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Area under Curve UV Spectrophotometric Method for Determination of Tadalafil In Bulk

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ABSTRACT
The aim of this work is to establish rapid, simple, precise and economical methods viz., area under curve were developed and validated for estimation of tadalafil in pharmaceutical dosage forms. Further,this study was designed to validate the developed methods as per ICH guidelines. The work was carried out to for estimation of Tadalafil in bulk pharmaceutical form by utilizing area under curve (AUC) method using UV-Visible Spectrophotometry. For this purpose the wavelength range 200-400 nm was selected. Methanol was used as a solvent throughout the work. Linearity was observed in concentration range 2-10 µm/ml(r^2 =0.9987) for the method.The developed method was found to be simple, linear, precise, accurate and sensitive which can be used for routine quality control analysis for spectrophotometric estimation of Active Pharmaceutical Ingredient.
Keywords: *Tadalafil, methanol, AUC method*

INTRODUCTION
Tadalafil is a Phosphodiesterase 5 inhibitor. Tadalafil is used to treatthe male erectile dysfunction (impotence) and pulmonary arterial hypertension (PAH). Tadalafil is metabolized by CYP3A4 to a catechol metabolite. Tadalafil is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) which is responsible for degradation of cGMP in the corpus cavernosum. Tadalafil chemically, (2R,8R,)-2-(2H-1,3-benzodioxol-5-yl)-6methyl-3,6.17-triazatetracyclo[8.7.0.0,3,6.0.0 11, 18] heptadeca-1(10), 11,13,15-tetraene-4,7dione (Fig.1). Tadalafil is an annulated 2,5-diketopiperazine. It is also a 1,2,3,4-tetrahydro-β –carboline.
Accordingly, the objective of this study was to develop and validate the simple spectrophotometric method for the estimation of tadalafil in bulk as per ICH guidelines. Drug was found to be freely soluble in methanol which was chosen for solvent proceeding studies. [1,2]
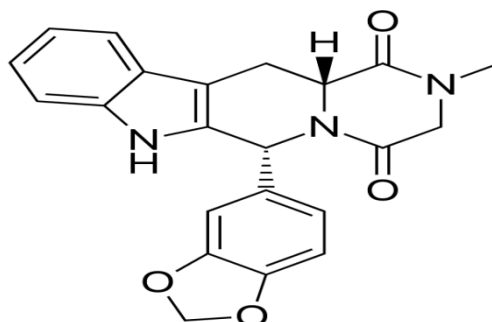

Figure 1: Chemical Structure of Tadalafil

MATERIAL AND METHODS
Chemicals
Tadalafil was a gift sample fromFlamingo 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. [3]
METHOD
Experimental Work
To check the solubility of Tadalafil
25 mg of Tadalafil was weighed and solubility of this sample was checked in 25 ml distilled water, methanol, ethanol.
To identify the λ max of Tadalafil:
Weigh10mg of the pure drug and dissolveit in small portion of distilled water and make up the volume upto 10 ml using methanolto give a standard stock solution of 1000μm/ml. From above solution 2.5 ml of the standard solution was withdrawn in volumetric flask and diluted to 25 ml to prepare 100ppm solution. Suitable dilutions were made with methanol to get standard solutions of concentrations: 2, 4, 6, 8, 10μm/ml. Spectrum peak details are shown in Figure 2. [4]
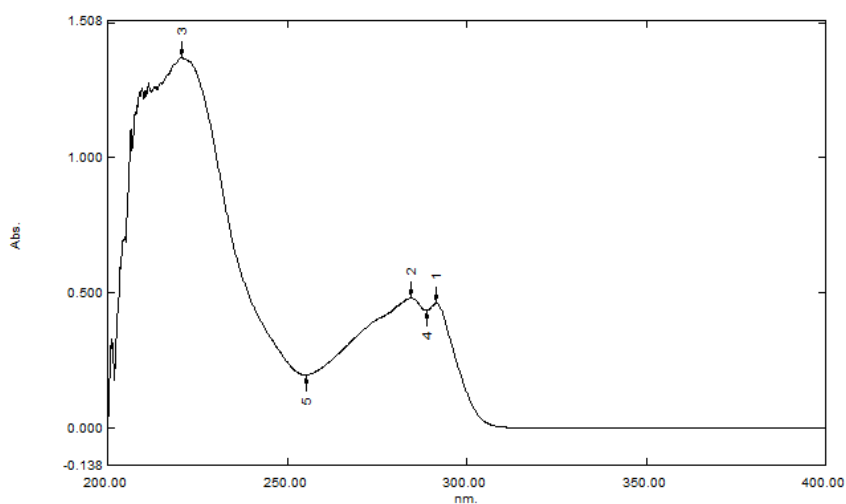
Table 1: Calibration curve of Tadalafil.

