



Area Under Curve UV Spectrophotometric Method for Determination of Sildenafil Citrate in Bulk

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ABSTRACT

To develop two simple UV spectroscopic methods for simultaneous estimation of Sildenafil citrate in bulk validates as per ICH guidelines. Method A involve Absorption maxima method which based on measurement of absorbance at λ max of Sildenafil citrate 292.20 nm and Method B involves Area Under Curve (AUC) method which based on the measurement of AUC in the range of 277.0 – 304.00 nm. The developed method validated for Linearity, Precision, LOD and LOQ as per ICH guidelines. Both the methods were found to be linear within concentration range 5-25 $\mu\text{g/ml}$ for Sildenafil citrate.

Keywords: Sildenafil citrate API, phosphodiesterase type inhibitors, Area Under Curve Method, λ max.

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INTRODUCTION

Sildenafil citrate is a potent and selective inhibitor of phosphodiesterase type 5 inhibitors. Chemically it is 5-[2-ethoxy-5-(4-methylpiperazin-1-yl)sulfonylphenyl]-1-methyl-3-propyl-6H-pyrazolo[4,3-d]pyrimidin-7-one. Sildenafil Citrate is the citrate salt of a pyrazolopyrimidinone derivative structurally related to zaprinast. Sildenafil selectively inhibits cyclic guanosine monophosphate (cGMP)-specific type 5 phosphodiesterase, resulting in vasodilation in the corpus cavernosum of the penis and penile erection. (NCI04). Accordingly, the objective of this study was to develop and validate the simple spectrophotometric method for the estimation of Sildenafil citrate in bulk as per ICH guidelines. Drug was found to be freely soluble in methanol which was chosen for solvent proceeding studies. [1,2]. In the present study was to develop two simple UV spectroscopic methods for simultaneous estimation of Sildenafil citrate in bulk validates as per ICH guidelines.

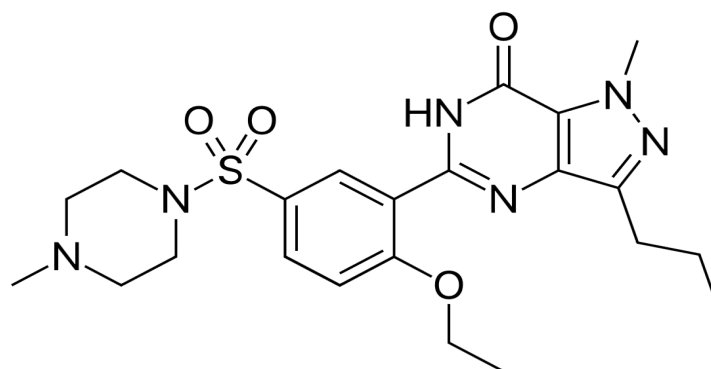


Figure 1: Chemical Structure of Sildenafil Citrate

MATERIAL AND METHODS

Chemicals

Sildenafil citrate was a gift sample from Flamingo Pharmaceutical, Taloja, Navi Mumbai, India. All chemicals and reagents used were of analytical reagent (AR) grade and purchased from Qualigens Fine Chemicals, Mumbai, India.

Instrumentation

Shimadzu (Kyoto, Japan) model UV- 1800 double beam UV- Visible spectrophotometer attached with computer operated software UV probe 2.33 with spectral width of 2 nm, and pair of 1 cm matched quartz cells was used to measure absorbance of the resulting solutions. Analytical balance of make Mettler Toledo (Model JL 1503- C) was used for weighing purpose.

METHOD

Experimental Work

A) To check the solubility of Sildenafil citrate:

25 mg of Sildenafil citrate was weighed and solubility of this sample was checked in 25 ml distilled water, methanol, ethanol. It is freely soluble in water, hence solvent selected as a distilled water [3].

B) To identify the λ max of Sildenafil citrate:

Weigh 10mg of the pure drug and dissolve it in small portion of distilled water and make up the volume up to 10 ml using distilled water give a standard stock solution of 1000 μ m/ml. From above solution 2.5 ml of the standard solution was withdrawn in volumetric flask and diluted to 25ml with distilled water to prepare 100ppm solution. Suitable dilutions were made with methanol to get standard solutions of concentrations: 5, 10, 15, 20, 25 μ m/ml. Spectrum peak details are shown in Figure 2.

