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ZIDOVUDINE: FORMULATION AND DEVELOPMENT OF MATRIX TABLETS

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ABSTRACT

The aim of the preset study was to formulate and evaluate controlled release matrix tablets of Zidovudine which was used as a model drug and by incorporating the drug in matrix forming hydrophilic polymers such as HPMC in different ratios, hydrophobic polymer such as Carbopol were used as release modulators. Primary objective of this study is to improve bioavailability, to prevent fluctuation of concentration of the drug in plasma, to reduce dosing frequency thereby to improve patience compliance through oral controlled release matrix systems. Study of pre-compressive parameters and post-compressive parameters for the prepared matrix tablets like; Hardness test, Weight variation test, uniformity of size and drug content, study of swelling behavior, In-vitro dissolution studies. The data will be subjected to statistical analysis mechanism and kinetics of release shall be studied and reported. Accelerated stability studies for the final formulations according ICH guidelines. Drug-excipients compatibility study by FTIR Spectroscopy.

KEYWORDS: Zidovudine, HPMC, Matrix, Hydrophilic gels.

INTRODUCTION

Oral route is the most preferred route for administration of drugs. Tablets are the most popular oral formulations available in the market and preferred by the patients and physicians alike. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses, and therefore have several disadvantages.[1] Controlled release (CR) tablet formulations are much desirable and preferred for such therapy because they offer better patient compliance, maintain uniform

drug levels, reduce dose and side effects, and increase safety margin for high potency drugs.[2]

The immediate release dosage forms have some limitations such as.

Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance. A typical peak-valley plasma conc. time profile is obtained which makes attainment of steady state condition difficult.

The unavoidable fluctuations in the drug concentration may lead to under medication or over medication as the Css values fall or rise beyond the therapeutic range.

To overcome these problems sustained release systems were introduced three decades ago. Sustained release, sustained action, prolonged release, controlled release, extended action, timed release, depot and repository dosage forms are the terms used to identify drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. The term "controlled release" has become associated with those systems from which therapeutic agents may be automatically delivered at predefined rate over long period of time.[3]

Many strategies are available for the design and development of modified-release drug delivery formulations. The primary purpose of these drug delivery devices is to improve the state of disease management by modifying the pharmacokinetic profiles of therapeutic agents normally administered as conventional tablets or capsules. Conventional oral dosage forms often produce fluctuations of drug plasma level that either exceed safe therapeutic level or quickly fall below the minimum effective level; this effect is usually totally dependent on the particular agent's biologic half-life, frequency of administration, and release rate. It is recognized that many patients can benefit from drugs intended for chronic administration by maintaining plasma levels within a safe and effective range.

Zidovudine (AZT) is the first anti-HIV compound approved for clinical use is widely used for treatment of AIDS either alone or in combination with other antiviral agents. However, the main limitation to therapeutic effectiveness of AZT is its dose dependent hematological toxicity, low therapeutic index, short biological half-life, and poor bioavailability. In the systemic circulation, it is first converted to AZT triphosphate, which is pharmacologically active and prevents the replication of the HIV virus. The biological half-life of AZT-

triphosphate is 4 hours, thus necessitating frequent administration (3 to 4 times a day) to maintain constant therapeutic drug levels. Treatment of AIDS using conventional formulations of AZT is found to have many drawbacks such as adverse side effects due to accumulation of drug in multidose therapy, poor patient compliance and high cost. So, CR formulations of AZT can overcome some of these problems. AZT is absorbed throughout the GIT. The drug is freely soluble at any pH, hence judicious selection of release retarding excipients is necessary for achieving constant in-vivo release. The most commonly used method of modulating the drug release is to include it in a matrix system.[4] Matrix based CR tablet formulations are the most popular and easy to formulate on a commercial scale in an industry. The matrix tablets can be prepared via wet granulation or by direct compression.[5] Many polymers have been used in the formulation of matrix based CR drug delivery systems. Reports are found on the use of hydrophilic polymers like hydroxyl propyl methylcellulose (HPMC), methylcellulose, sodium car boxy methylcellulose[6], carbopols[7] and polyvinyl alcohol[8] for the preparation of CR formulations of different drugs. Hydrophilic polymer matrix systems are widely used for designing oral controlled drug delivery dosage forms because of their flexibility to provide a desirable drug release profile, cost effectiveness, and broad regulatory acceptance.[9]

The hydrophilic polymers selected for the present study were HPMC, This polymer provide pH-independent drug release to oral dosage forms that can be used for formulating the sustainedrelease dosage forms. However, the use of hydrophilic matrix alone for extending drug release for highly water soluble drugs is restricted due to rapid diffusion of the dissolved drug through thehydrophilic gel network. For such drugs it becomes essential to include hydrophobic polymers in the matrix system.[10] Hence, in the present work, an attempt has been made to formulate the extended-release matrix tablets of AZT and tested for controlled delivery of drug using hydrophilic matrix material (HPMC) along or in combination with hydrophobic Carbopol-940.

MATERIALS AND METHODS

Zidovudine is obtained from Dr. Reddys laboratories, India, polymers like HPMC and CARBOPOL-940 from Sd fine chemicals, Mumbai, and all other common excipients were of L. R grade.

