# A sensitive spectrophotometric determination of tadalafil in pharmaceutical preparations and industrial wastewater samples

*Nief Rahman Ahmed**

Received 24, May, 2012
Accepted 4, December, 2012

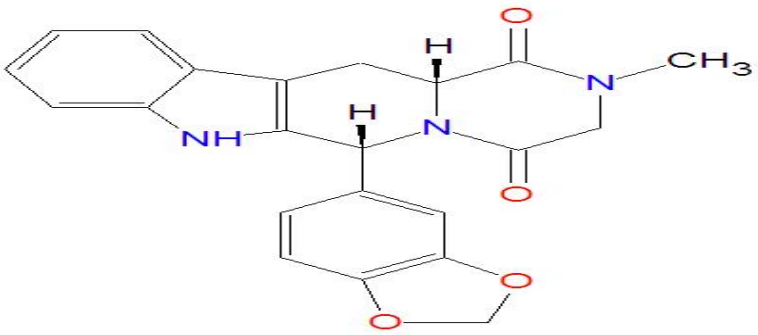
## Abstract

A simple, accurate, precise, rapid, economical and a high sensitive spectrophotometric method has been developed for the determination of tadalafil in pharmaceutical preparations and industrial wastewater samples, which shows a maximum absorbance at 204 nm in 1:1 ethanol-water. Beer's law was obeyed in the range of 1-7µg/ mL ,with molar absorptivity and Sandell's sensitivity of $0.783x10^5$l/mol.cm and 4.97 ng/cm$^2$respectively, relative standard deviation of the method was less than 1.7%, and accuracy (average recovery %) was 100 ± 0. 13. The limits of detection and quantitation are 0.18 and 0.54 µg .ml$^{-1}$, respectively. The method was successfully applied to the determination of tadalafil in some pharmaceutical formulations (tablets) and industrial wastewater samples. The proposed method was validated by sensitivity and precision which proves suitability for the routine analysis of tadalafil in true samples.

**Keywords:Tadalafil,Spectrophotometry,Pharmaceuticals,Industrialwastewater**

## Introduction

Tadalafil: (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..Popular known as Cialis and having the following structural formula,Fig(1).




**$C_{22}H_{19}N_3O_4$= 389.409**

**Fig(1) :Chemical structure of tadalafil**

*Department of Environmental Technology, College of Environment, University of Mosul, Mosul, Iraq

Tadalafil is a phosphor diesterase type 5 inhibitor which is used in the management of erectile dysfunction.It is not officially included in any of the pharmacopoeias .It is listed in the Martindale(complete drug reference ) [1].Extensive literature survey revealed that the determination of the drug in pure and dosage forms are not officially in any pharmacopoeia and there for, require much more investigation. There are several methods for determination of tadalafil such as HPLC [ 2-8],HPLC-EIMS [9] , capillary electrophoresis [10] , spectrophotometry [11-14] , densitometry [ 15], and by electro spray tandem mass spectrometry (ESI-MS-MS) [ 16] . The ultraviolet spectrophotometric method is used in industrial laboratories because of its simplicity, selectivity, as we know only two reports have been mentioned in the literature for the determination of tadalafil by UV method which was used at 284 nm [12,14] . For this reason, an attempt has been made to develop another UV method for determination of tadalafil in pharmaceutical preparations and environmental wastewater samples with higher absorption band at 204 nm .

## Methodology

### Apparatus

Spectro-scan 50 UV-visible(Sedico Ltd, Cyprus), (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurements.

### Reagents

All chemical used were of highest analytical grade and the tadalafil was provided from the state company for pharmaceutical industries (NDI) Mosul-Iraq.

Ethanol:Water (1:1)(v/v)was used as a solvent.

### Tadalafil standard solution25mg/L ($4.3x10^{-5}$M) :

This solution was prepared by dissolving 25 mg of tadalafil in 1000 ml of1:1 ethanol- distilled water in a volumetric flask.

### Recommended procedure

From the absorption maxima, calibration curve was constructed in the concentration range of 1-7 µg/ml. The absorbance was measured at 204 nm against ethanol-water 1:1 as a blank.

