granular (A-Tab) was replaced with Lactose, in this formulation release was high and released complete drug within 10 hrs. In formulation B6 drug to polymer ratio was increased (1:0.3) then also release was high .

In formulation B7 higher viscosity grade polymer i.e. HPMC K100 M

Was taken in drug to polymer ratio 1:0.2 in this formulation also release was high.

Formulation B8 was prepared by taking drug to polymer ratio 1:0.25 and it has given optimum release and all the physical parameters were within the Pharmacopoeial limit.So that this formulation was taken as the optimized formulation and coating was done with the Opadry AMB, 1.5% build was given to prevent from moisture contamination. The kinetic values obtained for formulation B8 were shown in Table No.30. The values of in-vitro release were attempted to fit into various mathematical models. The regression coefficients values for formulation B8 of zero order and first order plots were found to be 0.943 and 0.9802.Graphical representation of cumulative drug released as a function of square root of time. This Higuchi plot was almost linear with regression coefficient value 0.9925 for formulation B8. The linearity suggests that the release of Zidovudine from HPMC K100M was diffusion controlled Plot of log cumulative percent drug released vs. log time is shown in. Peppas-korsmeyer equation was given as

$$\% R = ktn$$

Where, R= drug release

K=constant

n=slope

t=time

This model is widely used when the release mechanism is not well know or when more than one type of release phenomenon was involved. The 'n' values can be used to characterize diffusion release mechanism as

'n'	**Mechanism**
0.5	Fickian diffusion
0.5<n<1	Non- fickian diffusion
1	Class II transport

The 'n'value for B8 was found to be 0.5062 which is indicates that the release approximates non-fickian diffusion mechanism.

Swelling Study

Swelling study was performed on all the batches (B5 to B8) for 12 hrs. The results of swelling index were shown in Table No. 14. Swelling index against time (hrs.) was plotted in Fig. No. 25 to Fig. No. 27. Swelling index was calculated with respect to time. Swelling index increased with time as the weight gain by the tablet was increased proportionally with the rate of hydration. The swelling index of the Batch B4 to B6 containing HPMC K15M was less as compare to the Batch B7 and B8 containing HPMC K100M, it might be due to the high viscosity of HPMC K100M than HPMC K15M. In case of batch B5 to B6 containing HPMC K15M in concentration of 12% and 18% respectively, showed considerable swelling and achieve 69.2% and 77.3% swelling in 4 hrs. and afterwards weight of the tablet decreases due to erosion of the polymer matrix.The Batch B7 and B8 containing HPMC K100M in 12% and 15% concentration initially swell slowly but achieve maximum swelling and achieve 92.5% and 96.3% swelling in 4 hrs. and afterwards weight of the tablet decreases due to erosion of the polymer matrix. In the present study, the higher swelling index was found for tablets of batch B7 and batch B8 containing HPMC K100M having nominal viscosity of more than 1, 00,000 cps. Thus, the viscosity of the polymer had major influence on swelling process and matrix integrity hence from the above results it can be concluded that linear relationship exists between swelling process and viscosity of polymer.

Table 5: Dissolution profile of batch no. B2 to B8

B. NO.	**Cumulative % drug release (hrs.)**						
	1	**2**	**4**	**6**	**8**	**10**	**12**
B2	27.72	37.55	52.49	65.69	76.03	85.10	93.10
B3	23.34	28.72	49.65	71.92	38.02	64.93	78.93
B5	37.91	46.83	68.01	86.63	96.85	101.03	-
B6	27.33	38.95	56.06	65.74	79.39	88.43	100.7
B7	31.81	40.73	53.06	69.12	83.10	91.22	98.09
B8	26.06	34.57	45.84	57.13	72.00	81.59	87.30
B8c	25.60	33.75	44.73	56.37	70.80	80.74	86.55

* B8 = Core Tablet

* B8c = Coated Tablet

Table 6 : Swelling index of tablets of batch B5 to B8

S. No.	Time (hrs.)	Swelling Index (%)			
		B5	B6	B7	B8
1	1	23.6	32.4	39.6	42.5
2	2	42.4	48.6	54.1	63.2
3	4	69.2	77.3	92.5	96.3
4	6	61.3	67.3	89.6	91.8
5	8	54.5	59.2	78.2	84.4
6	10	51.3	53.6	69.4	76.3
7	12	46.2	49.1	65.7	74.6