Preparation of Matrix tablets of Zidovudine: Matrix tablets containing 300 mg of Zidovudine along with various amounts of polymers such as HPMC, Carbopol-940, Microcrystlline

cellulose, sodium alginate and other excipients (such as magnesium stearate) were used and tablets prepared by wet granulation technique using isopropyl alcohol. All preparations were stored in airtight containers at room temperature for further studies.

Formulation of Zidovudine Matrix Tablet: Formula for one tablet: A total of 7 formulations (F1 to F7) were prepared each formulation contains zidovudine (ZDV) 300mg, HPMC and Carbopol in different ratios along with other common excipients. The formulas are shown in Table1.

Table No. 1: Composition of Zidovudine Matrix Tablets.

Sr. No.	INGREDIENTS	FORMULATIONS (mg)						
		F1	F2	F3	F4	F5	F6	F7
1	**ZIDOVUDINE(ZDV)**	300	300	300	300	300	300	300
2	**HPMC**	100	125	150	50	75	200	-
3	**CARBOPOL**	100	75	50	150	125	-	200
4	**SODIUM ALGINATE**	75	75	75	75	75	75	75
5	**ISOPROPL ALCOHOL**	q.s	q.s	q.s	q.s	q.s	q.s	q.s
6	**MICROCRYSTALLINE CELLULOSE**	150	150	150	150	150	200	200
7	**MAGNESIUM STEARATE**	5	5	5	5	5	5	5
8	**TOTAL WEIGHT**	**730**	**730**	**730**	**730**	**730**	**730**	**730**

Characterization

Fourier transformed infrared (FTIR) spectra of zidovudine was taken by using the KBr disk method. The scanning range was 400 to 4000 Cm^{-1}. The major peaks in recorded spectra were compared with standard spectra. These assignments are in full support of the given structures of drugs. The I.R. spectrum of zidovudine was shown in Fig.1.

Pre-Compressive parameters

1) Bulk Density[11]

a) Loose Bulk Density

An accurately weighed (2.5G) quantity of powder was transferred to a 10ml measuring cylinder and the volume occupied by the powder in terms of ml was recorded.

$$\textbf{Loose bulk Density (L.B.D)} = \frac{\textbf{Weight of powder in gm}}{\textbf{Volume of packing in mL}}$$

b) Tapped Bulk Density

The loosely packed powder in the measuring cylinder was to tapping 100 times on a plane hard wooden surface and volume occupied in mL was noted.

$$\textbf{Tapped bulk Density (T.B.D)} = \frac{\textbf{Weight of powder in gm}}{\textbf{Tapped volume in mL}}$$

2) Hausner's Factor[12]

Hausner found that the ratio D F / D O was related to inter-particle friction and, as such, could be used to predict powder flow properties.

$$\textbf{Hausner's factor} = \frac{\textbf{Tapped bulk density}}{\textbf{Poured bulk density}}$$

3) Carr's Compressibility Index[13]

$$\textbf{Carr's Index} = \frac{\textbf{TBD - LBD}}{\textbf{TBD}} \times 100$$

4) Angle of Repose[14]

It is measured to find frictional forces in loose powder or granules. It is the maximum angle possible between the surface of a pile of powder or granules and horizontal plane.

$$\textbf{Tan } \theta = h / r \textbf{ or } \theta = \tan^{-1} [h / r]$$

The values ≤ 30 indicates the free flowing powder and values ≥ 40 suggest poorly flowing material shown in table 2.

Post Compressive Parameters

(a) Thickness and Diameter

6 tablets were randomly picked from each batch, thickness and diameter of each tablet was measured using a calibrated dial caliper (A ±5%is allowed).

(b) Weight Variation Test (IP 1996 method)

6 Tablets were randomly selected from each batch and weighed on a electronic balance both weight of 6 tablets and individual tablet was considered mean and standard deviation (S.d) of weight was calculated from each batch and shown in table 3.

(c) Hardness Test[15]

6 Tablets were randomly selected from each batch and hardness of each tablet was

determined by using a monsanto hardness tester. A mean of S.d values were calculated for each batch and shown in table 3.

(d) Friability Test[16]

It is the ability of tablets to withstand mechanical shocks during handling and transportations. The % of friability of prepared tablet were shown in table 3 Tablets were randomly picked from each batch and weighed and placed in the Rochi friability test apparatus and operated at rate of 25 RPM for 4 minutes (or up to 100 revolutions),tablets were de-dusted and weighed again. The loss of tablet weight due to abrasion and fracture was measured in terms of % friability (A value of <1%F is acceptable}.

$$F = \frac{W_{INITIAL} - W_{FINAL}}{W_{INITIAL}} \times 100$$

(e) Disintegration Test[17]

Disintegration test was performed as per official Pharmacopoeial method. The tablet does not disintegrate but swelled and formed gel type of masses.

