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Development of two spectrophotometric methods in determination of tetracycline

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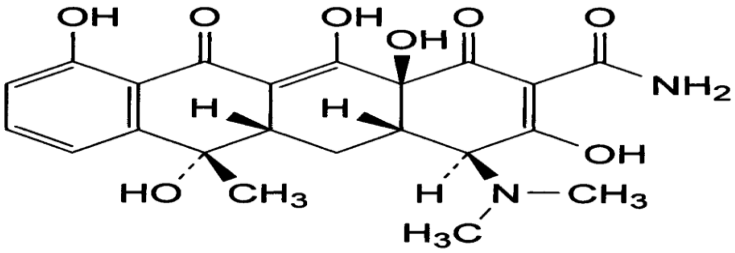
Abstract

Two spectrophotometric methods have been developed for the estimation of tetracycline as pure and in its pharmaceutical preparations. They were based on a reaction of tetracycline with concentrated sulphuric acid to produce a yellow product of tetracycline – sulphonic acid shows maximum absorption at 435 nm with a molar absorptivity of $8.31x10^3$ l./mol.cm. Sandell's sensitivity index, limit of detection (LOD) and limit of quantitation (LOQ) equal to 0.0534 µg /cm^2,0.108 and 0.360 µg/ml respectively. Beer's law is obeyed over the concentration range of 2-40 µg/ml, the relative error is from - 4 to 0.8 %. Method B included the same reaction principle as in method A, except the estimation via calculation of the area under the curve instead of the absorbance. The linearity is from 2 to 50 µg/ml with a molar absorptivity of $1.511x10^3$ l./mol.cm and Sandell's sensitivity index equal to 0.0294 µg /cm^2.The RSD% is not more than 0.142% and RE% not more than -3.4%. The proposed methods are characterized by simplicity and they are economical. The two methods used only one reagent, which is sulphuric acid, and thus reduce the possibility of contamination with organic materials and reagents. The two methods were successfully applied to the estimation of tetracycline in pharmaceutical preparations(capsules).

Introduction:

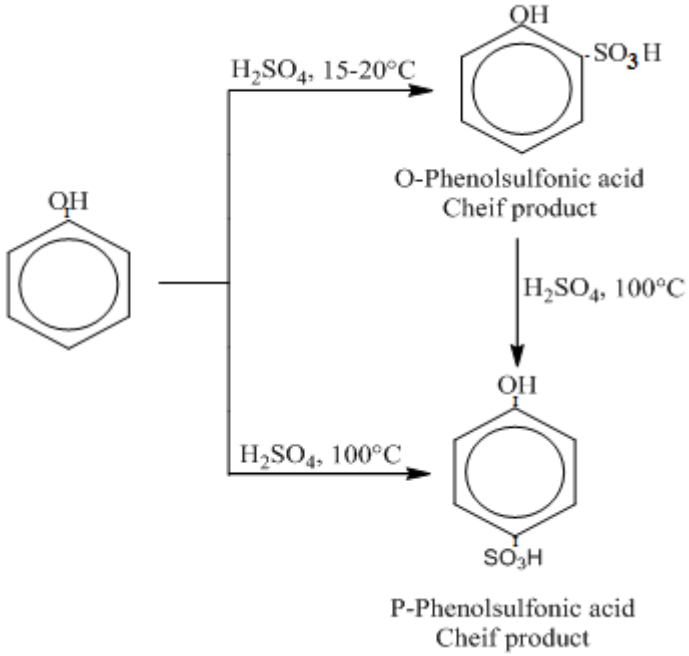
Tetracyclines are the group of an antibiotics contain tetracycline, minocycline, chlortetracycline, doxycycline, and oxytetracycline. Tetracyclines are broadly used in pharmaceutical and veterinary formulations. They are wide-spectrum, usually available and cheap. Tetracyclines are hydrophilic in nature and have a low volatile characteristic.

