Vol 2|Issue 2| 2012 |88-92.

International Journal
of
Pharmacy Review & Research
www.ijprr.com

e-ISSN: 2248 – 9207
Print ISSN: 2248 – 9193

SPECTROPHOTOMETRIC ESTIMATION OF ZIDOVUDINE IN BULK AND TABLET DOSAGE FORM

***G. Balammal, P. Habeeb khan, P. Jayachandra Reddy**

Department of Pharmaceutical Analysis, Krishna Teja Pharmacy College,
Chadalawada Nagar, Tirupati, Andhra Pradesh – 517 501, INDIA.

ABSTRACT

A simple, rapid and economical spectrophotometric was developed for the estimation of zidovudine in bulk and tablet dosage forms. The results obtained were found to be good and sensitive. The method was validated and was found to be accurate, precise and sensitive. The λ_{max} of the zidovudine was found to be at 266nm. Methanol used as a diluent. The method was found linear over the range of 5-25 µg per ml for zidovudine. The proposed method was validated as per the ICH and USP guidelines. The proposed method can be extended to different quality control labs and research and educational institutes for routine analysis of Zidovudine in bulk and dosage forms.

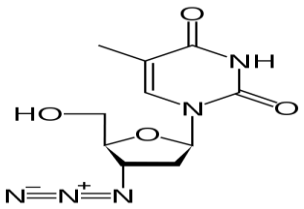
Key words: Estimation, UV Method, Zidovudine, Method.

INTRODUCTION

Zidovudine or azidothymidine is a nucleoside analogue reverse transcriptase inhibitor (NRTI), a type of antiretroviral drug. It was the first approved treatment for HIV. It is an analogue of thymidine [1-4].

I. PHYSICAL AND CHEMICAL PROPERTIES

- Molecular weight: 267.2413
- Chemical formula: $C_{10}H_{13}N_5O_4$
- IUPAC Name: 1-[(2R,4S,5S)-4-azido-5-(hydroxymethyl)oxolan-2-yl]-5-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione
- Structure:



- Properties:
  State: Solid
  Melting point: 106-112^{0}C
  water solubility - 10-50 g/L at 17^{0}C

TAXONOMY

- Kingdom:Organic
- Classes:Pyrimidines and Derivatives
- Substructures:
  - Hydroxy Compounds
  - Ethers
  - Azides
  - Alcohols and Polyols
  - Pyrimidines and Derivatives
  - Heterocyclic compounds
  - Aromatic compounds
  - Furans
  - Cyanamides

PHARMACOLOGY

Indication: For the treatment of human immunovirus (HIV) infections.

PHARMACOKINETICS

It is phosphorylated in the body to its active form zidovudine triphosphate which interferes in DNA synthesis of retroviruses by inhibiting DNA replication. Zidovudine inhibits the key enzyme reverse transcriptase. Human DNA polymerase is inhibited only at a concentration 100 times more than that required to inhibit viral reverse transcriptase.

***Corresponding Author G. Balammal** E mail: bala.hospira@gmail.com

ABSORPTION

Rapid and nearly complete absorption from the gastrointestinal tract following oral administration; however, because of first-pass metabolism, systemic bioavailability of zidovudine capsules and solution is approximately 65% (range, 52 to 75%). Bioavailability in neonates up to 14 days of age is approximately 89%, and it decreases to approximately 61% and 65% in neonates over 14 days of age and children 3 months to 12 years, respectively. Administration with a high-fat meal may decrease the rate and extent of absorption.

DISTRIBUTION

Protein binding is 30-38%.Crosses the placenta and blood-brain barrier; enters breast milk and semen.

METABOLISM

Hepatic. Metabolized by glucuronide conjugation to major, inactive metabolite, 3′-azido-3′-deoxy-5′- O-beta-D-glucopyranuronosylthymidine (GZDV).

EXCRETION

Urine (as unchanged drug and metabolites).As in adult patients, the major route of elimination was by metabolism to GZDV. After intravenous dosing, about 29% of the dose was excreted in the urine unchanged and about 45% of the dose was excreted as GZDV. Half life: 0.5-3 hours

Clearance

- 0.65 +/- 0.29 L/hr/kg [HIV-infected, Birth to 14 Days of Age]
- 1.14 +/- 0.24 L/hr/kg [HIV-infected, 14 Days to 3 Months of Age]
- 1.85 +/- 0.47 L/hr/kg [HIV-infected, 3 Months to 12 Years of Age]

PHARMACODYNAMICS [5-9]

Zidovudine is a nucleoside reverse transcriptase inhibitor (NRTI) with activity against Human Immunodeficiency Virus Type 1 (HIV-1). Zidovudine is phosphorylated to active metabolites that compete for incorporation into viral DNA. They inhibit the HIV reverse transcriptase enzyme competitively and act as a chain terminator of DNA synthesis. The lack of a 3'-OH group in the incorporated nucleoside analogue prevents the formation of the 5' to 3' phosphodiester linkage essential for DNA chain elongation, and therefore, the viral DNA growth is terminated.