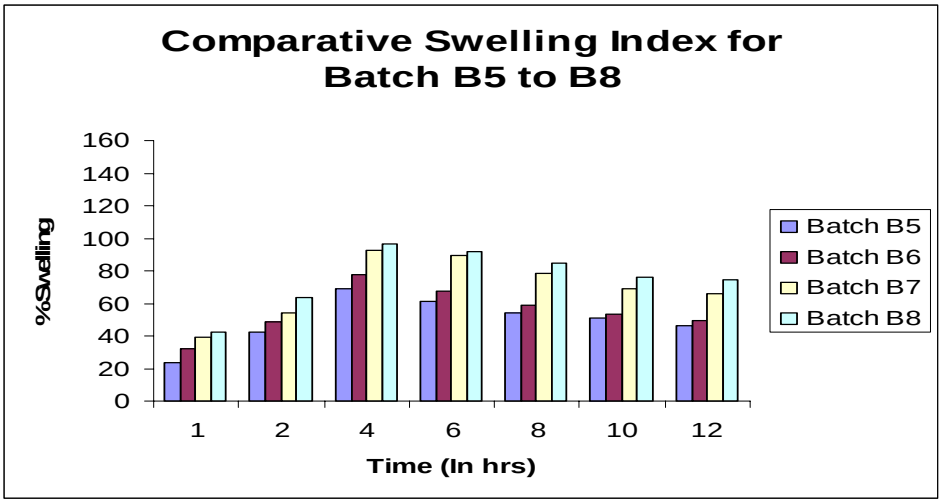

Fig. 1 : Comparative Swelling Index For Batch B5 To B8

Table 7 : In-vitro release profile of Zidovudine sustained release matrix tablets of B2 formulation

Time (hrs)	Root T	Log T	Cum drug release	% Cum drug retained	% Log Cum drug release	% Log Cum drug retained	(% % retained)$^{1\backslash 3}$
1	1	0	27.27	72.73	1.43	1.86	4.17
2	1.414	0.301	37.55	62.45	1.57	1.79	3.96
4	2	0.602	52.49	47.51	1.72	1.67	3.62
6	2.449	0.778	65.69	34.31	1.81	1.53	3.24
8	2.828	0.903	76.03	23.97	1.88	1.367	2.88
10	3.162	1	85.10	14.9	1.92	1.17	2.46
12	3.464	1.079	93.10	6.9	1.96	0.83	1.90

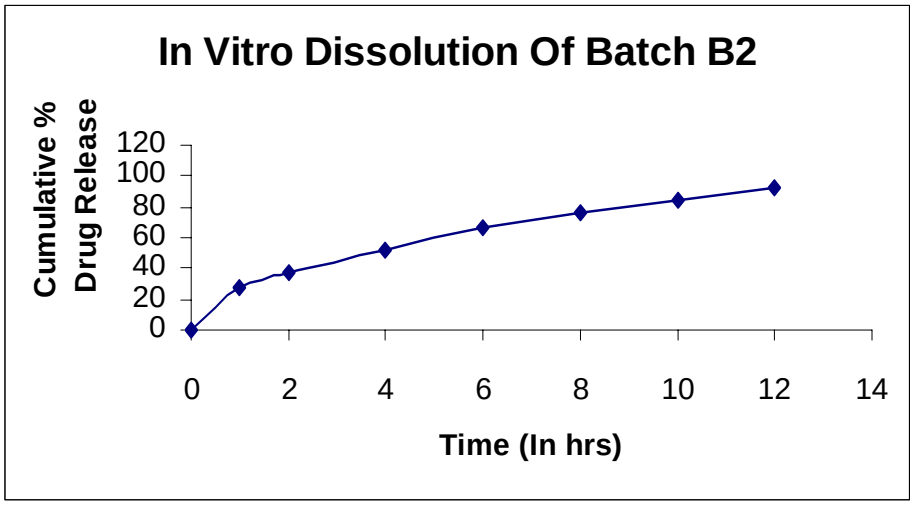

Fig. 2 : Dissolution profile of batch B2

Table 8 : In-vitro release profile of Zidovudine sustained release matrix tablets of B3 formulation