Tetracyclines are a group of broad-spectrum antibiotics. Tetracycline was present in 1953 and entered marketable use in 1978. It is mainly using in the treatment of infections that affect the respiratory and intestinal tracts, as well as in the treatment of chlamydia. Tetracycline is considered the best treatment for infections caused by chlamydia, such as thrombosis, and urethritis. Tetracycline has the following structure (Scheme 1) [1-4].



Scheme 1: Structure of tetracycline.

Sulphuric acid, a mineral a strong acid, a colourless, odourless, viscous liquid and miscible with water. The acid in its pure form is highly effective, as it corrodes other materials. It is also used as an oxidizing agent, to draw(adsorbed) water from many materials when added to them (except phosphorous pentoxide), and also easily absorbs water vapour from the air. Concentrated sulfuric acid enters oxidation and reduction reactions, it behaves as an oxidizing agent. Its interaction with phenol to form phenol-sulphonic acid in the ortho position at room temperature or in the para position at 100°C [5].



Scheme 2: The sulphonation of phenol.

Various methods and techniques have been listed in literature used in determination tetracycline as pure or in its formulations. These techniques comprised: High Performance liquid chromatography [6-9], UPLC-MS/MS [10], LC- MS [11], LC-MS/MS [12], adsorptive differential pulse cathodic stripping voltammetry [13], liquid membrane electrodes [15], adsorptive voltammetry using a multi walled carbon nanotube paste rotating disk electrode [16], modified glassy carbon electrode [17], flow-injection analysis [18], and spectrofluorimetric [19]. The spectrophotometric methods included using various reactions and reagents such as diazotisation and coupling with diazotised 4-aminoantipyrine in presence of cetylpyridinium chloride. [20], anthranilic acid [21], 4-aminopyridine [22], sulphanilic acid [23], oxidative coupling reaction with: sodium nitroprusside and hydroxylamine hydrochloride [24], N,N-Diethyl-p-phenylene diamine [25], 2, 4–dinitrophenyl hydrazine [26], and oxidation reaction with sodium hypochlorite in alkaline medium sodium

hypochlorite in alkaline medium[27]. The aim of present suggested procedures to estimate tetracycline in its formulation via ease and accurate methods.

Experimental

Apparatus

Absorbance measurements and absorption spectrum were carried out using a JASCOV-630 spectrometer. Glass cells were used with a 1 cm light bath

Chemicals

All materials used were of a high degree of purity.

Reagents solutions

Tetracycline solution (100 µg/ml)

0.0100 g of the pure tetracycline (supplied from the state Company for Drugs Industry and Medical Appliances (SDI) was dissolved in distilled water in a volumetric flask of 100 ml.

Concentrated sulfuric acid of 18.4 molarity.

Pharmaceutical preparation

Preparation of the solution for the tetracycline capsule.

Ten capsules of tetracycline hydrochloride content (each capsule containing 250 mg) were weighed and crushed finely. Then weigh the equivalent of one capsule accurately and dissolve in distilled water, mix well and filtrations it using filter paper, then the filter is diluted to 250 ml with distilled water to get 1000 µg/ ml. Diluted solutions were prepared by suitable dilution.

Procedure and calibration curve

To a series of 5 ml volumetric flasks, increasing volumes of pure tetracycline solution at a concentration of 100 µg/ml to cover the range 2-40 µg/ml was added to 0.5 ml of concentrated sulphuric acid. Then after standing for 5 minutes, dilution to the mark with distilled water and the absorbance was measured at the wavelength 435 nm (Figure 1), and the molar absorptivity, Sandell's sensitivity index, limit of detection (LOD) and limit of quantitation (LOQ) were calculated and equals to 8.31×10^3 l/ mol.cm., 0.0534 µg /cm^2,0.108 µg/ml and 0.360 µg/ml respectively.