### Procedures for pharmaceutical preparations

For the determination of tadalafil in tablet preparations, and in order to minimize a possible variation in the composition of the tablets. A mixed content of 20 tablets of the brand , was weighed and grounded to fine powder, then the powder equivalent to 25 mg of tadalafil was stirred well with about 90 ml of 1:1 ethanol-water for 20 minutes and the volume was completed to 100mL with distilled water ,filtered through whatman No. 41 filter paper and 10 ml of this solution was diluted to100 ml by ethanol - distilled water 1:1 to get 25µg/ml solution and aliquot of this solution was treated as described above for recommended procedure.

**Procedure for real water samples**

To demonstrate the practical applicability of the proposed method, real water samples were analyzed by this method. Industrial waste water from the state company for drug industries and medical appliances Mosul-Iraq, were fortified with the concentrations in the range of 2,4,6 µg/ml of tadalafil .The fortified water samples were analyzed as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

## Result and Discussion

The standard solution of tadalafil (5µg/mL ) was scanned in the range of200-400nm which shows two maxima located at 204 and 284 nm Fig 2. The higher absorption band at 204 nm. Therefore 204 nm wavelength was selected for the construction of calibration curve.

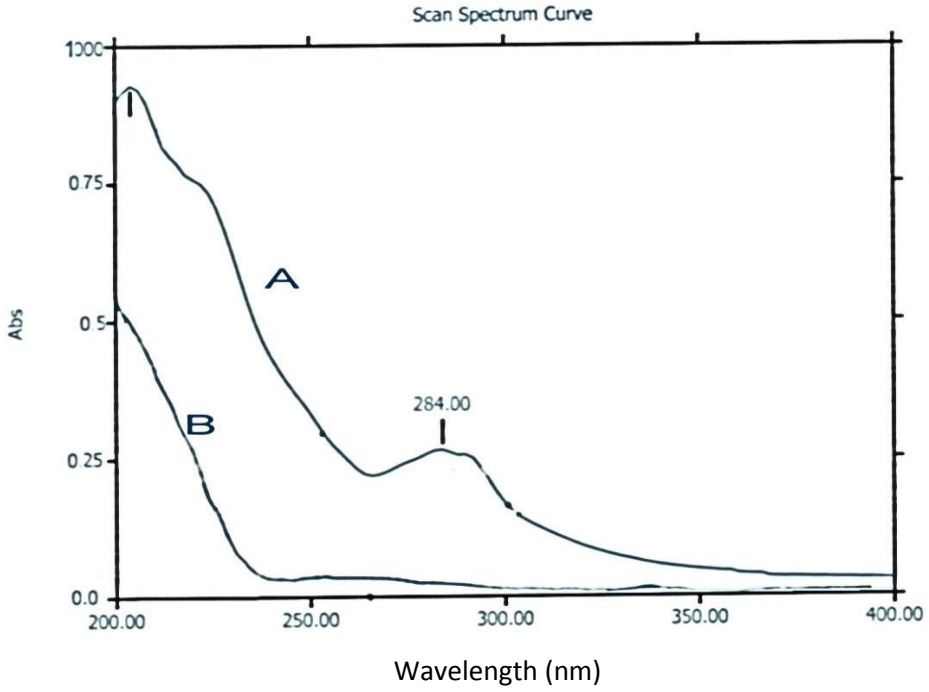



**Fig (2);-Absorption spectra of (A)5µg/ml tadalafil against blank (1:1 ethanol : water), (B) blank against distilled water**.

Beer's law was obeyed in the concentration range of 1-7 µg/mL ( Fig 3) with correlation coefficient of 0.999. The conditional molar absorptivity was found to be $0.783x10^5$l/mol.cm ,and the Sandell's sensitivity was 4.97 ng/cm$^2$.The limit of detection (LOD) and limit of quantification(LOQ) were

calculated according to the current ICH guideline as the ratio of 3.3 and 10 standard deviation of the blank (n=11),respectively, and the slope of the calibration line [17].The limit of detection was 0.18µg/mL and the limit of quantification as the lowest standard concentration which could be determined with acceptable accuracy, and precision was 0.54µg/mL .