Time (hrs)	Root T	Log T	Cum drug release	% Cum drug retained	% Log Cum drug release	Log % Cum drug retained	(% % retained)$^{1\backslash 3}$
1	1	0	23.34	76.66	1.36	1.88	4.24
2	1.414	0.301	28.72	71.28	1.45	1.85	4.14
4	2	0.602	38.02	61.98	1.58	1.79	3.95
6	2.449	0.778	49.65	50.35	1.69	1.70	3.69
8	2.828	0.903	64.93	35.07	1.81	1.54	3.27
10	3.162	1	71.92	28.08	1.85	1.44	3.03
12	3.464	1.079	78.93	21.07	1.89	1.32	2.76

Fig. 3: Dissolution profile of batch B3

Table 9: *In-vitro* release profile of Zidovudine sustained release matrix tablets of B5 formulation

Time (hrs)	Root T	Log T	Cum drug release	% Cum drug retained	% Log Cum drug release	% Log Cum drug retained	% (% retained)$^{1\backslash 3}$
1	1	0	37.91	62.03	1.57	1.79	3.95
2	1.414	0.301	46.83	53.17	1.67	1.72	3.76
4	2	0.602	68.01	31.99	1.83	1.50	3.17
6	2.449	0.778	86.63	13.37	1.93	1.12	2.37
8	2.828	0.903	96.85	3.15	1.98	0.49	1.46
10	3.162	1	101.03	-1.03	2.00	-0.012	-1.00

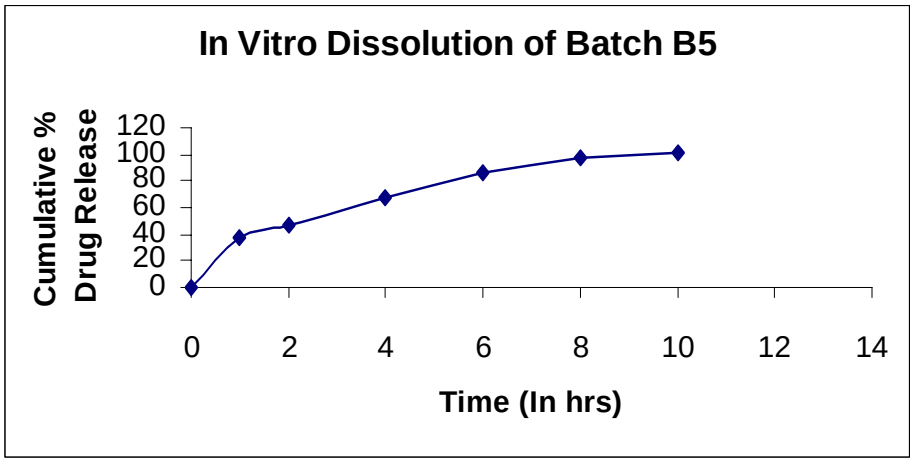

Fig. 4 : Dissolution profile of batch B5

Table 10: *In-vitro* release profile of Zidovudine sustained release matrix tablets of B6 formulation

Time (hrs)	Root T	Log T	Cum drug release	% Cum drug retained	% Log Cum drug release	% Log Cum drug retained	% (% retained)$^{1\backslash 3}$
1	1	0	27.33	72.67	1.43	1.86	4.17
2	1.414	0.301	38.95	61.05	1.59	1.78	3.93
4	2	0.602	56.06	43.94	1.74	1.64	3.52
6	2.449	0.778	65.74	34.26	1.81	1.53	3.24
8	2.828	0.903	79.39	20.61	1.89	1.31	2.74
10	3.162	1	88.43	11.57	1.94	1.06	2.26
12	3.464	1.079	100.7	-0.7	2.00	0.15	-0.88

Fig. 5 : Dissolution profile of batch B6

Table 11: *In-vitro* release profile of Zidovudine sustained release matrix tablets of B7 formulation

