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Research Article

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RP-HPLC method development and validation of tadalafil in tablet dosage form

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ABSTRACT

Tadalafil is a PDE_5 inhibitor, indicated for the treatment of erectile disfunction. The objective of this study is to develop a simple and accurate RP-HPLC method for the estimation of Tadalafil in tablet dosage form. A sharp peak was obtained at 3.068min, on a Agilent Eclipse XBD C_{18} column (150 X 4.6mm i.d., 5µm particle size) with mobile phase, acetonitrile and buffer solution (50:50v/v), delivered in isocratic mode at a flow rate of 1.2ml/min. at 282nm, methanol was used as diluent. The linear dynamic response was found to be in the concentration range of 10-150µg/ml and shows a correlation coefficient (R^2) of 0.999. Accuracy was determined by recovery studies from tablet dosage form and ranges from 100.3-100.8%. The intraday and interday precision was found to be 0.54% and 0.52% respectively.

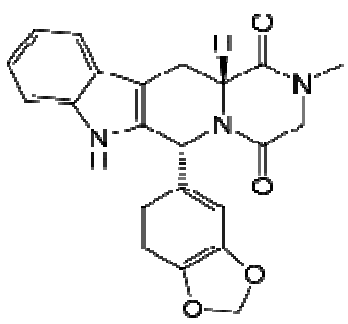
Key words: Tadalafil, HPLC, Isocratic, Validation.

INTRODUCTION

Tadalafil is a selective inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) Chemically it is a (6*R-trans*)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-pyrazino [1', 2':1,6] pyrido[3,4-*b*]indole-1,4-dione (Fig1). Initially it was licensed to treat erectile dysfunction. Later, it was also approved for the treatment of bladder symptoms due to an enlarged [1].

A few RP-HPLC methods have been reported in the literature for the estimation of Tadalafi in tablet dosage form [2-10]. An attempt has been made to develop a simple and reliable RP-HPLC method for the estimation of Tadalafil in tablet dosage form. The results of analysis were validated in accordance with ICH guidelines [11].

Fig.1 Structure of Tadalafil



EXPERIMENTAL SECTION

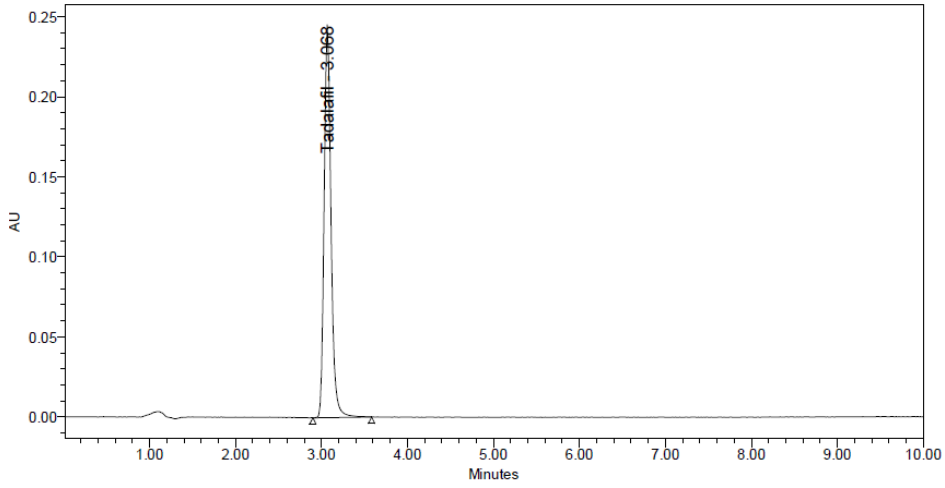
Apparatus and chromatographic conditions:
Chromatographic separation was carried out at room temperature with Agilent Eclipse XBD C_{18} (150X 4.6mm with 5µm particles) column by using EMPOWER 2 Software. A mixture of acetonitrile and potassium dihydrogen orthophosphate buffer adjusted to pH 6 with sodium hydroxide (50:50v/v) was used as mobile phase and delivered at a flow rate of 1.2ml/min with injection volume of 10µl. Methanol was used as a diluent. Detection was carried out at 282nm by using PDA detector at ambient temperature. The total run time was set at 8min.

Chemicals and reagents:
Pure standard of Tadalafil was obtained from Chandra labs, Hyderabad. Tadalafil tablets (10mg) from local drug store. Methanol, Acetonitrile, Potassium dihydrogen orthophosphate and Sodium hydroxide used were of HPLC grade.

Preparation of mobile phase:
Potassium dihydrogen orthophosphate (6.8gm in 1000ml water) buffer (pH 6 adjusted with NaOH) and acetonitrile (50:50v/v) was employed as mobile phase. Prior to use, the mobile phase was degassed and filtered through 0.45µ membrane filter.

