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Oral Extended Release Matrix Tablets of Zidovudine Formulation Development and *In-Vitro* Evaluation

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A B S T R A C T

The aim of the present study was to develop sustained release formulation of Zidovudine to maintain constant therapeutic levels of the drug for over 12 hrs. Various polymers such as Guar gum, HPMCK100 M, PEG 6000 AND Carbopol 934 p were employed as polymers. Zidovudine dose was fixed as 100 mg. Total weight of the tablet was considered as 400 mg. Polymers were used in the concentration of 100, 150 and 200 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e.,96.10 % in 12 hours. It followed zero order release kinetics mechanism.

Keywords: Zidovudine, Guar gum, HPMC, PEG 6000 and sustained release tablets.

A R T I C L E I N F O

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1. Introduction

Oral Drug Delivery:

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Extended-release drug products. A dosage form that allows at least a twofold reduction in dosage frequency as compared to that drug presented as an immediate-release (conventional) dosage form. Examples of extended-release dosage forms include controlled-release, sustained-release and long-acting drug products [1, 2].

Advantages:

Maintenance of plasma drug concentration within an optimal therapeutic range for prolonged duration of treatment. Make use of special effects, e.g. Sustained-release aspirin for morning relief of arthritis by dosing before bed time. Economy i.e. reduction in health care costs. The average cost of treatment over an extended time period may be less, with lesser frequency of dosing, enhanced therapeutic benefits and reduced side effects [3,4].

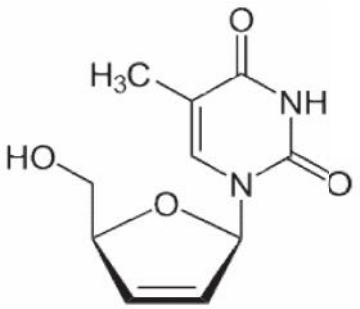
Disadvantages:

a. Increased variability among dosage units.
b. More rapid development of tolerance.
c. Need for additional patient education and counselling.
d. Reduced potential for dose adjustment of drugs normally administered in varying strengths [5,6].

Drug Profile [7]:

Generic Name: Zidovudine

Chemical structure:



Chemical Name: 1-[(2R,5 S)-5-(hydroxymethyl)-2,5-dihydrofuran-2-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione

Molecular Formula: C10H13N5O4

Molecular weight: 224.213 g/mol

Category: nucleoside analog reverse-transcriptase inhibitor (NARTI) active against HIV

2. Materials and Methods

Pre-formulation parameters:

a. The tests includes,
b. Angle of response
c. Bulk density
d. Tapped density
e. Measures of powder compressibility

Formulation development of Tablets:

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 6.3.The tablets were prepared as per the procedure Zidovudine. Total weight of the tablet was considered as 600mg.

Procedure:

a. Zidovudine and all other ingredients were
b. Individually passed through sieve no 60.
c. All the ingredients were mixed thoroughly by triturating up to 15 min.
d. The powder mixture was lubricated with talc.
e. The tablets were prepared by using direct compression method.

3. Results and Discussion

The present study was aimed to developing extended release tablets of Zidovudine using various polymers. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

Analytical Method: Graphs of Zidovudine was taken in Simulated Gastric fluid (pH 1.2) and in p H 6.8 phosphate buffer at 256 nm and 260 nm respectively. Tablet powder blend was subjected to various pre- formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.43±0.07 to 0.58±0.06 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.52 to 0.67 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 16 to 18 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

Quality Control Parameters For tablets: Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

***In-vitro* quality control parameters for tablets:**

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

***In-Vitro* Drug Release Studies:**

From the dissolution data it was evident that the formulations prepared with guar gum as polymer were unable to retard the drug release up to desired time period i.e., 12 hours. Whereas the formulations prepared with HPMCK100M retarded the drug release in the concerntrationentration of 200 mg (F6) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.10% in 12 hours with good retardation. The formulations prepared with PEG 6000 showed more retardation even after 12 hours they were not shown total drug release. Hence they were not considered. Application of Release Rate Kinetics to Dissolution Data: Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer- Peppas release model.

