Research Article

UV SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF NEW DRUG, DACLATASVIR DIHYDROCHLORIDE

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ABSTRACT

Daclatasvir dihydrochloride (DCH) is a new drug gained its FDA approval on July 24, 2015 for treatment of hepatitis C. As there are no reported UV spectrophotometric methods for estimation of daclatasvir dihydrochloride, the present work was aimed at development of accurate and precise spectrophotometric method for its estimation by absorbance maxima method. The working standard solution of 10 µg/ml was scanned in the wavelength range of 400-200 nm. Absorption maximum, λ_{max} was found at 214 nm. Calibration curve was obtained with good correlation coefficient value of 0.986. Linearity was observed in concentration range of 2-12 µg/ml. Method accuracy was revealed by recovery studies obtained in between 99.95 and 100.09.

KEY WORDS: daclatasvir dihydrochloride, new drug, UV method of estimation, Accuracy, Precision.

INTRODUCTION

Daclatasvir dihydrochloride (DCH) is a new drug useful for treatment of hepatitis C (HCV). It was developed by Bristol-Myers Squibb and was approved in Europe on 22 August 2014 and gained its FDA approval on July 24, 2015 in United States. It is approved for Hepatitis C genotype 3 infections[1] and inhibits the HCV nonstructural protein NS5A[2]. Chemically it is Dimethyl N,N'-(biphenyl-4,4'-diylbis(1H-imidazole-5,2-diyl-((2S)-pyrrolidine-2,1-diyl)((1S)-1-(1-methylethyl)-2-oxoethane-2,1-diyl))) dicarbamate dihydrochloride .

Recent research suggests that it targets two steps of the viral replication process, enabling rapid decline of HCV RNA. Modeling shows that the NS5A inhibitor, daclatasvir has two modes of action and yields a shorter estimate of the hepatitis C virus half-life[3]. Daclatasvir has been tested in combination regimens with pegylated interferon and ribavirin as well as with other direct-acting antiviral agents including asunaprevir and sofosbuvir.[4]

Hence it is such that this drug has wide scope for formulations to be developed for effective treatment of HCV. Till now, there is no reported UV method for its estimation in literature. Hence present research work was aimed at development of accurate, precise UV method of estimation of daclatasvir dihydrochloride[5].

MATERIALS AND METHODS

UV-visible Spectrophotometer, Shimadzu UV JAPAN 1801, Electronic balance, Shimadzu, Sonicator etc. Daclatasvir dihydrochloride was obtained as a gift sample from Mylan laboratories Ltd., Hyderabad, India**.**

Spectrophotometric method

Standard Solution
Daclatasvir dihydrochloride, 100 mg was weighed accurately and transferred to 100 ml volumetric flask. Distilled water, 25 ml was added and mixed well to dissolve the drug. The volume was made up to 100 ml with distilled water.

Working standard solution
The standard solution was suitably diluted with distilled water to produce 10 µg/ml of daclatasvir dihydrochloride.

Scanning of absorption maxima
The working standard solution, 10 µg/ml of DCL was scanned in the wavelength range of 400-200 nm against the reagent blank to obtain the absorption maxima using UV-visible Spectrophotometer (Shimadzu). The spectrum of drug obtained is shown in Figure 1 and it was used to determine absorption maxima. Peak absorbance was obtained at 214 nm.Hence 214 nm was considered as absorption maxima, $\lambda_{max.}$

Calibration curve construction
The standard solution of daclatasavir dihydrochloride was subsequently diluted with water to obtain series of dilutions containing 2, 4, 6, 8 and 10 µg/ml daclatasavir dihydrochloride. The absorbance of these solutions was measured using UV-visible Spectrophotometer at 214 nm against reagent blank. All the estimations were done in triplicate and the average values are reported. The concentrations of daclatasavir dihydrochloride and the corresponding absorbencies are given in the Table 1. The standard graph for estimation daclatasavir dihydrochloride was plotted and is shown in Figure 2. The value of correlation coefficient (r) for the curve was calculated.

Reproducibility
Reproducibility of the method in the present investigation was studied by analyzing three individually weighed samples of drug

and analyzing the drug as described above. Relative standard deviation (RSD) which is used to express the reproducibility was calculated and reported in Table 2.