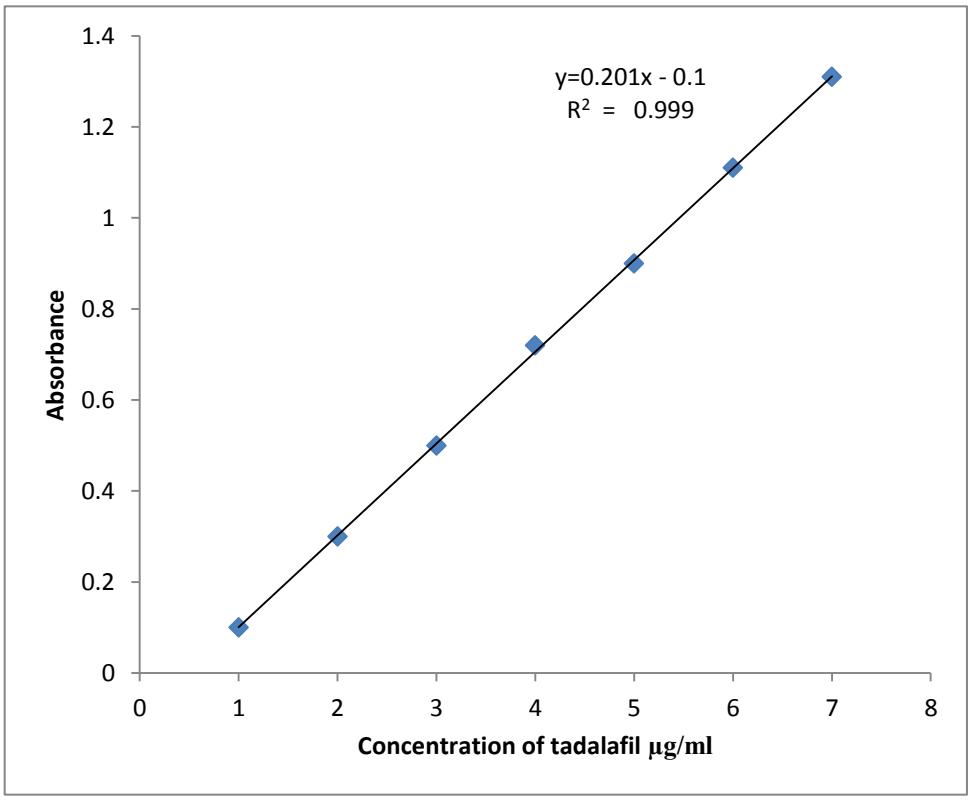



**Fig. (3): Calibration graph of tadalafil.**

In order to determine the accuracy and precision of the method, a pure drug solution was analyzed at three different concentrations ,each determination being repeated six times. The relative error(%) and relative standard deviation values are summarized in Table 1.

From Table 1 the values of standard deviation were satisfactory and the recovery studies were close to 100%,.The RSD% value is less than 1.7.

**Table( I) Accuracy and precision of the proposed method.**

| Tadalafil taken ( µg/ml) | Tadalafil found(µg/ml) | Er (%)[a] | RSD(%) (n=6) |
|---|---|---|---|
| 2 | 2.022 | 1.1 | 1.3 |
| 4 | 4.048 | 1.2 | 1.6 |
| 6 | 6.072 | 1.2 | 1.4 |

a: Mean of six determinations.

The proposed method was compared with other reported UV spectrophotometric methods and found to be superior ,(Table 2).