(f) Swelling Characteristics of Matrix Tablet[18]

The swelling properties of matrix tablets were determined by placing the tablet in the dissolution medium at 37± 0.5ºC. The tablets were removed periodically from dissolution medium. After draining off the free water from the surfaces, they were measured for weight gain. Swelling characteristics of matrix tablets were expressed in terms of percentage Swelling index (SI %) it is calculated by using the equation.

$$SI\ \% = \frac{\text{Wt. of swollen tablet} - \text{Initial wt. of tablet}}{\text{Initial wt. of tablet}} \times 100$$

(g) Drug Content Estimation

Standard Solution

100 mg of pure Zidovudine drug was dissolved phosphate buffer pH 7.4 in a volumetric flask and the volume was makeup to100ml mark with the same solvent and sonicated for 5 minutes. 10 ml of above solution was diluted with phosphate buffer pH 7.4 to 100ml and sonicated for 5 minutes, from this respective dilutions are taken such that 2,4,6,8,10 µg/mL.

From each batch of prepared tablets, 10 tablets were collected randomly and powdered. A quantity of powder equivalent to 300 mg was transferred into a 100 ml volumetric flask, 100

ml of phosphate buffer pH 7.4 was added and the solution was sonication for about 30 min. The solution was made up to 100 ml with phosphate buffer pH 7.4, filtered and suitable dilutions were made with phosphate buffer pH 7.4.The absorbance of the resulting solution was measured at the 266 nm using blank in the reference cell. The total content of drug in the solution was calculated using the absorbance of a standard solution. The above test was done in triplicate.

In-Vitro Release Studies

In vitro drug release studies of the prepared matrix tablets were conducted for a period of 14 hours using an eight station USP XXII type 2 apparatus (Dbk Instumrnts, India) at 37±0.5ºC the paddle speed was 50 ± 1 rpm. The dissolution medium used in each flask was 900 ml of buffer media pH – 7.4. At every 1 hour interval samples of 10 ml were withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant and maintain sink conditions. After filtration and appropriate dilution, the sample solutions were analyzed at 266 nm by using double beam U.V/visible spectrophotometer (ELICO SL 244) and dissolution medium as blank. Experiments were performed in triplicates. The amount of drug present in the samples was calculated with the help of calibration curve constructed from reference standard.

Accelerated Stability Studies

The optimized matrix tablets formulation was subjected to accelerated stability studies upto3 months at 25^0c with 60% RH, 30^0 C with 75% and 40^0 c with 75%, samples were withdrawn after one, two and three months and analyzed.

RESULTS AND DISCUSSIONS

FT-IR of zidovidine

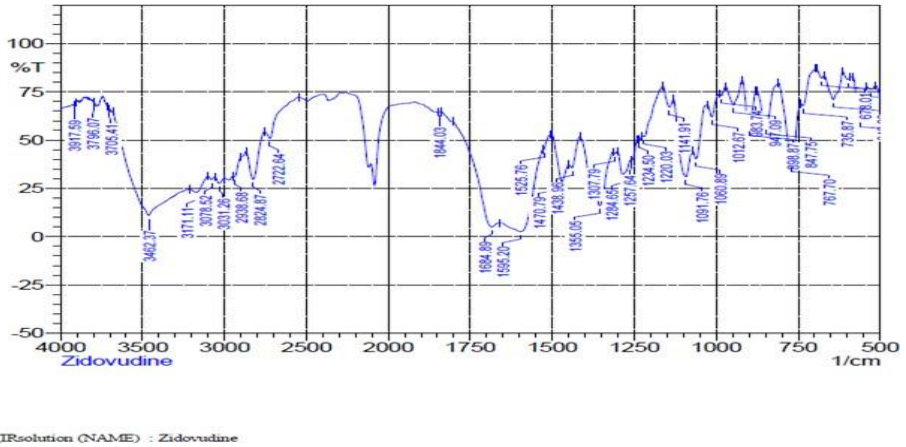

Fig. 1: Shows FTIR peaks of various functional groups of the zidovudine.

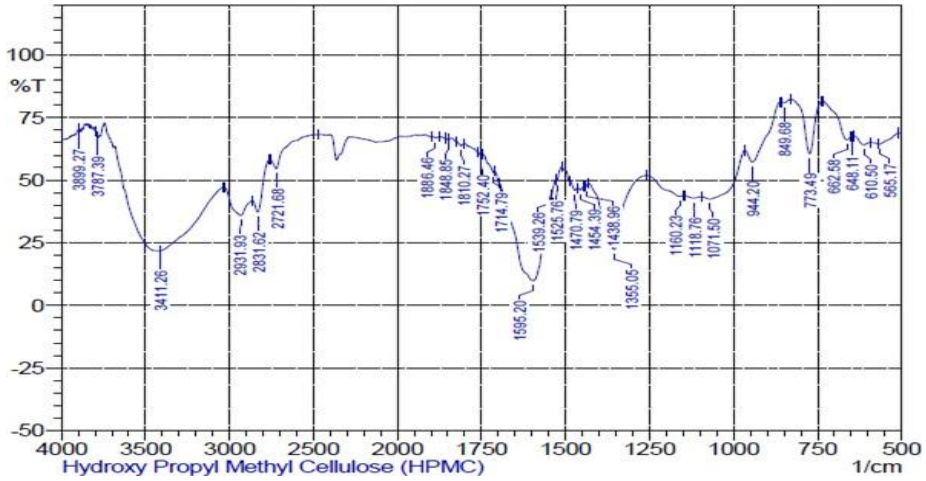

Fig. 2: Shows FTIR Peaks of Various Functional Groups of Polymer HPMC.

