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RESEARCH ARTICLE

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A VALIDATED UV SPECTROPHOTOMETRIC DETERMINATION OF AN ANTIVIRAL DRUG - ADEFOVIR DIPIVOXIL FROM TABLET FORMULATIONS

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ABSTRACT

Simple, sensitive and specific spectrophotometric method was developed and validated for quantification of Adefovir dipivoxil in tabltet dosage form. Drug showed the absorption maxima in water at 260nm and was linear for a range of 2-10µg/ml with a correlation coefficient of 0.9999. The validation of the above method was done by carrying out precision and accuracy studies. The Limit of detection and Limit of Quantification for Adefovir dipivoxil was found to be 0.82mcg/ml and 2.76mcg/ml. The percentage recovery was found to be 99.3% and showed good repeatability with relative standard deviation less than 2. So, the proposed method can be applied for the routine analysis of Adefovir dipivoxil from formulations.

KEY WORDS

Spectrophotometry, Adefovir dipivoxil, water, Beer's law.

INTRODUCTION

Adefovir dipivoxil[1] is chemically 9-[2-[Bis[(pivaloyloxy)methoxy]phosphinyl]methoxy]ethyl]
adenine . the structural formula is C20H32N5O8P and molcular weight is 501.48. Adefovir dipivoxil is a diester prodrug of the active moiety Adefovir, it is an acyclic nucleotide analogue of adenosine monophosphate. It is a novel antiviral drug, which is highly efficient in the treatment ofhuman hepatitis B virus (HBV) and HIV. It was reported that Adefovir dipivoxil dose at 10 mg, once daily taken orally in the treatment of chronic hepatitis in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. Adefovir[5] is phosphorylated to the active metabolite, Adefovir diphosphate, by cellular kinases, Adefovir diphosphate inhibits HBV DNA polymerases4 (reverse transcriptase) by competing with the natural substrate deoxyadenosine triphosphate and by causing DNA chain termination after its ncorporation into viral DNA. Adefovir dipivoxil is absorbed rapidly & extensively after oral administration, and approximate oral bioavailability of Adefovir from Adefovir dipivoxil is 59%5. *In vitro* binding of Adefovir to human plasma or human serum proteins is 4% over the Adefovir concentration range of 0.1 to 25 mg/mL. Metabolism involves the rapid onversion of Adefovir dipivoxil to Adefovir, 45% of the dose. Adefovir is renally excreted by a combination of glomerular filteration & active tubular secretion. Since, Adefovir dipivoxil is widely used in the antiviral therapy, it is important to develop and validate analytical methods for its determination in pharmaceutical dosage form. The present work reports the development and validation of a UV spectrophotometric method[3] for the estimation of Adefovir dipivoxil in bulk and in tablets, the present work reports a rapid and sensitive method with UV detection[2] for routine quality control of Adefovir dipivoxil in bulk and in pharmaceutical formulations. The method was validated by parameters such as correlation coefficient, intercept and slope.

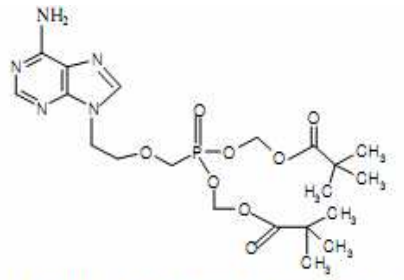

Figure 1. Structure of adefovir dipivoxil.

EXPERIMENTAL

Shimadzu UV-VIS (1700 series) double spectrophotometer equipped with 10mm matched quartz cells.

CHEMICALS

Adefovir dipivoxil was obtained from Hetero drugs Ltd., Hyd, was used as such without further purification. Different brands of tablets of given drug were supplied from local pharmacy.

RECOMMENDED PROCEDURE AND CALIBRATION CURVE

Adefovir dipivoxil (10 mg) was accurately weighed and dissolved in 100 mL of water to form a stock solution (100 µg/mL). 10 mL of the above solution was diluted to 100 mL with water in a 100 mL volumetric flask to give a

concentration of 10 µg/mL and this was then scanned in UV range. This showed an absorption maximum at 260 nm (Figure 2). Aliquots (2,4,6,8 and 10) mL of working standard solution (10 µg/mL) corresponding to 2-10 µg were taken in a series of 10 mL volumetric flask and volume made up with water. The absorbance measurements of these solutions were carried out against water as blank at 260 nm. A calibration curve of ADD was plotted. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

Absorption spectrum of Adefovir dipivoxil

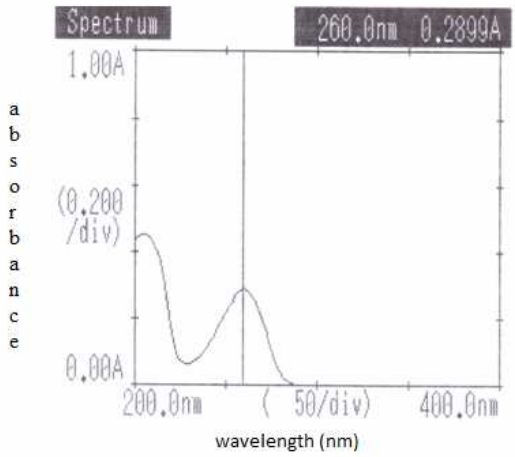

Figure 2.
Adefovir dipivoxil scanned in UV range (in water).