Time (hrs)	Root T	Log T	Cum % drug release	Cum % drug retained	Log Cum % drug release	Log Cum % drug retained	(% retained)$^{1\backslash 3}$
1	1	0	31.81	68.19	1.50	1.83	4.08
2	1.414	0.301	40.73	59.27	1.60	1.77	3.89
4	2	0.602	53.06	46.94	1.72	1.67	3.60
6	2.449	0.778	69.12	30.88	1.83	1.48	3.13
8	2.828	0.903	83.10	16.9	1.91	1.22	2.56
10	3.162	1	91.22	8.78	1.96	0.94	2.06
12	3.464	1.079	98.09	1.91	1.99	0.28	1.24

Fig. 6: Dissolution profile of batch B7

Table 12: In-vitro release profile of Zidovudine sustained release matrix tablets of B8 formulation (core tablet)

Time (hrs)	Root T	Log T	Cum % drug release	Cum % drug retained	Log Cum % drug release	Log Cum % drug retained	(% retained)$^{1\backslash 3}$
1	1	0	26.06	73.94	1.41	1.86	4.19
2	1.414	0.301	34.57	65.43	1.53	1.81	4.02
4	2	0.602	45.84	54.16	1.66	1.73	3.78
6	2.449	0.778	57.13	42.87	1.75	1.63	3.49
8	2.828	0.903	72.00	28.00	1.85	1.44	3.03
10	3.162	1	81.59	18.41	1.91	1.26	2.64
12	3.464	1.079	87.30	12.7	1.94	1.10	2.33

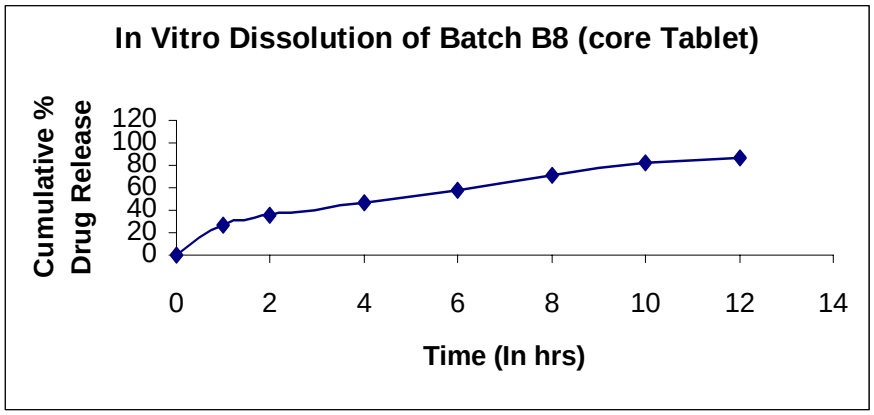

Fig. 7: Dissolution profile of batch B8 (Core Tablet)

Table 13 : In-vitro release profile of Zidovudine sustained release matrix tablets of B8 formulation (coated tablet)

Time (hrs)	Root T	Log T	Cum % drug release	Cum % drug retained	Log Cum % drug release	Log Cum % drug retained	(% retained)$^{1\backslash 3}$
1	1	0	25.60	74.4	1.40	1.87	4.20
2	1.414	0.301	33.75	66.25	1.52	1.82	4.04
4	2	0.602	44.73	55.27	1.65	1.74	3.80
6	2.449	0.778	56.37	43.63	1.75	1.63	3.52
8	2.828	0.903	70.80	29.2	1.85	1.46	3.07
10	3.162	1	80.74	19.26	1.90	1.28	2.68
12	3.464	1.079	86.55	13.45	1.93	1.12	2.37