Concentration	Absorbance
2	0.059
4	0.171
6	0.307
8	0.421
10	0.560

Spectrum Peak Pick Report

24-08-2019 12:27:53

Data Set: File_190824_122508 - RawData

Measurement Properties
Wavelength Range (nm.): 200.00 to 400.00
Scan Speed: Medium
Sampling Interval: 0.2
Auto Sampling Interval: Enabled
Scan Mode: Single

Instrument Properties
Instrument Type: UV-1800 Series
Measuring Mode: Absorbance
Slit Width: 1.0 nm

No.	P/V	Wavelength	Abs.	Description
1	⬆	291.60	0.463	
2	⬆	284.40	0.481	tadalafil
3	⬆	220.60	1.371	
4	⬇	288.80	0.435	
5	⬇	255.20	0.196	

Figure 2: Spectrum Peak Pick.

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 λ1 and λ2. 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.[5]

Analytical Method Development and Validation:
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 Tadalafil (2, 4, 6, 8, and 10μm/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 284.40nm and range of 200 – 400 nm for two methods respectively against distilled water as blank. Calibration Curve table of tadalafil is shown in Table. 1. Calibration curve of tadalafil.

RESULTS AND DISCUSSION
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 3). Regression analysis was made for the slope, intercept and and correlation coefficient values. The regression equations of calibration curve were y = 0.1252x - 0.072(r^2 =0.9987) at 284.40 nm for absorption maxima the range was found to be 2 -10μm/ml for the UV spectrophotometric analysis. Calibration Curve is shown in Table. 1. Calibration Curve of tadalafil. Calibration curve of tadalafil is shown in Figure. 3. [6]
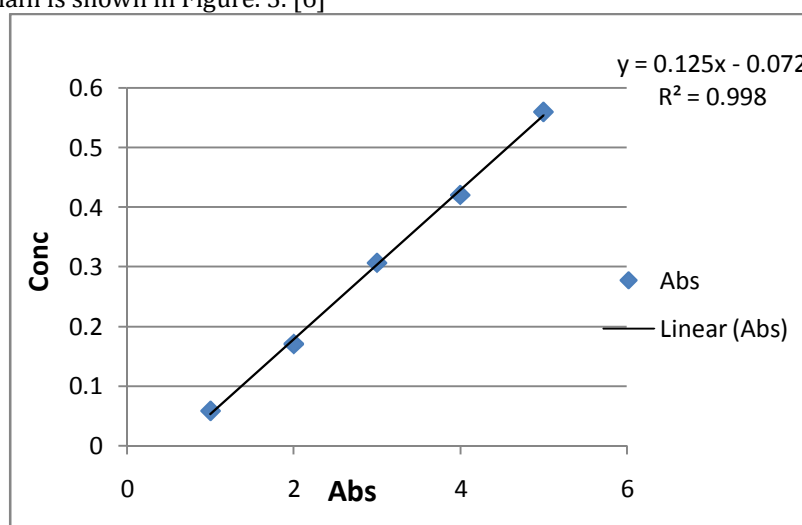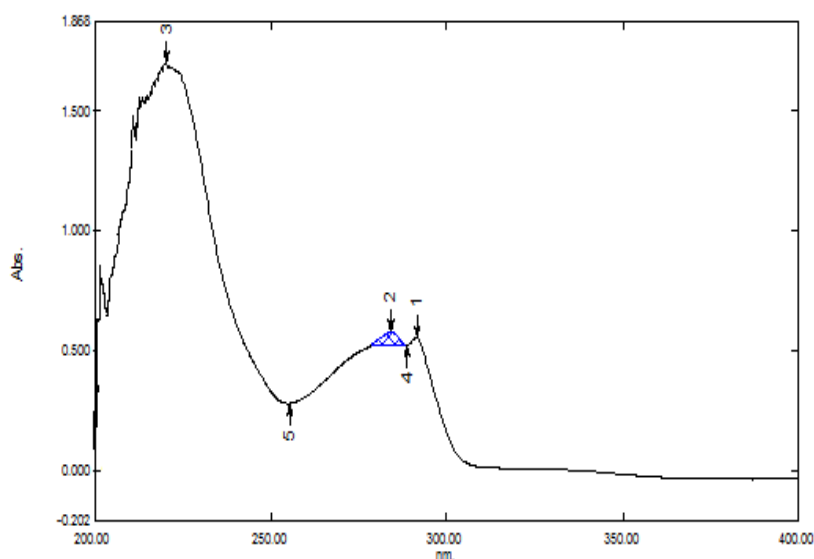

Figure 3: Calibration Curve of Tadalafil.

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 = 0.1252x - 0.072 (r^2 = 0.9987) at 200 – 400 nm for Area Under Curve spectrophotometry analysis. The range was found to be 2-10 μm/ml for the Area Under Curve UV spectrophotometric analysis.

Spectrum Peak Area Report

23-08-2019 13:18:36

Data Set: 00 - RawData

Region	Color	Start	End	Divisor	Area	Result	Description
1		279.00	288.20	1.000	0.274	0.274	TADALAFIL
2							

Figure 4: Area Under Curve Of Tadalafil.

Table 2: Area Under curve of Tadalafil.

Parameter	AUC
Wavelength Range (nm)	200 – 400
Concentration Range (μm/ml)	2-10
Slope (m)	0.1252
Intercept (c)	0.072
Correlation Coefficient (r^2)	0.9987

CONCLUSION

The simple and economic UV spectrophotometric AUC methods have been developed for the determination of Tadalafil. 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 Tadalafil 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.

ACKNOWLEDGEMENT

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