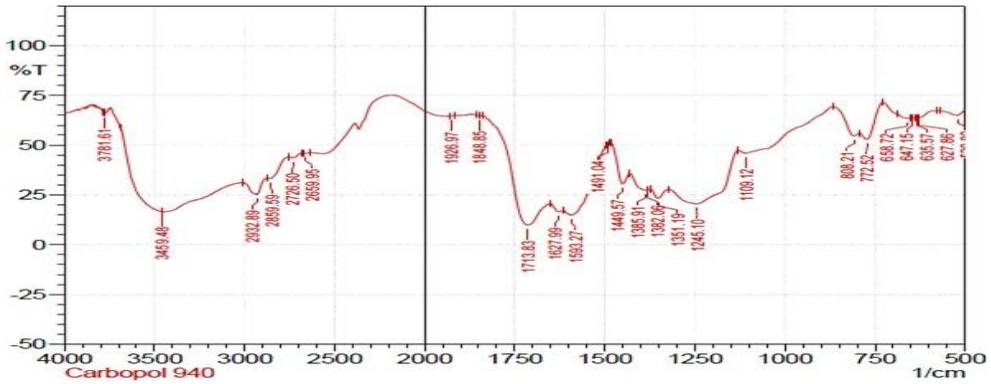

Fig. 3: Shows FTIR Peaks of Various Functional groups of Polymer CARBOPOL-940.

Drug - Excipients Compatibility

The possible chemical interaction of drug with polymer drug excipients compatibility was carried out for 3 weeks. At the end of three weeks pure drug, drug-excipients physical mixtures were analyzed by IR spectroscopy. The IR peaks in pure drug and drug excipients physical mixture are shown in fig.4. No changes in peaks this study reveals the compatibility between drugs and excipients.

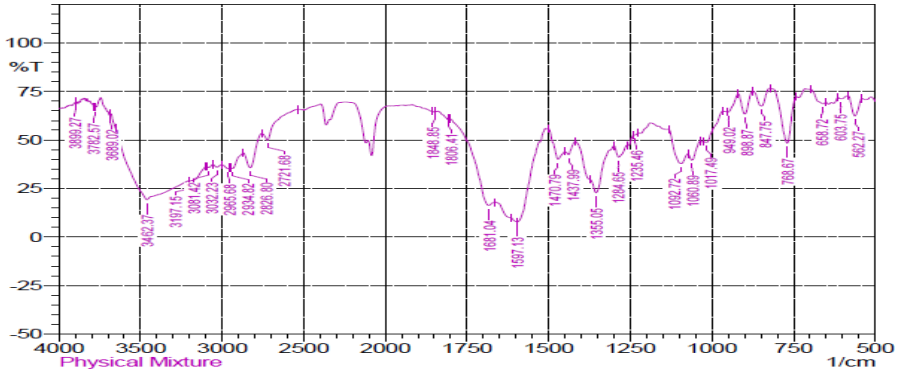

Fig. 4: Shows FTIR Peaks of Various functional groups of Physical Mixture.

Evaluation of powder flow properties:

Pre compression parameters of granules were analysed, angle of repose values of all the formulations are in region of $17.35^0 \pm 0.03$ and $20.35^0 \pm 0.04$, bulk density was found to be in a range of 0.381± 0.04 to 0.450 ± 0.03 gm/cc, and tapped density was found to be in a range of 0.436 ± 0.06 to0.480 ± 0.02 gm/cc, Hausner Ratio from1.046± 0.08 to 1.131± 0.02 and Carr's Index was found to be 4.442± 0.03 to 11.620± 0.01% Thus all the formulations were found to suitable for compression as tablets given in Table 2.

Table No. 2: Values of pre- compressive parameters of prepared formulations.

Formulation Code	Angle of Repose	Bulk density (g/ml)	Tapped Density (g/ml)	Hausner Factor	Carr's Index %
F1	20.09±0.010	0.4509±0.002	0.4803±0.006	1.066 ±0.011	6.252 ±1.051
F2	18.32±0.015	0.4426±0.001	0.4743±0.003	1.068 ±0.024	6.388 ±0.882
F3	19.50±0.017	0.3817±0.004	0.4368±0.005	1.131 ±0.045	11.620 ±0.08
F4	17.35±0.030	0.4218±0.003	0.4570±0.002	1.071 ±0.031	6.664 ±0.095
F5	19.29±0.039	0.4371±0.005	0.4501±0.006	1.046 ±0.026	4.442 ±0.069
F6	19.86±0.041	0.4462±0.008	0.471±0.004	1.068 ±0.019	6.387 ±0.108
F7	20.35±0.051	0.4349±0.006	0.4620±0.005	1.069 ±0.046	6.528 ±0.092

Evaluation of Post-Compressive Parameters of Zidovudine Matrix Tablets

The tablet formulations were subject to various post- compressive evaluation tests, such as thickness, diameter, and uniformity of weight, drug content, and hardness, friability, swelling characteristics, and in vitro dissolution studies. The results for all the formulations were shown in Table 3.

