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## Spectrophotometric Determination of Adefovir Dipivoxil in bulk and Pharmaceutical Formulation

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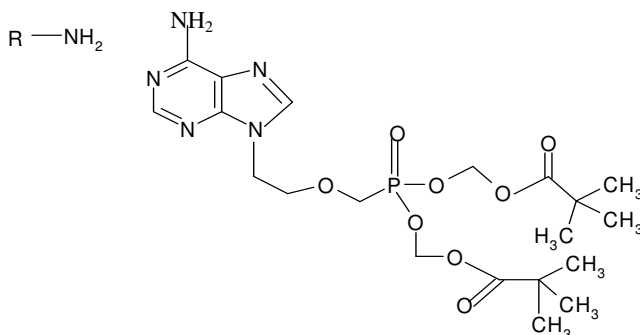
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**Abstract:** Two selective and sensitive spectrophotometric methods have been developed for the estimation of adefovir dipivoxil in bulk and pharmaceutical preparations. Adefovir dipivoxil was subjected to acid hydrolysis and the hydrolysed product used for the estimation. The methods are based on the reaction with 3-methyl-2-benzothiazolinone hydrazone in the presence of ferric chloride, to form a colored species with absorption maxima at 627 nm. The second method is based on the reaction of drug with 1,2 naphthaquinone -4-sulphonic acid sodium salt, under alkaline conditions which absorbs maximally at 454 nm. Beers law is obeyed in the concentration range of 5-25 µg/mL and 2-10 µg/mL respectively. These methods were extended to pharmaceutical formulations and there was no interference from excipients and diluents. The analytical parameters were evaluated.

**Keywords:** Adefovir dipivoxil, MBTH, Folin's reagent.

### Introduction

Adefovir dipivoxil is an antiviral drug and chemically [ 2-(6-aminopurine-9yl) ethoxy methyl-(2,2-dimethyl propanoyloxy methoxy phosphoryl) oxy methyl 2,2-dimethyl propanoate<sup>1,2</sup>. Adefovir dipivoxil is a prodrug of adefovir. Adefovir is an acyclic nucleotide analog of adenosine monophosphate<sup>3</sup>. It is a new generation antiviral drug which is active *in-vitro* against HBV. It is indicated for the treatment of chronic hepatitis-B and HIV. It is not official in any pharmacopoeia. Literature survey reveals that no visible methods are reported however a few bio-analytical methods were reported using human plasma by HPLC<sup>4</sup> & LCMS/MS<sup>5</sup>.



**Figure 1.** Structure of adefovir dipivoxil.

The present investigation has been undertaken to develop two simple visible spectrophotometric methods in which, the colored species obtained in method A, can be considered to be the oxidative coupling product between the acid hydrolyzed drug and MBTH in the presence of ferric chloride as an oxidant<sup>6</sup>, with a  $\lambda_{\text{max}}$  at 627 nm. Method B is based on the formation of colored chromogen at  $\lambda_{\text{max}}$  454 nm when it reacts with 1,2 - naphthaquinone - 4- sulphonate under alkaline conditions<sup>7</sup>.

## Experimental

Shimadzu model 1700 double beam UV-visible spectrophotometer with a pair of 1 cm matched quartz cells was used to measure absorbance of the resulting solutions. All the chemicals used were of AR grade procured from qualigens Mumbai.

### Preparation of reagents

#### 3- Methyl -2- benzo thiazolinone hydrazones (0.2 %)

200 mg of MBTH was dissolved in 100 mL of distilled water.

#### Ferric chloride (0.2 %)

Ferric chloride 0.2% was freshly prepared by dissolving 200 mg of ferric chloride in 100 mL of distilled water.

#### Folins reagent (sodium 1,2-naphthaquinone -4- sulphonate ) (1 %<sup>w/v</sup>)

Folins reagent was prepared by dissolving 1 g of sodium 1, 2-naphthaquinone-4- sulphonate in 100 mL of distilled water.

#### Sodium hydroxide (5 %<sup>w/v</sup>)

Sodium hydroxide solution was prepared by dissolving 5 g in 100 mL of distilled water.

## Method A

### Preparation of sample solutions

Twenty tablets were powdered and an amount equivalent to 100 mg of drug was dissolved in 50 mL of distilled water, 9.0 mL of concentrated HCl was added, refluxed for 2 h and the solution was diluted to 100 mL with distilled water to obtain 1 mg/mL solution. The hydrolyzed drug solution was filtered and further diluted with distilled water to obtain a concentration of 100  $\mu\text{g/mL}$ .