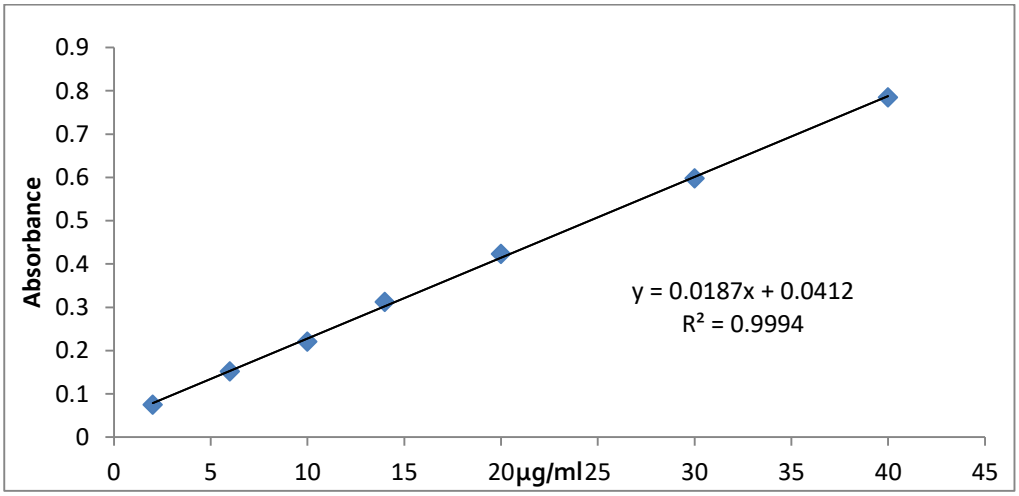


Fig. 1: Calibration curve for the determination of tetracycline.

Preliminary experiment

When tetracycline (20 µg/ml) reacts with concentrated sulphuric acid (0.5 ml) and leaving the solution for five minutes at room temperature, then completing the volume with distilled water to the mark of 5 ml, and the absorption spectral scan of the yellow product was taken against the blank solution and it was found that its highest absorption was at a wavelength of 435 nm. The maximum absorption of 435 nm was recommended in the subsequence experiments.

Results and Discussion

When concentrated sulphuric acid is added to tetracycline, electrophilic compensation occurs (sulphonation of the phenol ring in tetracycline) as mention before in Scheme 2.

Setting optimal conditions

The effect of concentrated sulphuric acid volume

Different volumes of concentrated sulphuric acid were taken from 0.25 to 1 ml, and through the absorptions of yellow products (Figure 2), show that the optimal volume to complete the reaction and gave the highest absorbance is 0.5 ml, and it is fixed in subsequent experiments.