MECHANISM OF ACTION

Zidovudine, a structural analog of thymidine, inhibits the activity of HIV-1 reverse transcriptase (RT) both by competing with the natural substrate dGTP and by its incorporation into viral DNA.

Reconstitution

Required dose to be removed from vial and added to 5% dextrose injection solution to achieve a concentration <4 mg/ml.

LIST OF CONTRAINDICATIONS

Zidovudine and Pregnancy

Caution when used during pregnancy. Category C: Either studies in animals have revealed adverse effects on the foetus (teratogenic or embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the foetus.

PRECAUTIONS

Anaemia or myelosuppression, renal and hepatic impairment, elderly, pregnancy. Monitor patients with risk factors for liver disease. Blood tests should be carried out regularly, reduce dose if neutrophil or haemoglobin count is low. Monitor serum CK concentration every 3 months in patients who have received >6 months of treatment. Patients to contact doctor if they experience muscle weakness, shortness of breath, symptoms of hepatitis or pancreatitis.

STORAGE

- Intravenous: Store at 15-25°C (59-77°F).
- Oral: Store at 15-25°C (59-77°F).

MATERIALS & METHODS

INSTRUMENTS

Metler Analytical Balance, Analytical technology solution UV-Spectrophotometer with two matched quartz cells with a 1cm path length were employed in the method. MATERIALS: Pure Zidovudine bulk drug drug was obtained as a gift sample from Dr.Reddy's, AR grade methanol was obtained from Merck Chemicals, Mumbai, India. VIRO-Z TAB, 300mg (RANBAXY) and RETROVIR TAB, 300mg (CIPLA) were obtained from local market.

CHOICE OF SOLVENT

Different Solvents like Water, Methanol, 0.1N HCl, 0.1N NaOH and Phosphate buffer P^H 6.4 were employed for the optimisation of the method. Methanol gave a single distinct peak with good absorbance for the Zidovudine. So, methanol was employed as the solvent.

Preparation of Stock solutions

Standard Zidovudine 100 mg was weighed and dissolved in 100 mL of methanol in a 100 mL volumetric flask. The flask was shaken and volume was made up to the mark with methanol to give a solution containing 1000 µg / mL (stock solution I). From the stock solution I, pipette out 10 mL and placed into 100 mL volumetric flask. The volume was made up to mark with distilled water to give a stock solution containing 100 µg / mL (stock solution II).

Determination of λ_{max}

From the standard stock solution II of Zidovudine, appropriate aliquots were were made with methanol to obtain working standard solutions of concentrations from 1 to 100 µg / mL. Absorbance for

these solutions were measured in the range of 200-400nm and the spectra was recorded.

Procedures for Tablet Dosage Forms

Twenty Tablets were taken, weighed and finely powdered. The powder equivalent to 100 mg of Zidovudine was accurately weighed and transferred to volumetric flask of 100 mL capacity containing 25 mL of the methanol and sonicated for 15-20 min. The flask was shaken and volume was made up to the mark with methanol to give a solution of 1000 µg / mL (stock solution I). The above solution was filtered through Whatmann filter paper. From this solution, 10 mL was taken and diluted to 100 mL with distilled water to give a solution of 100 µg / mL (stock solution II) and used for the estimation of Zidovudine. The solutions were measured for their absorbance at 266nm, using methanol as a blank.

RESULTS AND DISCUSSION

DETERMINATION OF λmax

The λ_{max} of the Zidovudine was found to be at 266nm as shown in the figure.1.