Spectrum Peak Pick Report

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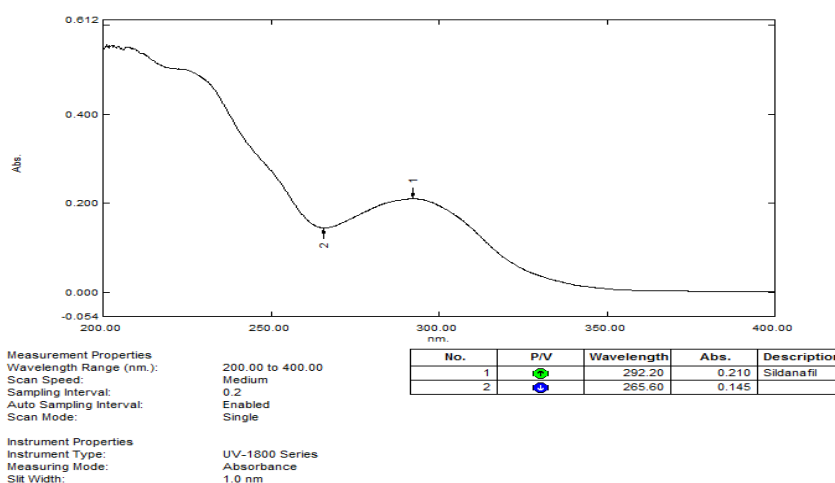


Figure 2: Spectrum peak report of sildenafil citrate.

C) Area Under Curve Method:

In case of AUC (Area under Curve) method is applicable where there is sharp peak or broad spectra are obtained. It include the calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ_1 and λ_2 . Area calculation processing item are calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by the entering the wavelength ranges over which area has to be calculated. This wavelength ranges are selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. The above mentioned spectrums are used to calculate AUC. Thus, the calibration curve can be plotted concentration versus AUC.[4]

D) Analytical Method Development and Validation:

1.Linearity:

The linearity of an analytical procedure is the interval between the upper and lower concentration of analyte in the sample. For which demonstrated that the analytical procedure is of linearity. The standard solution of Sildenafil citrate (5, 10, 15, 20, and 25 μ m/ml) was pipette out in a separated series of 10ml volumetric flask. Make up the volume with distilled water and mixed well. The absorbance maxima and area under curve for the solutions was measured at 292.20nm and range of 200 – 400 nm for two methods respectively against distilled water as blank. Calibration Curve table of Sildenafil citrate is shown in figure 3.[5-9]

RESULTS AND DISCUSSION

A) Calibration Curve for Drug Absorbance maxima method

In the Experimental conditions described, the graph obtained for the absorbance maxima for pure drug showed linear relationship (Figure 2). Regression analysis was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curve were $y = 0.105x + 0.003$ ($r^2 = 0.999$) at 292.20 nm for absorption maxima the range was found to be 5-25µm/ml for the UV spectrophotometric analysis. Calibration curve of Sildenafil citrate is shown in Figure. 3.

A) Area Under Curve Method

In the Experimental conditions described, the graph obtained for the Area Under Curve (AUC) spectra showed linear relationship (Figure 4). Regression analysis was made for the slope, intercept and correlation values. The equation is $y = 0.788x - 0.586$ ($r^2 = 0.990$) at 200 - 400 nm for Area under Curve spectrophotometry analysis. The range was found to be 5-10 µm/ml for the Area Under Curve UV spectrophotometric analysis.

Table 1: Calibration Curve of Pure Sildenafil citrate.

Concentration	Absorbance
5 ppm	0.109
10 ppm	0.211
15 ppm	0.323
20 ppm	0.431
25 ppm	0.526