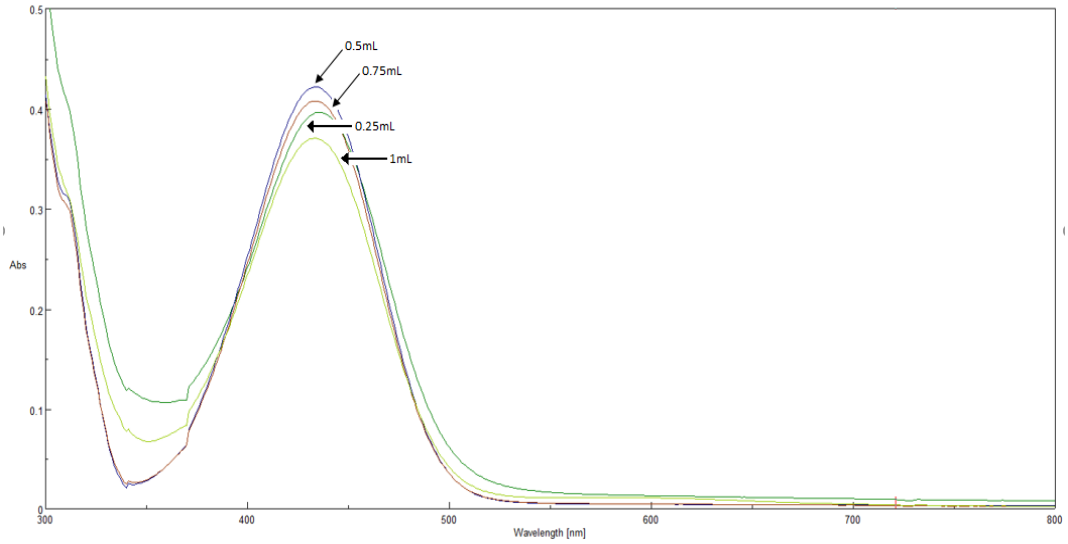


Fig. 2: Choosing the optimal volume of concentrated sulphuric acid.

The ratio of acid to water

Different proportions of acid and water were taken and the results are listed in Table 1.

Table 1: The ratio of acid to water.

Ratio of H_2SO_4: H_2O	Absorbance
Concentrated*	0.423
1:1	0.326
1:3	0.044
1:5	0.023
1:9	0.015

The results in Table 1 indicated that concentrated sulphuric acid gave the highest absorbance compared with acid diluted in different proportions with distilled water.

Therefore, adding concentrated acid is recommended. Also, the standing time before dilution was studied and the results indicated that the highest absorbance was achieved when left the flask for 5 minutes. This time was fixed in the subsequence methods.

The effect of solvents on the spectrum of product

The effect of solvents of different polarities was studied on the absorption spectrum of the coloured product consisting of sulphonation of tetracycline with concentrated sulphuric acid (Figure 3), and Table (3).

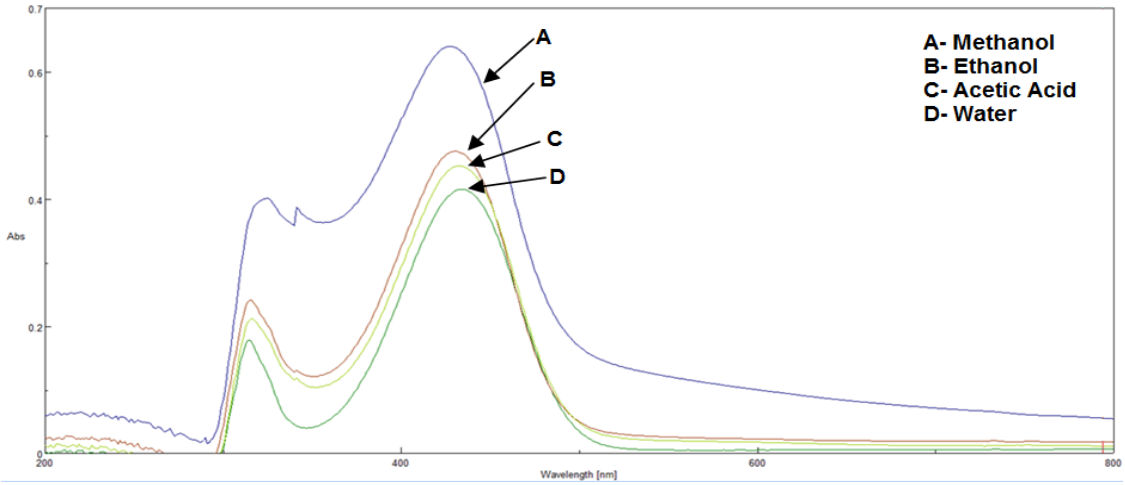


Fig. 3: Absorption spectrum for using different solvents.

Table 2: Effect of solvents on absorbance and molar absorptivity.

Solvent	λmax	Absorbance	£, l/mol.cm
Ethanol	430	0.474	1.053×104
Methanol	427	0.640	1.400×104
CH_3COOH	433	0.451	1.022×104
Water	435	0.415	0.9×104

The results cited in Figure 3 and Table 2 show that organic solvents give more absorbance than water. The use of water for dilution was maintained at subsequent experiments, because of the availability, cheapness and non-toxicity.

Effect of addition sequence.

In order to choose the best sequence for adding the two reactants, the sequences shown in Table 3.