Precision and accuracy of the method
A dilution containing 50 µg of daclatasavir dihydrochloridewas assayed repeatedly (n=10) by the proposed method. The precision is a measure of the agreement among the values obtained when the same solution is repeatedly assayed. While accuracy is the agreement between the estimated value and true value standard errorand standard deviation (s.d.) are the measures of precision and accuracy respectively.The results of precision and accuracy of the method are given in Table 2.
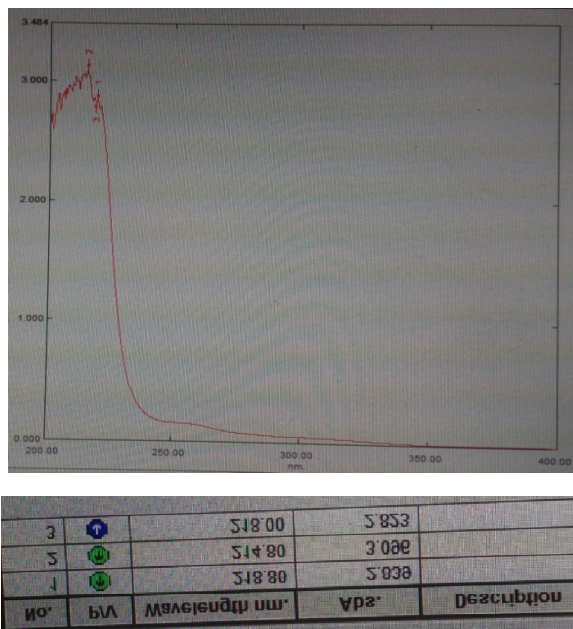

Figure 1: UV absorption spectrum of 10 µg/ml of daclatasvir dihydrochloride

Table 1: Concentration vs. absorbance values of daclatasavirdihydrochloride in 2% w/v SLS (n = 3)

Concentration of DCH (µg/ml)	Absorbance ± s.d.	RSD (%)
2	0.214±0.0042	1.96
4	0.343±0.0045	1.31
6	0.515±0.0026	0.50
8	0.565±0.0070	1.23
10	0.812±0.0026	0.32

Y=0.079X, where X is the concentration of the drug and Y is the corresponding absorbance value.
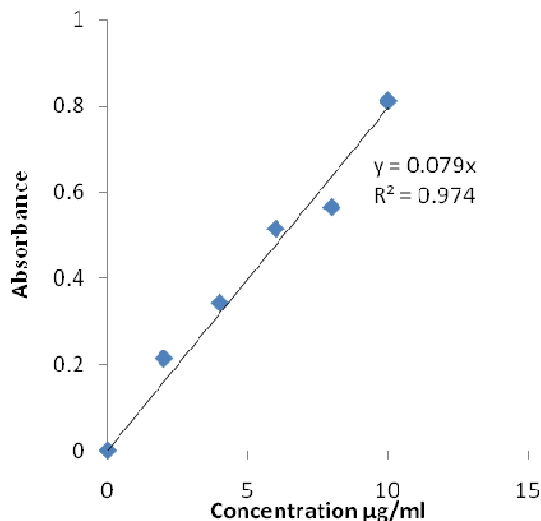r = 0.956

Figure 2: Calibration curve for the estimation of daclatasavir dihydrochloride

Table 2: Precision and accuracy data

True amount (μg)	Amount estimated (μg)	Mean (μg)	Standard deviation	Standard error
100	100.02, 100.09, 100.08, 100.09, 100, 99.98, 100.02, 100.03, 100.05, 99.95	100.03	0.058	0.018

RESULTS AND DISCUSSION

Water was selected as solvent as daclatasvir dihydrochloride as it is soluble in water.

The spectrum of 10 μg/ml of DCL shown in Figure 1 indicated peak absorbance at 214 nm. Hence 214 nm was considered as absorption maxima, $\lambda_{max.}$

The results of concentrations of daclatasavir dihydrochloride and the corresponding absorbencies are shown in the Table 1 and calibration curve is represented in Figure 1. The curve was obtained with correlation cofficientr value of 0.987, which indicated a positive correlation between concentrations of daclatasvir dihydrochloride and the corresponding absorbance values. The method obeyed Beer's law in the range of 2-12μg/ml.

Very low values of standard deviation value of 0.058 and standard error of 0.018 shown in Table 2 indicated the precision and accuracy of the present method.

Hence it is concluded that this method is suitable for the estimation of daclatasvir dihydrochloride content in various formulations and other studies.

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