Table No. 3: Physical characteristics of prepared matrix tablets.

Formulation Code	Thickness (mm)	Hardness (kg/cm^2)	Weight variation	Friability	Drug content (%)
F1	4.10 ±0.10	6.5 ±0.20	2.1 ±0.102	0.096 ±0.012	98.1 ±0.70
F2	4.05 ±0.22	7.2 ±0.35	2.4±0.148	0.081 ±0.042	95.2±0.66
F3	3.98 ±0.29	6.8 ±0.22	1.5 ±0.192	0.075 ±0.065	95.8±0.79
F4	3.96 ±0.41	5.9 ±0.45	1.03±0.167	0.065 ±0.047	97.7±1.15
F5	4.35 ±0.58	6.9 ±0.50	2.8 ±0.182	0.095 ±0.028	98.8±1.55
F6	4.41 ±0.64	7.8 ±0.60	1.79 ±0.196	0.091 ±0.068	98.9±0.98
F7	4.49 ±0.69	8.1 ±0.41	2.92 ±0.249	0.084 ±0.088	98.5±1.55

Thickness Test: reveals that all the formulations showed uniform thickness.

Weight Variation Test

It was carried out as per official method and the average percentage deviation of all the formulation was found to be within the limit (as per Pharmacopoeial standard the deviation

should not be more than 5% for tablet having weight 400 mg).All formulations showed values within ranges.

Content Uniformity: was also carried out as per official method and it was found that all batches shows good content uniformity. It was found that all batches shows percent drug content more than 95 percent.

Hardness Test: States that all the formulations were found in the range 6 to 8 kg/cm^2.

Friability Test: Another measure of tablet hardness was the friability. Compressed tablets that lose less than 1% of their weight are generally considered acceptable. For all formulation tried here the weight loss was <1% hence acceptable.

Drug Content: The values for all the formulations were in the ranges from 95.20 to 98.90%.

Disintegration Test: The tablet of all the batches does not disintegrated but formed swelled masses.

Swelling behaviour of the Matrix Tablets

The swelling behaviour of some selected matrix tablets were measured by percentage swelling index at various time intervals and were shown in table 4. The percentage swellings in the formulations F1 to F7 were done. Formulation 5 shown a good swelling behaviour and formulation shown a low swellable behaviour during the first 2-6 hrs followed by gradual increase in the swelling. The swelling characteristics of matrix tablets were studied and the results are shown in table 4, fig.5.

Table No. 4: Swelling indices of matrix tablets in Phosphate buffer pH 7.4.

FORMULATION CODE	Initial weight (mg)	Final weight (mg)	Swelling index (%)
F1	725.20	1280.21	76.53
F2	730.10	1188.62	62.80
F3	728.51	1250.98	71.71
F4	735.20	1170.60	59.22
F5	720.80	1290.65	79.05
F6	730.56	1185.45	62.26
F7	732.84	1160.84	58.40

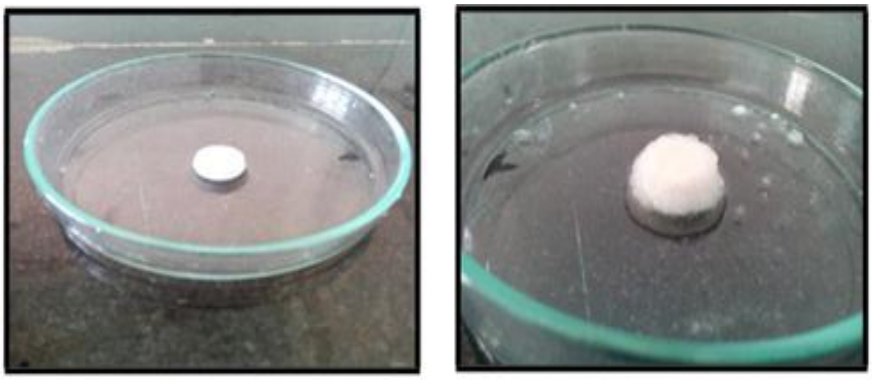

Fig. 5: Matrix tablet of ZDV in Petri dish at 0 Hrs and After Hrs.

In-Vitro Release

The in vitro release studies were carried out for all formulations in the phosphate buffer pH-7.4 as a medium, sampling was done at every one hour.

The Formulation F5 Shown a 98.90% with 75 mg of HPMC and 125mg of carbopol-940 and F1, F2, F3, F4, F6 and F7 shown improved rate of dissolution 95.10%, 96.58%, 93.56%, 95.11%, 98.90%, 92.80% and 94.30% of zidovudine respectively at 14 hours. From the group of formulations F5 formulation was observed as optimum formulation with improved dissolution rate compared to other formulations. Dissolution release was shown in figures 6 to 9. This illustrates the importance of obtaining complete tablet dissolution in order to obtain a high level of drug release. The drug release profiles are as shown in table 5.

Formulation containing 75mg of HPMC and 125mg of CARBOPOL-940 had shown maximum dissolution of zidovudine.

Table No. 5: In-vitro cumulative % release of drug from matrix tablets of Zidovudine.

