A sensitivespectrophotometric determination of tadalafil in pharmaceutical preparations and industrial wastewater samples

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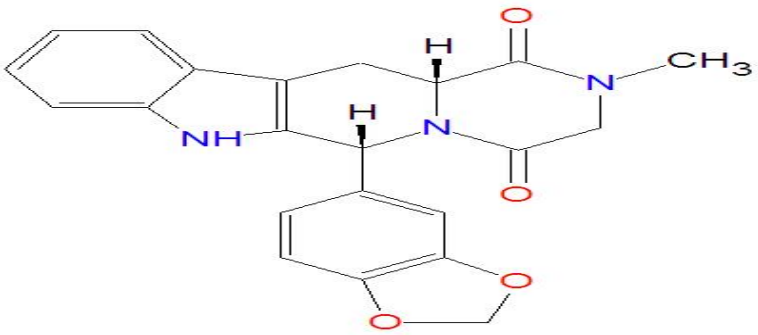
Abstract

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 amaximum 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^2respectively, 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

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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 anypharmacopoeia and therefor, require much more investigation. There are severalmethods 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 literaturefor the determination of tadalafilby 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(SedicoLtd,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 oftadalafil 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 inorder 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 wereanalyzed as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

ResultandDiscussion

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 bandat 204 nm.Therefore 204 nm wavelength was selected for the construction of calibration curve.

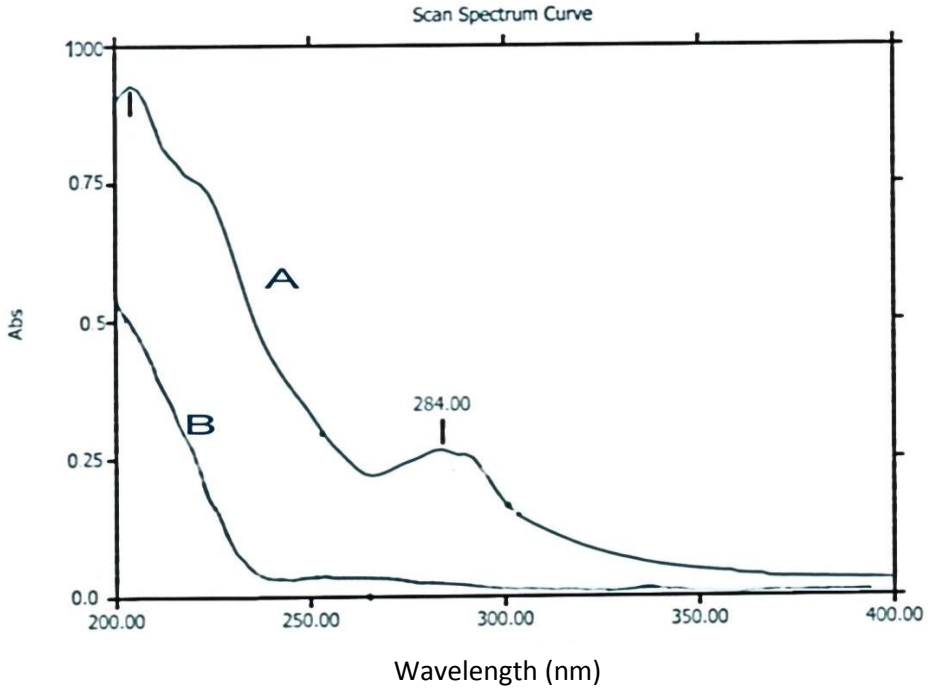

Fig (2);-Absorption spectra of (A)5µg/ml tadalafil against blank (1:1 ethanol : water), (B) blank against distilled water.

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 ofquantification as the lowest standard concentration which could be determined with acceptable accuracy,and precision was 0.54µg/mL.