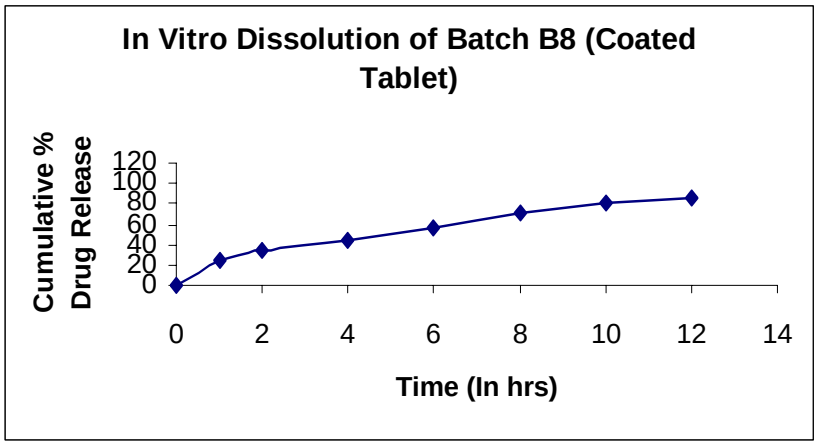

Fig. 8: Dissolution Profile Of Batch B8 (Coated Tablet)

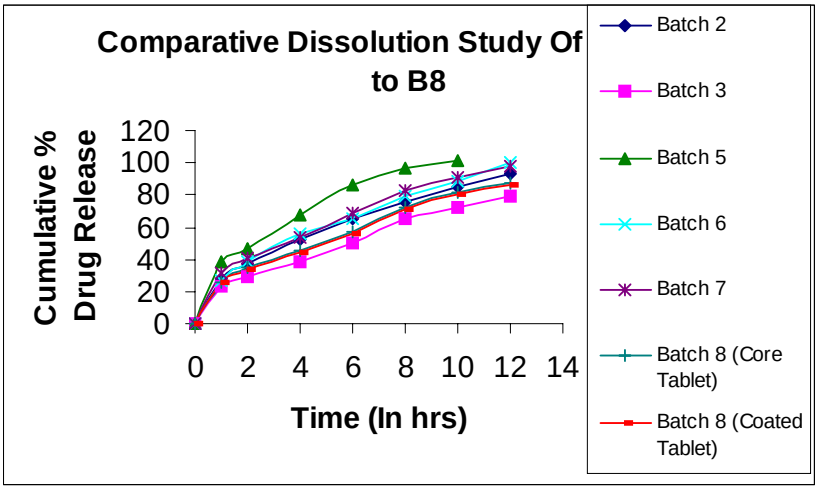

Fig. 9: Comparative Dissolution Profile Of Batch B2 To B8

Table 14: Kinetic values obtained from *in-vitro* released data of formulation B8

Kinetic values obtained from invitro released data of formulation B8			
Kinetic Model	**Intercept**	**Slope**	**R^2**
Zero-order plot	14.468	6.5765	0.943
First-order plot	1.9809	-0.0685	0.9802
Higuchi plot	-1.2769	25.05	0.9925
Peppas-korsmeyer	1.3771	0.5062	0.9891
Hixson Crowell	4.4221	-0.1692	0.9919

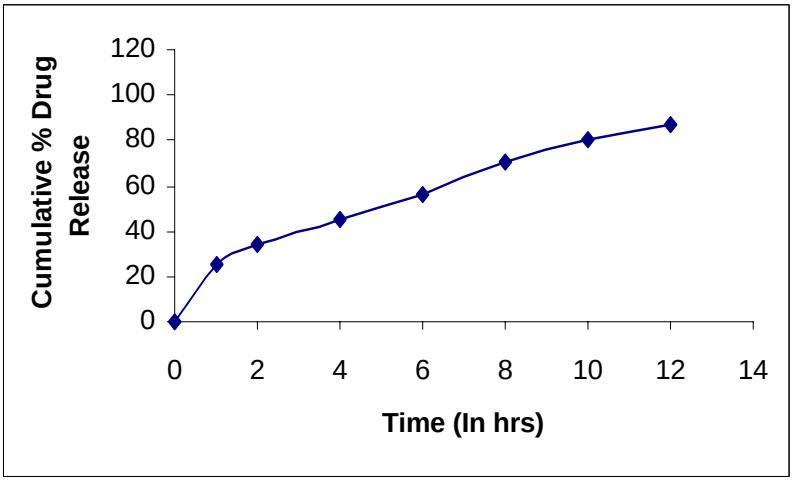

Fig. 10: *In vitro* cumulative % drug release v\s time for formulation (B8) of zidovudine (zero order release)

Fig. 11: Log cumulative % drug retained v/s time for formulation (b8) of zidovudine [first order plot]