Figure 1. Graph showing the λ_{max} of the Zidovudine

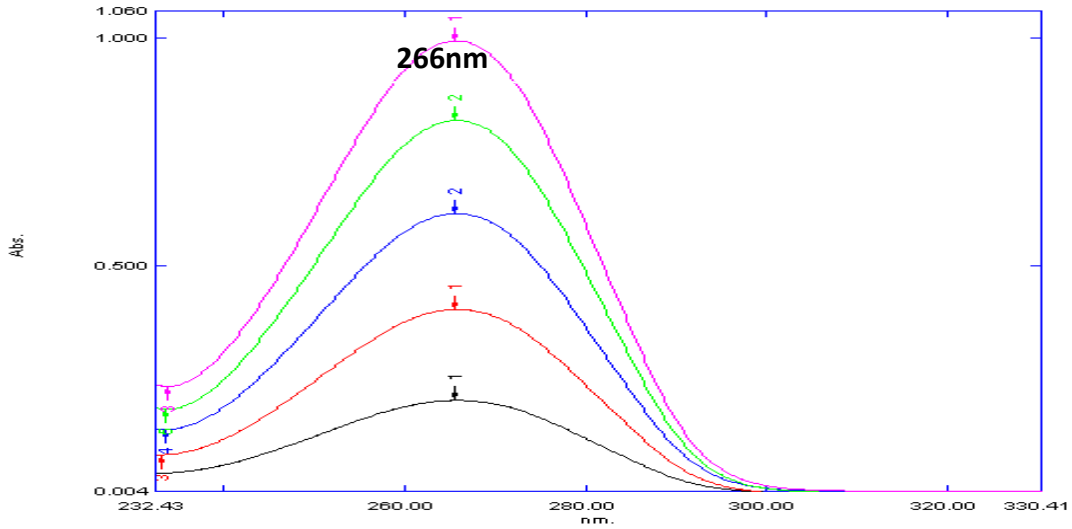


Table 1. Calibration of Standard Zidovudine bulk drug

S.No.	Concentration (µg / mL)	Absorbance at 266nm
1	5	0.203
2	10	0.406
3	15	0.614
4	20	0.819
5	25	0.994

Figure 2. Linearity of Standard Zidovudine bulk drug

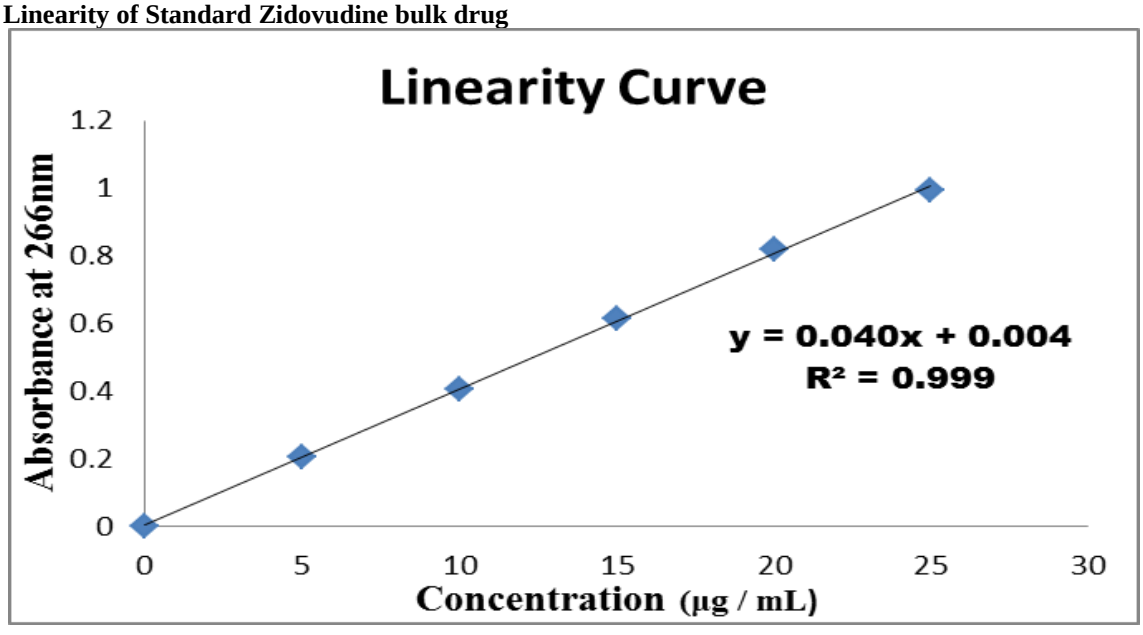


Table2. Linearity Parameter Results

Parameter	Result
λ_{max} of the Drug	266nm
Beer's Limit	2-25(µg / mL)
Linearity: Regression Equation : Y = mX + C Slope (m) Intercept (C)	 y = 0.040x + 0.004 0.040 0.004
Correlation Coefficient (r^2)	0.999
Molar absorptivity	0.0406 X 10^4
LOD	0.33(µg / mL)
LOQ	1.00(µg / mL)

Table 3. Comparative Results of Two Products

S.No.	Sample	Repeatability % RSD (n=5)	Inter-day Precision % RSD (n=15)
1.	Viro-Z Tab (Ranbaxy)	0.62	1.24
2.	Zidovir Tab (Cipla)	0.57	1.15

Table 4. Assay Results of Two Products

S.No.	Sample	Label Claim(mg)	Amount Found(mg)	% Label Claim found
1	Viro-Z Tab (Ranbaxy)	300mg	303.25	101.83
2.	Zidovir Tab (Cipla)	300mg	302.45	100.81