Time in hours	Cumulative % drug release						
	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	4.50±0.858	3.02±1.20	3±1.45	4.5±1.22	4.95±1.31	1.5±0.98	3±0.96
2	9±1.55	4.5±1.62	6±1.22	9.30±0.68	9.75±1.34	5.25±1.12	6.75±1.67
3	1510±1.27	6.75±1.34	9.76±1.41	15.01±1.08	18.01±1.21	9.01±1.06	13.57±1.78
4	4.03±1.21	12.83±1.54	19.52±1.37	20.78±1.31	26.28±1.20	18.01±0.84	22.52±1.67
5	28.55±1.45	29.39±1.57	29.29±1.06	27.05±0.78	36.81±1.26	24.03±1.16	26.29±1.14
6	30.09±1.44	32.31±1.40	33.07±0.96	33.08±1.29	45.10±1.28	30.06±1.27	30.09±0.91
7	37.62±1.62	39.09±1.51	36.85±1.88	42.11±1.67	52.65±1.42	38.34±1.44	34.60±1.62
8	45.16±1.22	46.64±1.40	45.14±1.09	45.16±1.26	54.20±0.82	42.13±1.65	42.14±1.27
9	52.71±1.23	54.19±1.98	51.19±1.79	57.21±1.20	58.76±1.98	51.18±1.29	49.69±0.99
10	60.27±1.29	61.75±1.21	57.25±1.27	60.27±1.89	63.33±1.96	58.73±1.21	59.49±1.21

11	69.34±1.44	72.31±1.66	66.31±1.56	72.34±1.41	75.40±1.07	67.80±1.27	69.30±1.85
12	78.41±1.55	81.39±1.47	73.14±1.77	82.92±1.37	82.96±1.96	75.37±1.20	76.88±1.88
13	87.50±1.84	90.48±1.67	82.97±0.77	88.26±1.61	92.80±1.20	86.70±1.33	82.96±1.87
14	95.10±1.33	96.58±0.99	93.56±1.23	95.11±1.27	98.90±1.11	92.80±1.87	94.30±1.22

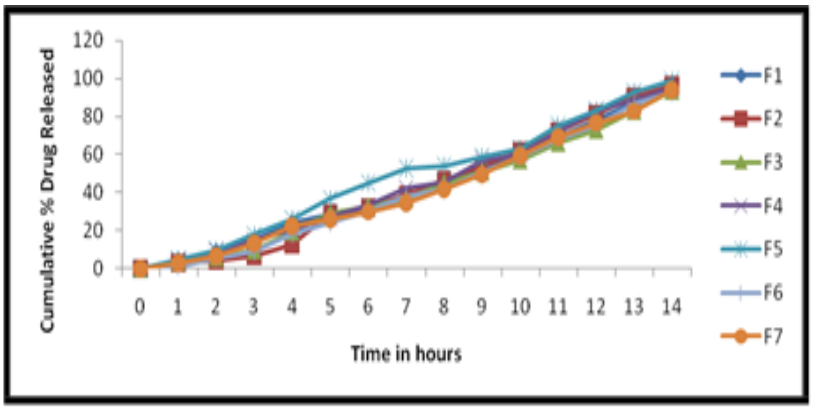

Fig. 6: Cumulative % Drug Release of All Formulations.

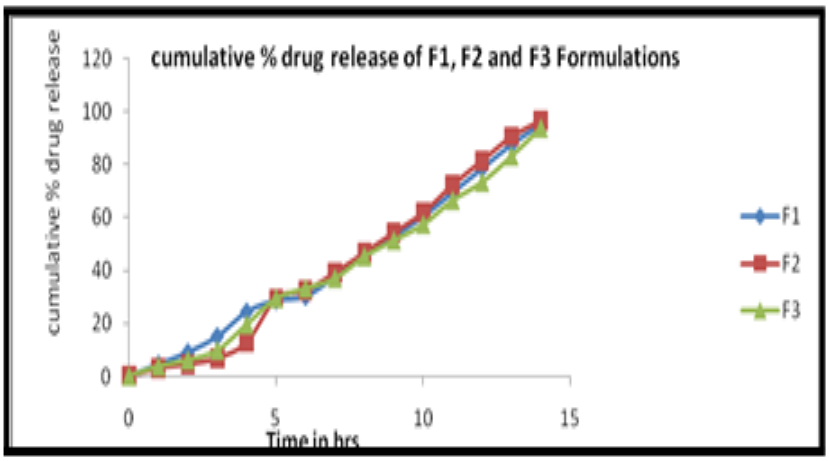

Fig. 7: Cumulative % Drug Release of F1, F2 and F3 Formulations.