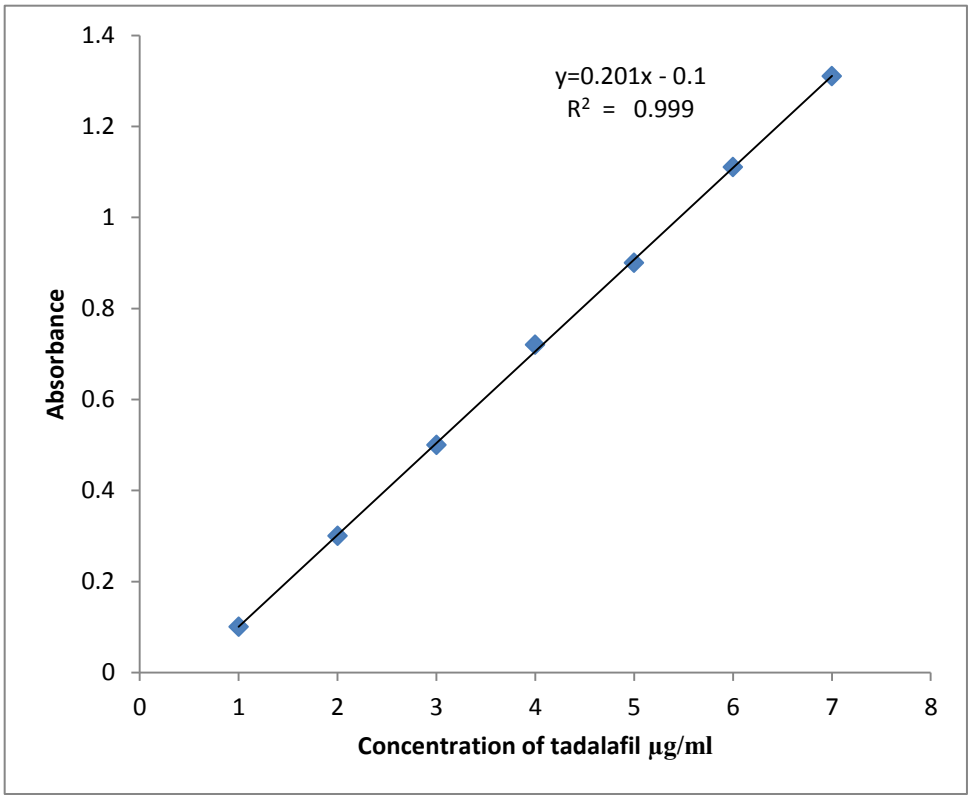

Fig. (3): Calibration graph oftadalafil.

In order to determinethe 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 summarizedin Table 1.

From Table 1 the valuesof standard deviation were satisfactory and the recoverystudies 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)	Tadalafilfound(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 reportedUV spectrophotometric methods and found to besuperior ,(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 andindustrial 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 oftadalafil. 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

Theproposed method was satisfactorily appliedto the determination of tadalafil in its pharmaceutical preparations tablets and wastewater samples,the results of the assay of the pharmaceutical preparations revels that thereis close agreement between the results obtained by the proposed method and the labelclaim, Table4and the results of water samples Table 5 show that the recovery values obtained were closed to100%

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Table(4): Determination of tadalafil in pharmaceutical formulations

Pharmaceutical formulations	Labelamount (mg)	Founded* (mg)	Recovery%
Tablets	20mg/tab	19.96	99.8
[Tadananine(NDI)]	10mg/tab	10.02	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 usedfor routine quality control analysis of tadalafil in pure form,bulk, pharmaceutical formulations and environmental wastewater samples.

Acknowledgments

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التقدير الطيفي للتدالافيل في المستحضرات الصيدلانية والمياه الصناعيةالمطروحة

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ألخلاصه:

تمتطوير طريقة طيفية في المنطقة فوق البنفسجية تمتاز بالبساطة والدقة والضبطوالسرعة 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 مقداره0.783×10^5 لتر\مول سم ودلاله ساندل4.97نانوغرام/سم^{2}وان الانحراف القياسي النسبيللطريقة 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