Beer's plot of Adefovir dipivoxil

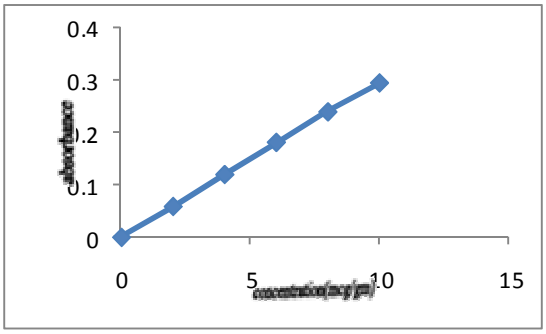

Figure 3.
Standard plot of Adefovir dipivoxil.

PROCEDURE FOR TABLETS

Two commercial formulations, Hespera (M/s GSK) and Preveon (M/s Cipla LTD.,) were purchased from local pharmacy. The contents of 20 tablets were mixed and accurately weighed amount of the contents equivalent to 10 mg of ADD was transferred into a 100 mL volumetric flask. 70 mL of water was added and the contents of the flask were shaken for 5 min. The solution was then diluted to the mark with the water to get a stock solution of 100 µg/mL The content of the flask was filtered through Whatman filter paper No.1 and 10 mL of the filtrate was diluted to 100 mL with water in a 100 mL volumetric flask to give a concentration of 10 µg/mL Suitable volume of this solution was taken in 10 mL volumetric flask and volume was made up with water. Absorbances were read and concentrations of ADD determined using the calibration curve. Calculations were then made with the dilution factor to find out the concentration of the drug in tablets. The experiments were repeated five times to check its reproducibility.

RESULTS AND DISCUSSION

The proposed method for determination of Adefovir dipivoxil showed molar absorptivity of 0.97 x 104 L/mol.cm. Linear regression of absorbance on concentration gave the equation y = 0.0322x + 0.0042 with a correlation coefficient (r) of 0.9998. The optical characteristics such as Beer's law[6] limit, Sandell's sensitivity, % Range of error (0.05 and 0.01 confidence limits) were calculated and are summarized in Table 1. Statistical analysis of commercial formulations has been shown in Table 2.

Table 1
Optical characteristics of Adefovir dipivoxil

Parameters	Results
λmax, nm	260
Beer's law limit, µg/mL	2-10
Molar absorptivity, L mole-1 cm-1	0.97x104
Sandell's sensitivity (µg cm-2 / 0.001 absorbance unit)	0.0319
Regression equation (Y = a + bC)	
Slope (b)	0.0294
Intercept (a)	0.0014
Correlation coefficient (r)	0.9997
% Range of error (Confidence limits)	
0.05 level	0.1923
0.01 level	0.2845

Table 2
Statistical analysis of Adefovir dipivoxil tablets.

Brand	Label amount mg/capsule	Amount found mg/tablet	% label claim ± FD*
Hespera	10	9.9965	99.98+ 0.14
Preveon	10	9.9997	99.99+ 0.23

*average of five determinations.

Table 3
Recovery studies of Adefovir dipivoxil tablets.

Brand	Amount added, mg	Amount found, mg	% recovery ± FD*
Hespera	5	14.98	99.73±0.24
Preveon	5	14.96	99.66±0.21

CONCLUSION

In this study a simple, rapid, sensitive, accurate and precise UV spectrophotometric method for the determination of Adefovir dipivoxil in bulk and pharmaceutical formulation has been developed and validated. It was found that the common excipients present in the formulation did not interfere with the proposed method and can be used for the routine quality control analysis of Adefovir dipivoxil in bulk as well as in marketed tables.

REFERENCES

1. Brunton L L, Parker K S and Lazo J S, In: Goodman and Gillman's, the Pharmacological Basis of Therapeutics, 11th Ed. London: McGraw Hill Publishing; 2005, 1338.
2. Beckett H A and Stenlake B J, Practical Pharmaceutical Chemistry; 4th Ed.,CBS Publishers, New Delhi, 2001, 274.
3. Ewing's Analytical Instrumentation Hand book; 3rd edition, Edited by Jack Cazes, Special Indian Edition, 127-129.
4. Douglas A. Skoog, F. James Holler and Stanley R. Crouch, Instrumental Analysis, Indian edition, Cengage Learning India Pvt Ltd, 381
5. H. P. Rang, M. M. Dale, J. M. Ritter, R. J. Flower, Pharmacology, 6th edition, 685.
6. Roger. E. Schirmer, Modern Methods of Pharmaceutical Analysis, 2nd edition, vol-I, CRC Press, 35-38.
7. O' Neil M J. The Merck Index - an encyclopedia of chemicals, drugs and biologicals,
   13th Ed., New Jersy, Merk & Co., Inc., 2001.z