**Table (2):Comparison of the existing UV spectrophotometric methods with the proposed method for tadalafil.**

| Parameters | Method 1 | Method 2 | Method 3 |
|---|---|---|---|
| Ref | 12 | 14 | Proposed |
| λ Max(nm) | 284.5 | 284 | 204 |
| Solvents | Methanol:$H_2O$ 80 : 20 | Methanol | Methanol:$H_2O$ 50 : 50 |
| Linear range µg/ml | 5-30 | 2-20 | 1-7 |
| ε (l/mol.cm) | $0.66x10^4$ | $1.65x10^4$ | $0.783x10^5$ |
| RSD% | Less than 2 | 0.28 | Less than 1.7 |
| Application | Pharmaceuticals | Pharmaceuticals | Pharmaceuticals and industrial wastewater |

## Interference studies

In order to assess the possible applications of the proposed method, the effect of substance that often accompany with tadalafil in (Tablets) were studied by adding different amount of substances to 5 µg of tadalafil. An attractive feather of the method is its relative freedom from interference by the usual diluents and excipients in amounts for in excess of their normal occurrence in pharmaceutical preparations. The results are given in Table (3).

**Table (3) Determination of 5 µg of tadalafil in the presence of excipients and other substances.**

| Interfering substances | Amount added/mg of interfering | Amount of drug found*µg | Er (%)[a] | RSD % |
|---|---|---|---|---|
| Lactose | 40 | 5.06 | 1.2 | 0.71 |
| Microcrystalline cellulose | 20 | 4.96 | -0.8 | 0.64 |
| Corn starch | 30 | 4.97 | -0.6 | 0.78 |
| Povidone | 30 | 5.05 | 1.0 | 0.79 |
| Magnesium stearate | 40 | 5.07 | 1.4 | 0.91 |
| Hydroxylpropyl methyl cellulose | 40 | 4.97 | -0.6 | 0.93 |
| Poly ethylene glycol | 20 | 5.01 | 0.2 | 0.91 |
| Titanium dioxide | 10 | 5.05 | 1.0 | 0.88 |

*Average of six determinations.

## Analytical application

The proposed method was satisfactorily applied to the determination of tadalafil in its pharmaceutical preparations tablets and wastewater samples, the results of the assay of the pharmaceutical preparations revels that there is close agreement between the results obtained by the proposed method and the label claim, Table 4 and the results of water samples Table 5 show that the recovery values obtained were closed to100%

.

**Table(4): Determination of tadalafil in pharmaceutical formulations**

| Pharmaceutical formulations | Label amount (mg) | Founded*(mg) | Recovery% |
|---|---|---|---|
| Tablets [Tadananine(NDI)] | 20mg/tab<br>10mg/tab | 19.96<br>10.02 | 99.8<br>100.2 |

*mean value of ten determinations

**Table(5): Determination of tadalafil in wastewater samples**

| Wastewater samples | Added µg/ml | Found* (µg/ml) | Recovery %(n=10) |
|---|---|---|---|
| Industrial wastewater | 2 | 2.02 | 101 |
| | 4 | 3.98 | 99.5 |
| | 6 | 6.08 | 101.3 |

* mean value of ten determinations.

## Conclusion

The developed method is found to be high sensitive, accurate, simple, precise and economical ,and can be used for routine quality control analysis of tadalafil in pure form, bulk, pharmaceutical formulations and environmental wastewater samples.

## Acknowledgments

The author wishes to express gratitude to his former company[ the state company of drug industries and medical appliance (NDI) Nineveh – Iraq for providing gift samples of tadalafil standard material and tablets.

## References:

1- SwetmanS.C; Martindale .2005 .The complete Drug References, 34 Edn, Pharmaceutical Press London, p.1751.

2- Reddy.B,Amarnadh.K and Reddy. M . 2010.;Validation and stability indicating RP- HPLC method for the determination of tadalafil in pharmaceutical formulations: Res. Pharm. Biotech., 2(1):,1-6.

3-Aboul-Enein .H.Y and Ali.I; 2005 .Determination of tadalafil in pharmaceutical preparation by HPLC using mono lithic silica column;Talanta,,65(1):,276-280.

4-Ching-Lingand Chen-His.Chou. Ch . .2005. .;determination of tadalafil in small volumes of plasmaby HPLC with UV detection ;J. Chromato. B,822(1):,278-284.

5-Rabbaa-Khabbaz.L. and AbiDaoud. R; . 2006. .Asensitive and simple HPLC method for quantification of tadalafilin human serum; J. A. Res ,6(1):,170-175.