### *Preparation of standard solutions*

Accurately 100 mg of drug was dissolved in 50 mL of distilled water, 9.0 mL of concentrated HCl was added, refluxed for 2 h and the solution was diluted to 100 mL with distilled water to obtain 1 mg/mL solution. The hydrolyzed drug solution was filtered and further diluted with distilled water to obtain a concentration of 100 µg/mL.

### *Assay procedure*

Aliquots of standard drug solution ranging from 0.5 – 2.5 mL (100 µg/mL) were transferred to a series of 10 mL volumetric flasks. To each, 0.2 mL of 0.2% MBTH, 0.2 mL of 0.2% of ferric chloride were added and stand for 20 minutes and the volume was made up to the mark with distilled water. The absorbance at 627 nm against a reagent blank was measured. The colored species was stable for 2.0 h and the amount of the unknown sample was computed from its calibration graph.

## **Method B**

### *Preparation of standard solution*

Standard solution of adefovir dipivoxil was prepared by dissolving 100 mg in 100 mL of methanol and further diluted with methanol to get 100 µg/mL .

### *Preparation of sample solution*

Twenty tablets were weighed and powdered. The tablet powder equivalent to 100 mg of adefovir dipivoxil was transferred into 100 mL volumetric flask containing 50 mL of methanol and the flask was kept for ultrasonication for 5 min. It was then diluted up to the mark with methanol and the solution was filtered. Further it was diluted with methanol to obtain a concentration of 100 µg/mL and used for analysis.

### *Assay procedure*

Aliquots of adefovir dipivoxil ranging from 0.2 –1.2 mL of standard solution were transferred into a series of 10 mL volumetric flasks. To each flask 0.2 mL of sodium 1,2-naphthaquinone-4-sulphonate (1 %<sup>w/v</sup>) and 2 mL of sodium hydroxide (5 % w/v) solutions were added to each flask. It was kept for 20 min at room temperature. The solutions were made up to the mark with distilled water. The absorbance was measured at 454 nm against a reagent blank. The colored species was stable for several hours and the amount of the unknown sample was computed from its calibration graph.

## **Results and Discussion**

The optical characteristics such as Beer's law limits, sandell's sensitivity, molar absorptivity, and percent relative standard deviation, (calculated from the eight measurement containing  $\frac{3}{4}$ <sup>th</sup> of the amount of the upper Beers law limits) were calculated and the result are summarized in Table 1.

**Table 1.** Optical characteristics and precision of the proposed method A and B

Parameter	Method A	Method B
$\lambda_{max}$ , nm	627	454
Beers law limits, $\mu\text{g mL}^{-1}$ , (c)	5-25	2-10
Sandell's sensitivity $\mu\text{g/cm}^2/0.01\text{A.U}$	0.045	0.010
Molar absorptivity, $\text{L mol}^{-1} \text{cm}^{-1}$	$0.217 \times 10^4$	$0.965 \times 10^4$
Regression equation, $Y^*$		
Intercept (a)	0.0219	0.0944
Slope (b)	0.0003	0.0046
Correlation Coefficient (r)	0.9999	0.9996
Relative standard deviation, %	0.3082	0.1839
% Range of error**		
Confidence limit, 0.05 level	0.0011	0.0008
0.01 level	0.0016	0.0012

\* $Y = a+bc$ , where 'C' is the concentration of adefovir dipivoxil in  $\mu\text{g/mL}$  and Y is the absorbance at the respective  $\lambda_{max}$ . \*\* for eight measurements.

**Table 2.** Assay and recovery of adefovir dipivoxil in pharmaceutical formulations.

S.No	Amount of drug in tablet, mg	Amount of pure drug added, mg	Method-A		Method-B	
			Content of drug found, mg	Pure drug percentage of recovery **	Content of drug found, mg	Pure drug percentage of recovery**
Tablet-I	10.0	5	14.98	99.73	14.92	99.46
Tablet-II	10.0	5	14.96	99.66	14.90	99.33

\*\* Recovery amount was the average or six determinations \*\*

## Conclusions

Commercial formulation of adefovir dipivoxil tablet was successfully analyzed by the proposed method. The accuracy and validity of the proposed methods were further ascertained by performing recovery studies. Pre-analyzed sample was spiked with pure drug and the total quantity was found by the proposed methods. The recovery of the pure drug added was quantitative and revealed that there is no interference of excipients in the determination. The results of recovery study were shown in Table 2. In conclusion the proposed spectrophotometric method for the estimation of adefovir dipivoxil is simple, sensitive, and accurate and can be used for the routine quality control of the drug in bulk as well as in pharmaceutical formulations.

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