Table 2: Observations for graph of Zidovudine in 0.1N HCl (256nm)

Concerntration [µg/l]	Absorbance
5	0.104
10	0.205
15	0.302
20	0.411
25	0.503
30	0.608
35	0.710

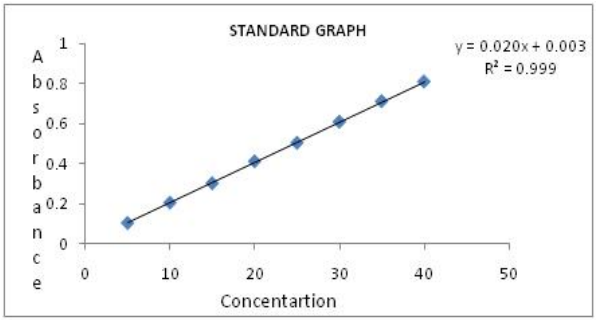


Figure 1: Standard graph of Zidovudine in 0.1N HCl

Table 3: Preformulation parameters of powder blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	25.11	0.49±0.04	0.54±0.04	16.21±0.06	0.86±0.06
F2	25.67	0.52±0.09	0.52±0.04	16.87±0.05	0.98±0.05
F3	25.54	0.50±0.05	0.58±0.05	17.11±0.01	0.64±0.03
F4	25.43	0.51±0.06	0.54±0.07	17.67±0.08	1.12±0.04
F5	25.34	0.52±0.03	0.57±0.03	16.92±0.04	1.2±0.08
F6	24.22	0.53±0.04	0.56±0.06	17.65±0.09	1.06±0.09
F7	25.18	0.54±0.06	0.59±0.04	16.43±0.05	0.76±0.03
F8	24.22	0.58±0.04	0.67±0.02	17.97±0.02	1.15±0.09
F9	25.05	0.55±0.08	0.5 2±0.03	17.54±0.09	1.17±0.02
F10	25.43	0.51±0.06	0.54±0.07	17.67±0.08	1.12±0.04
F11	25.34	0.52±0.03	0.57±0.03	16.92±0.04	1.2±0.08
F12	24.22	0.53±0.04	0.56±0.06	17.65±0.09	1.06±0.09

Table 4: Quality Control Parameters

Formulation	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
	412.5	4.5	0.50	6.8	99.76
F1	405.4	4.5	0.51	6.9	99.45
F2	398.6	4.4	0.51	4.9	99.34
F3	410.6	4.5	0.55	6.9	99.87
F4	409.4	4.4	0.56	6.7	99.14
F5	410.7	4.5	0.45	6.5	98.56
F6	402.3	4.1	0.51	6.4	98.42
F7	401.2	4.3	0.49	6.7	99.65
F8	398.3	4.5	0.55	6.6	99.12
F9	410.6	4.5	0.55	6.9	99.87
F10	409.4	4.4	0.56	6.7	99.14
F11	410.7	4.5	0.45	6.5	98.56

Table 5: Release kinetics data for optimised formulation

Cumulative (%) Release	Time (T)	LOG (%) Release	LOG (%) Remaining	Release Rate (Cumulative % Release / t)	1/CUM% Release	Peppas log Q/100	% Drug Remaining
0	0		2.000				100
14.62	0.5	1.165	1.931	29.240	0.0684	-0.835	85.38
19.86	1	1.256	1.904	19.860	0.0504	-0.702	80.14
22.35	2	1.349	1.890	11.175	0.0447	-0.651	77.65
31.45	3	1.498	1.836	10.483	0.0318	-0.502	68.55
39.8	4	1.600	1.780	9.950	0.0251	-0.400	60.2
45.25	5	1.656	1.738	9.050	0.0221	-0.344	54.75
58.24	6	1.765	1.621	9.707	0.0172	-0.235	41.76
66.73	7	1.824	1.522	9.533	0.0150	-0.176	33.27

71.34	8	1.853	1.457	8.918	0.0140	-0.147	28.66
75.52	9	1.878	1.389	8.391	0.0132	-0.122	24.48
82.17	10	1.915	1.251	8.217	0.0122	-0.085	17.83
87.1	11	1.940	1.111	7.918	0.0115	-0.060	12.9
96.1	12	1.983	0.591	8.008	0.0104	-0.017	3.9

From the above results it was evident that the formulation F6 was followed Zero order release kinetics.

4. Conclusion

The aim of the present study was to develop sustained release formulation of Zidovudine to maintain constant therapeutic levels of the drug for over 12 hrs. Various polymers such as Guar gum, HPMCK100 M, PEG 6000 and Carbopol 934 p were employed as polymers. Zidovudine dose was fixed as 100 mg. Total weight of the tablet was considered as 400 mg. Polymers were used in the concentration of 100, 150 and 200 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e.,96.10 % in 12 hours. It followed zero order release kinetics mechanism.

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