6-Barot.T,Patel. 2010. Determination of tadalafil in pure powder and tablet dosage form by HPLC, JAOAC,93(2):516-522.

7-Farthing .C, Farthing .D, Koka. S, Larus. T, Fakhry. I, Xi. L, Kukreja. R, Sica .D, and Gehr .T 2010 A simple and sensitive HPLC fluorescence method for etermination of tadalafil in mouse plasma.; J. Chromat. B. Anal. Technol. Bio .Life. Sci, 878(28):, 2891-2895.

8-Satish.A,Natvarlal.J .2011 .HPTLC method for determination of tadalafil in tablet dosage form;AJPTR,1(3):,138-146.

9- Zhu.X., Xaiao.S,Chen.B, Zhang .F,Yao.S,Wau.Z and Hau.H 2005.Simultaneous determination of sildenafil, vardenafil and tadalafil as forbidden components in natural dietary supplements for male sexual potency by HPLC electro spray ionization mass spectrometry; J. Chromatogr A,1066,89-95.

10-Aboul-Enein .H.Y and Ali.I.2004. .Validated method for tadalafil analysis in pharmaceutical preparations by capillary electrophoresis; Chromatographia , 60,187-191.

11-NesalinJ.A.,Babu.C.J,Kumar.G.V and Mani.T.T.2009.Validated extractive spectrophotometeric estimation of tadalafil in tablet dosage form ;E-J Chem,6(3):,611-614.

12- Anandakumar.K,Varadharajan.K ,Subathrai.R and Siavn.G 2010 .Estimation of tadalafil in bulk and formulation by uv –visible spectrophotometry;Asian. J. Res. Chem,3(1),54-58.

13- Ali .A,andAymana.G 2011 Spectrophotometric determination of tadalafil in pure and dosage forms ; Chem. Indus. Chem. Engineer. Quat 17 (2) 125−132.

14-Mohmmad.Y, Gowri.D., Pragatikumar. Band Shahul.H 2010 UV Spectrophotometric method for the estimation of tadalafil in bulk and tablet dosage form; E-J Chem, **7(3),** 833-836.

15- Berniati.H.T,Endang.S,Dwi.S.S, Siti.C, Farina.W.K and Gunawan.I, 2006Densitometric determination of tadalafil citrate in tablets:Validation of the method ;J. Liq Chrom.Relat.Tech,29,2753-2765.

16-Abdel-Hamid.M.E .2006 ..Determination of sildenafil ,tadalafil and vardenafil in tablets and adulterated herbal product by ESI-MS-MS;J. Liq.Chrom. Relat Tech.,29(4):,591-603.

17- Valcarcel. M.2000.Principles of Analytical Chemistry , Atext book, Spring verlager ,Berlin Heidelberg, First edn .69, 207.

# التقدير الطيفي للتدالافيل في المستحضرات الصيدلانية والمياه الصناعية المطروحة

***نايف رحمان احمد****

***جامعه الموصل كليه البيئة**

**ألخلاصه:**

تم تطوير طريقة طيفية في المنطقة فوق البنفسجية تمتاز بالبساطة والدقة والضبط والسرعة والحساسية العالية لتقدير عقار التدالافيل في مستحضراته الدوائية وفي المياه الصناعية المطروحة حيث تم قياس كميات تتراوح بين 7,1 جزء بالمليون وبمعامل امتصاص مولاري مقداره$0.783\times10^5$ لتر\مول سم ودلاله ساندل4.97نانوغرام/سم$^2$وان الانحراف القياسي النسبي للطريقة اقل من 1.7%والدقة(معدل الاسترجاعية)0.13±100وان حدي الكشف والكمي للطريقة هما0.18 و 0.54 مايكرو غرام /مل على التوالي.وطبقت الطريقة بنجاح لتقدير الدواء في مستحضراته الصيدلانية (أقراص) وفي المياه الصناعية المطروحة واقترحت الطريقة للتحليل الروتيني كونها ذات حساسية عالية وبسيطة وسريعة وذات دقة جيدة