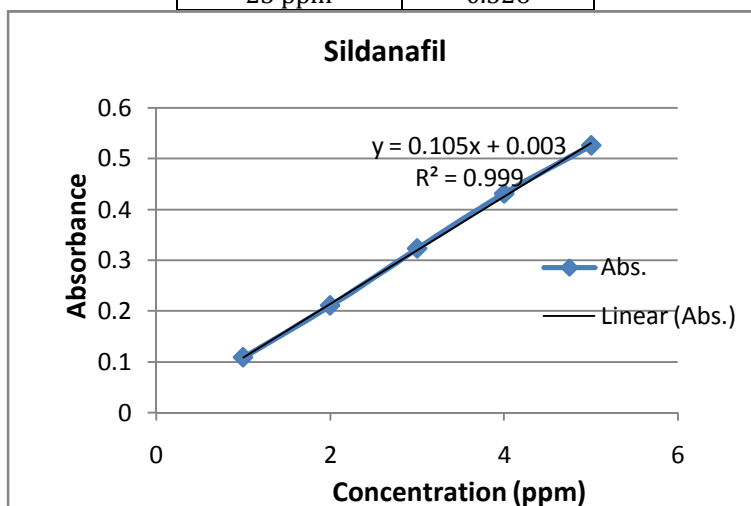


Figure 3: Linearity of Sildenafil Citrate

Spectrum Peak Area Report

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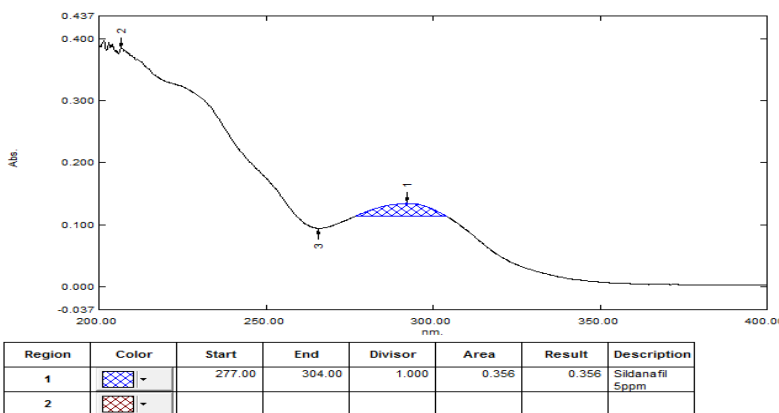
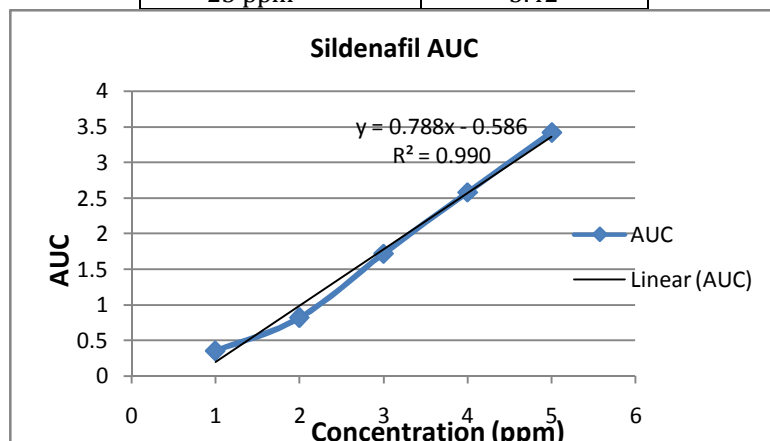


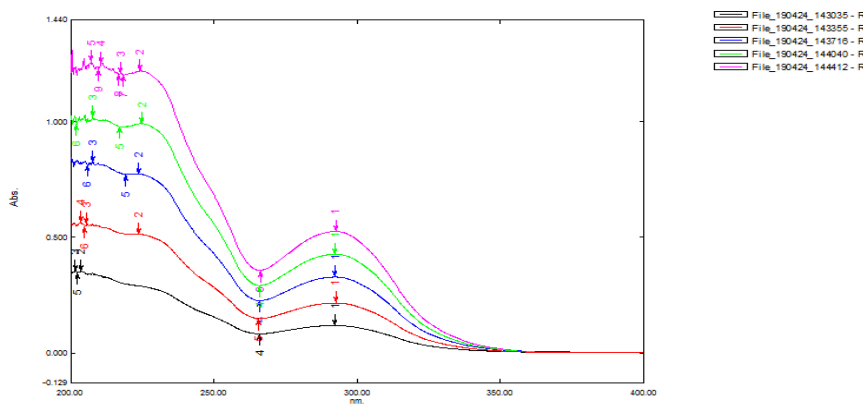
Figure 4: Area Under Curve of Sildenafil citrate

Table 2: Calibration Curve of Pure Sildenafil by AUC.

Concentration	AUC
5 ppm	0.356
10 ppm	0.822
15 ppm	1.72
20 ppm	2.58
25 ppm	3.42

**Figure 5: Linearity of Sildenafil by AUC****Overlay Spectrum Graph Report**

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Figure 6: Overlay spectrum of Sildanafil Citrate**Table 3: Spectroscopic parameters.**

Parameter	AUC
Wavelength Range (nm)	200 - 400
Concentration Range ($\mu\text{m}/\text{ml}$)	5-25
Regression Equation	$y = 0.788x - 0.586$
Slope (m)	0.788
Intercept (c)	0.586
Correlation Coefficient (r^2)	0.9900

CONCLUSION

The simple and economic UV spectrophotometric AUC methods have been developed for the determination of Sildenafil citrate. Because of cost-effective and minimal maintenance, the present UV spectrophotometric methods can be preferred at small scale industries and successfully applied and suggested for the qualitative analysis of Sildenafil citrate in pharmaceutical formulations for QC, where economy and time are essential and to assure therapeutic efficacy. The results show the UV spectrophotometric method was found to be accurate, precise and sensitive.

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