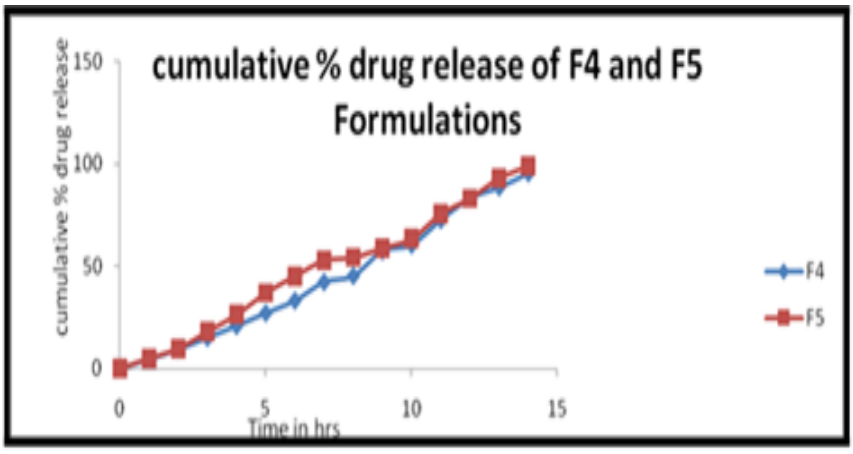

Fig. 8: Cumulative % Drug Release of F4 and F5 Formulations.

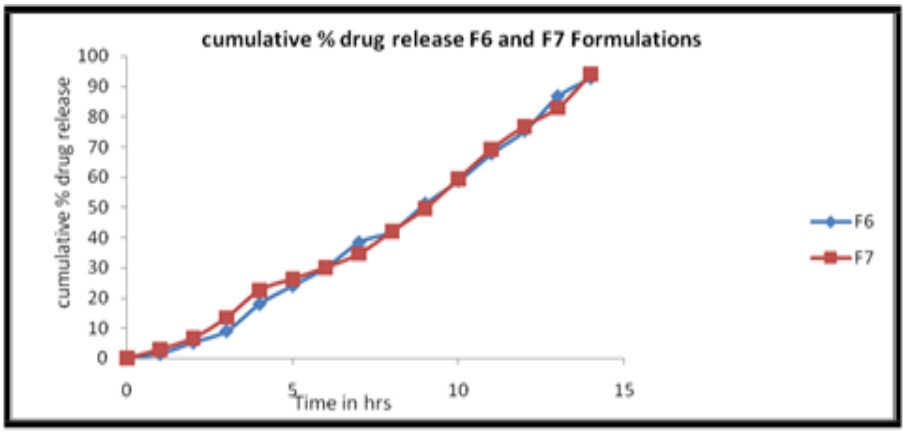

Fig. 9: Cumulative % Drug Release of F6 and F7 Formulations.

Drug Release Kinetics

The cumulative amount of zidovudine released from the formulated matrix tablets at different time intervals were fitted in to several kinetic models such as Zero order kinetics, first order kinetics, Higuchi model and Korsemayer-peppas model to characterize mechanism of drug release.

By studying the release kinetics of zidovudine matrix tablets, as clearly indicated in table 6 and Figures 10 to 13, the formulations did not follow a first-order release pattern. When the data were plotted according to the first-order equation, the formulations showed regression values between 0.711 and 0.826, and the data were plotted according to the zero-order equation shown in table 6, the formulations showed a fair linearity, with regression values between 0.982 and 0.991. Release kinetics of zidovudine matrix tablets formulations followed a zero-order release pattern. Due to which shows more linearity in zero order rather than first order.

Mechanism of Drug Release

The in vitro release profiles of drug from all the formulations could be best expressed by Higuchi's equation, as the plots showed high linearity with R^2 values between 0.852 and 0.914 shown in table 6 and figure 10-13. It indicating that diffusion mechanism involved in the release of the drug from the tablets. To confirm the diffusion mechanism, the data were fit into Korsmeyer Peppas equation. From the plots slope n values ranging from 0.969 to 0.997, it indicating that diffusion mechanism involved in formulations F1 to F7.

Table No. 6: Coefficient of Determinations for Prepared Matrix Tablets of Zidovudine

Formulation Code	Coefficient of Determination (R^2)			
	Zero order	First order	Higuchi square root	Peppas
F1	0.986	0.793	0.871	0.994
F2	0.982	0.786	0.852	0.969
F3	0.987	0.804	0.871	0.990
F4	0.989	0.820	0.875	0.997
F5	0.991	0.711	0.914	0.990
F6	0.986	0.826	0.857	0.993
F7	0.983	0.796	0.861	0.993

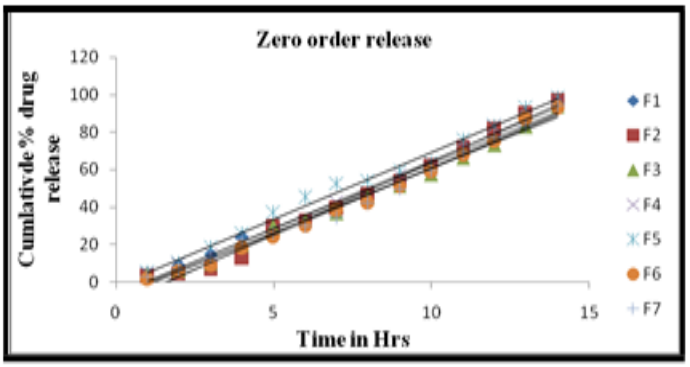

Fig. 10: Zero Order Release of All Formulations.