Fig. 12: Cumulative % drug released v/s root time for formulation (B8) of zidovudine [Higuchi Matrix]

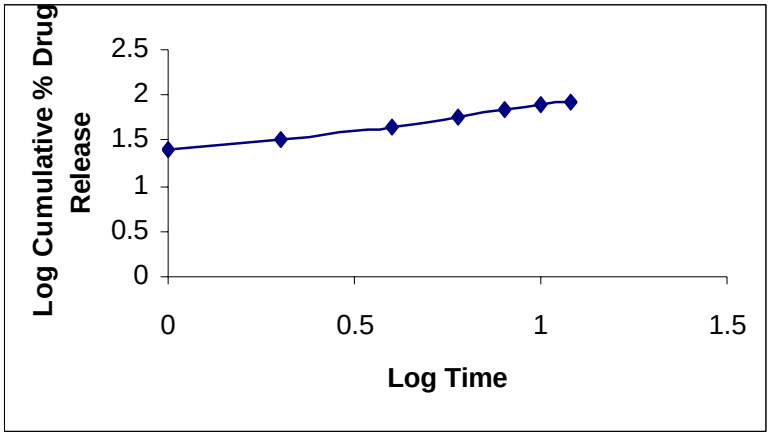

Fig. 13: Log cumulative % drug released v/s log time for formulation (B8) Of Zidovudine [Peppas]

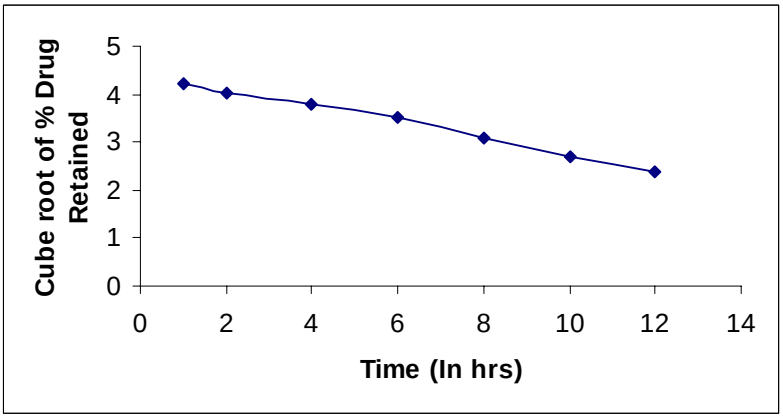

Fig. 14: Cube Root Of % Drug Retained V/S Time For Formulation (B8) Of Zidovudine [Hixson-Crowell]

SUMMARY AND CONCLUSION

The present study was undertaken with an aim to formulate and evaluate the Zidovudine sustained release matrix tablets by using different polymers. Preformulation study was done initially and results directed for the further course of formulation. Based on Preformulation studies different batches of Zidovudine were prepared by using selected excipients. Granules were evaluated for Bulk density, tapped density, compressibility index, Porosity, Angle of repose, Hausner's ratio before being punched as tablets. Various formulations of sustained release matrix tablets of Zidovudine were formulated using various polymers viz, kollidon SR, HPMC K15M and HPMC K100M in different ratio by direct compression and by wet granulation technique. The tablets were evaluated for physical characterization, *in- vitro* release study and stability studies. Observation of all formulations for

physical characterization had shown that, all of them comply with the specifications of official pharmacopoeias and/or standard references. Results of *in- vitro* release profile indicated that among all the formulations, B8 was the most promising formulation as it showed that 86.55% drug release within 12 hrs. and all the physical parameters and release profile was according to the specification, and these formulation was coated with opadry AMB to prevent from moisture contaimination. The *in-vitro* release data was plotted for various Kinetic models. The R^2 value for Higuchi plot was found to be 0.9925 which indicates drug release was governed by diffusion mechanism and slope value of korsmeyer - peppas equation was found to be 0.5062 which indicate that drug was released by non-fickian release mechanism. From the above points, it was concluded that formulation B8 is an ideal or optimized formulation for 12 hours release as it fulfills all the requirements for sustained release tablets. In future *in-vivo* study will be carried out to correlate with *in-vitro* release data for establishing the product.

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