Preparation of standard stock solution:
10mg of standard Tadalafil was accurately weighed and transferred to a 10ml volumetric flask and dissolved in 6ml diluent. The flask was sonicated for 10min. the flask was shaken and volume was made up to the mark with diluent to get the concentration of 1000µg/ml. Appropriate volume of aliquot from Tadalafil standard solution was further diluted with diluent to obtain final concentration of 10µg/ml. The standard solution was injected and the chromatogram was recorded (Fig.2).

Fig No.2 Typical chromatogram of Tadalafil



Analysis of tablet formulation:
Not less than 5 tablets each containing 10mg Tadalafil were accurately weighed and powdered. A quantity equivalent to 50mg of Tadalafil was weighed accurately and transferred to 50ml volumetric flask. 30ml of diluent was added to it and sonicated for 10min.The flask was shaken and volume was made up to the mark with diluent and filtered through a 0.45µ membrane filter. Appropriate volume of aliquot from sample solution was further diluted with diluent to get the concentration of 100µg/ml.From the above solution 1ml was pipetted out and transferred to 10ml volumetric flask and the volume made up to 10ml to get the concentration of 10µg/ml. The results were shown in table1.

Table: 1 Determination of active ingredients in tablets

Sample	Label claimed	Amount found (mg)	% Amount found
Cialis	10mg/Tab	9.901	99.01

RESULTS AND DISCUSSION

Linearity:
Linearity was determined from calibration curve plotted using peak area response versus concentration of standard solutions. It shows good linearity in the range of 10-150µg/mL with correlation coefficient (r^2) of 0.999. The regression equation was found to be Y=11491X-13524 (Fig 3&Table 2).

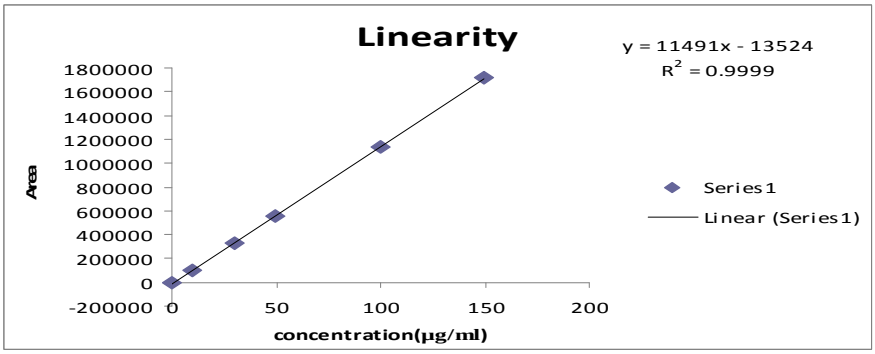


Fig 3 Calibration curve of Tadalafil

Table:2 Linearity data

Conc.(µg/ml)	Area
0	0
10	96075
30	326176
50	553461
100	1136938
150	1712988

Precision:
Repeatability was evaluated by injecting 100µg/ml sample solution for 6times. Intraday and interday % RSD were calculated. The precision results showed good reproducibility (Table-3).

Table: 3 Validation parameters

Parameters	results	
Linearity range(µg/ml)	10-150	
Std. Regression equation	Y=11491X-13524	
Correlation coefficient	0.999	
LOD (ng/ml)	0.15	
LOQ (ng/ml)	0.46	
Precision at 100µg/ml	Intra day	Interday
	0.54	0.52

Recovery studies:
The accuracy of the method was evaluated by using standard addition method at 3 different levels i.e., 50%, 100% &150%. The % recovery values were calculated. The recovery values meet the acceptance criteria of 100±2%, indicated that the accuracy of the method (Table 4).

Table: 4 Recovery data

Level of addition (%)	Amount added (µg/ml)	Amount recovered(µg/ml)	Average % recovery	% RSD
50	100	4	100.3	0.57
100	100	5	100.4	0.39
150	100	7.5	100.8	0.69

Sensitivity (Detection limit and Quantitative limit):
Limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.15ng/ml and 0.46ng/ml respectively.

System suitability:
To evaluate the suitability of the system a freshly prepared standard stock solution of Tadalafil was used. Retention time, asymmetry factor and number of theoretical plates were determined (Table 5).

Table: 5 System suitability parameters

Retention time	3.068
No. of theoretical plates	7033
Asymmetry factor	1.20

CONCLUSION

The proposed RP-HPLC method was simple, sensitive, precise and accurate for determination of Tadalafil in tablet dosage form. The results obtained for all validated parameters were within the limits. Hence the proposed method can be easily applied for the quantification of Tadalafil in routine quality control pharmaceutical laboratories.

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