Figure 3. Amount of zidovudine estimated in bulk and formulation

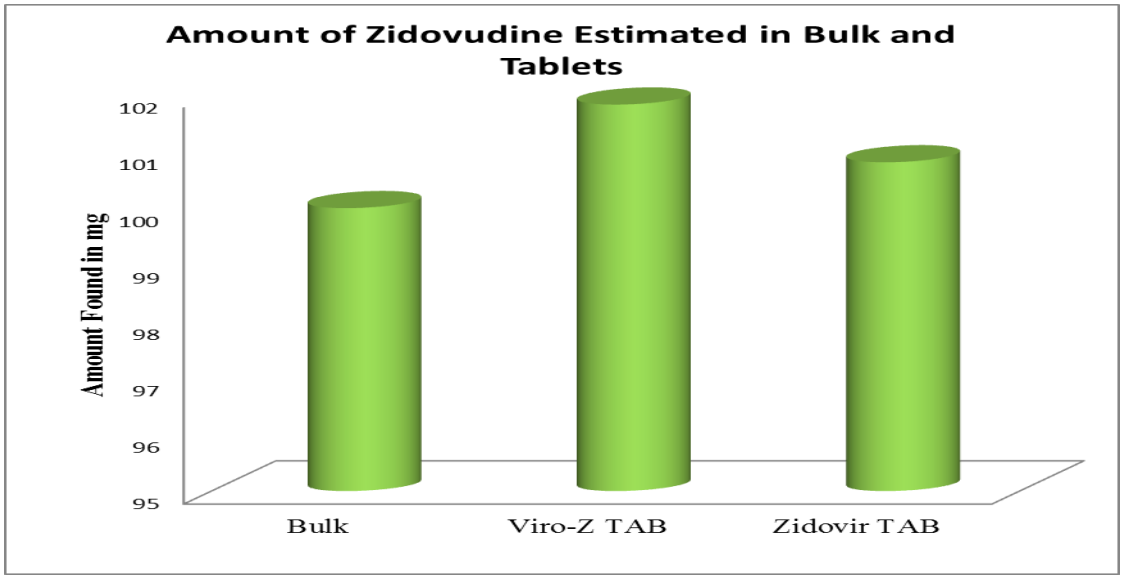


Table 5. Recovery Studies

S.No.	Sample	Amount Present(mg)	Amount Added(mg)	Amount Found(mg)	% Recovery
1	Viro-Z Tab (Ranbaxy)	300 300 300	240 300 360	534.2 589.9 649.3	98.92 98.31 98.37
2.	Zidovir Tab (Cipla)	300 300 300	240 300 360	536.4 592.3 654.2	99.33 98.71 99.12

Standard solution was prepared in the concentration range of 5, 10, 15, 20, 25 µg / mL. Measured the absorbance at 266 nm. The results are given in table1. The linearity range found to be 5-20 µg / mL (figure 2). Based on linearity results, Slope (m), Intercept (C), Molar absorptivity, LOD, LOQ was calculated. Assay Results of two Products have been compared (table 3&4) found to be reproduciable. Three replicate samples are prepared and measured % recovery (table 5). Based on recovery results method found to be accurate and linear.

CONCLUSION

A simple, rapid and economical spectrophotmetric was developed for the estimation of Zidovudine in bulk and tablet dosage forms. The results obtained were found to be good and sensitive. The method was validated and was found to be accurate, precise and sensitive. The tablet dosage forms were assayed by this method. And the results showed good correlation between bulk and tablet dosage forms. The proposed method can be extended to different quality control labs and research and educational institutes for routine analysis of Zidovudine in bulk and dosage forms.

REFERRENCES

1. ICH harmonised tripartite guideline, Validation of Analytical Procedures, Q2 (R1).
2. Remington. The Science and Practice of Pharmacy, 1, 21st Edition, 2005: 647-650.
3. A. H. Beckett and J. B. Stenlake. Practical Pharmaceutical Chemistry, Part two, 4th edition, 1988: 275-284.
4. Vogel's Text book of Quantitaive Chemical Analysis, 5th Edition, ELBS Longman, 2007: 661-672.
5. J. Michael Hollas. Modern Spectroscopy, 4th Edition, 2004: 289-313.
6. Donald L Pavia, Gary M Lampman, George S Kriz. Introduction to Spectroscopy, 3rd Edition, 2001: 353-389.
7. Douglas A Skoog, Donald M West, F James Holler, Stanley R Crouch. Fundamentals of Analytical Chemistry, 8th Edition, 2004: 710-783.
8. Günter Gauglitz, Tuan Vo-Dinh. Handbook of Spectroscopy, 2006: 37-47.
9. G. Chatwal, SK. Anand. Instrumental Methods of Chemical Analysis, 5th Edition, 2002: 2.149-2.184.