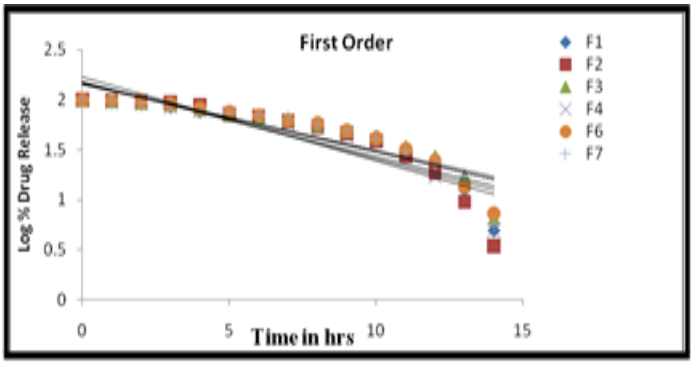

Fig. 11: First Order Release of All Formulations.

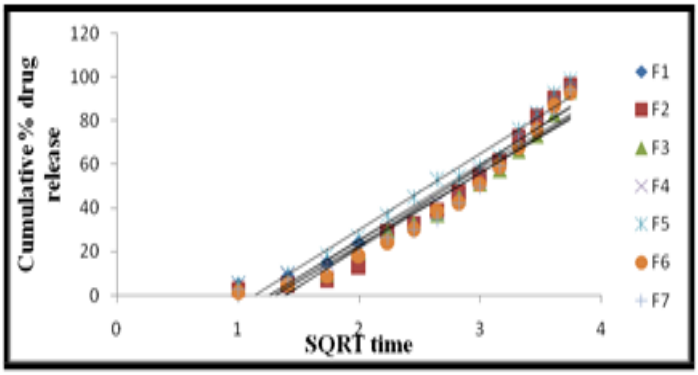

Fig. 12: Higuchi model for all formulations.

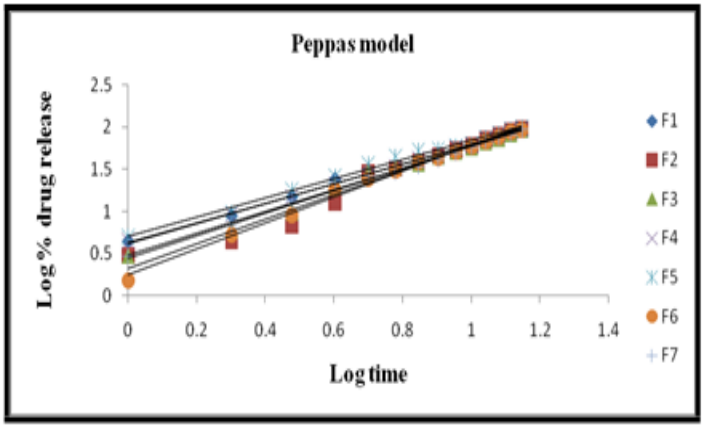

Fig. 13: Peppas model for all formulations.

Stability Study

The stability data of formulation F5 was summarized in table 7. After accelerated stability study, there were no significant changes in the appearance, swelling index properties visual grading and drug content. Hence stability study confirmed that, formulation F5 was physico-chemically stable.

Table No. 7: Results of stability studies of F5 Formulation.

Tests	Initial	3 Month 25°C/60% RH	3 Month 30°C/75% RH	1 Month 40°C/75% RH	2 Month 40°C/75% RH	3 Month 40°C/75% RH
Assay (%)	100.3	99.1	98.3	98.1	98.3	98.6
Dissolution	99.9	97.4	99.2	99.1	99.6	98.2

CONCLUSION

Zidovudine matrix tablets were prepared by wet granulation technique as controlled release matrix tablets with HPMC and Carbopol. The matrix tablet formulations prepared with HPMC and Carbopol was found suitable for extending the drug release up to 14hrs. The matrix tablet formulations gave slow release of drugs upto 14hrs. Drug release from all the tablets followed both diffusion and dissolution mechanisms. The incorporation of polymers in the matrix tablet formulations has significant influence on drug release. Log percentage drug udissolved *versus* time plots for zero order release rate constant of all the prepared matrix tablets were found to be linear with R2 values of 0.982-0.991. The cumulative amount of drug released *versus* square root of time plots for Higuchi's dissolution rate constant of all the matrix tablet formulations were found to be linear with R2 values of 0.852-0.914. Log Mt/ Log M versus log time for Korsermeyer peppas constant were found to be linear with 'n' values ranging from 0.969-0.997 indicating the mechanism of drug release from all the

matrix tablet formulations by both combinations of dissolution and diffusion controlled mechanisms. FTIR spectral studies of selected formulations of zidovudine exhibited no major interactions between the drug and polymers. Swelling index studies on selected formulations of zidovudine indicated the influence of polymers on the swelling behavior of matrix tablet formulations by altering the matrix and gel structure during the drug release process. Accelerated stability studies were carried out for some selected matrix tablets, indicated no significant change in physical parameters such as weight uniformity, hardness, friability and drug content. The drug release from the matrix tablets after storage at different conditions, remain unaltered and was quiet stable.

Thus the present studies clearly indicated that these formulations were found to be suitable for once a day matrix tablet administration.

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