Table 3. Effect of the order of adding reagents.

NO	Reaction components	Absorbance
I*	S + H + H_2O	0.414
II	H + S+ H_2O	0.422
III	H_2O + S +H	0.359
IV	H_2O + H +S	0.280

* Tetracycline(S) +Sulphuric acid(H) + Distilled water (H_2O).

It was noted from the above results that sequence II (the same order in the previous experiment) gave the highest absorbance, and therefore the order II is recommended to use in the subsequent experiments.

Effect of time on the stability of the product.

The stability of the coloured product formed by using two concentrations of 10 and 20 µg tetracycline /ml was studied. It was found that the reaction was stable for a period of time up to 90 minutes (Table 4).

Table 4: Effect of time on the absorbance of coloured product.

µg/ml	Absorbance/ minute								
	Immediately	5	10	20	30	40	50	60	90
10	0.209	0.210	0.211	0.211	0.212	0.212	0.211	0.210	0.212
20	0.420	0.421	0.421	0.422	0.421	0.421	0.423	0.421	0.421

Absorption spectrum

After preparing the optimal conditions for the method, an absorption spectrum of the coloured product was taken, which consisted of 20 µg of tetracycline with concentrated sulphuric acid. Figure 4 shows that the highest absorption of the colored product at the wavelength of 435 nm.

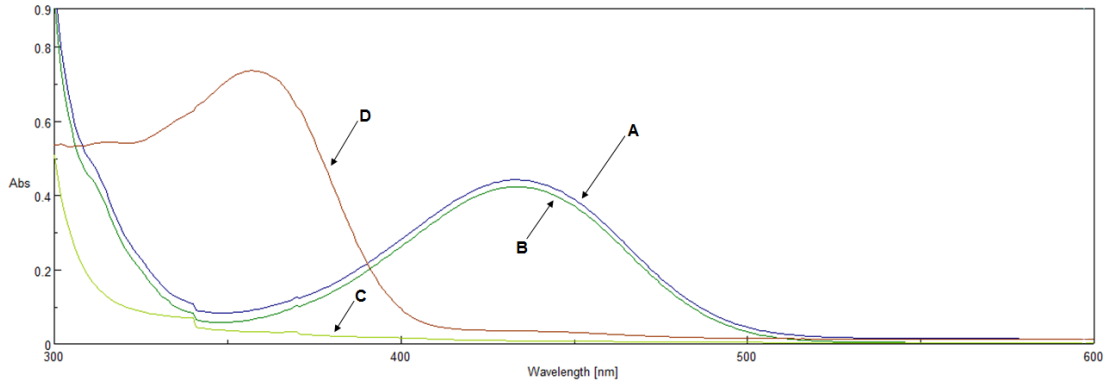


Fig. 4: Absorption spectrums:

(A) Spectrum of 20 µg/ml tetracycline versus distilled water, (B) spectrum of tetracycline versus blank solution, (C) blank solution versus distilled water, and (D) tetracycline versus distilled water

Application of the proposed method

The proposed method was applied to estimation of tetracycline in pharmaceutical preparations (capsules from two different companies), the results cited in Table 5.

Table 5: The results of the application part.

Pharmaceutical preparation	Certified Value (mg)	Amount present (µg/ml)	Recovery*%	Drug content found (mg)
Tetracycline capsules / S.D.I	250 mg	6	100.80	252.00
		10	100.50	251.25
Tetracycline capsules/ India	250 mg	6	96.60	241.50
		10	96.00	240.00

*Average of three determinations.

The calculated drug content for the S.D.I. and Indian capsule are with an acceptable analytical error which indicates the success of the method.

Standard addition method

In order to prove that the suggested method success in estimation tetracycline, and its freedom from additive interactions, the standard addition method was applied to the estimation of tetracycline in capsule/S.D.I via taking 6 and 10 µg/ml of capsule pharmaceutical preparation solution, the results as cited in Figure 5.

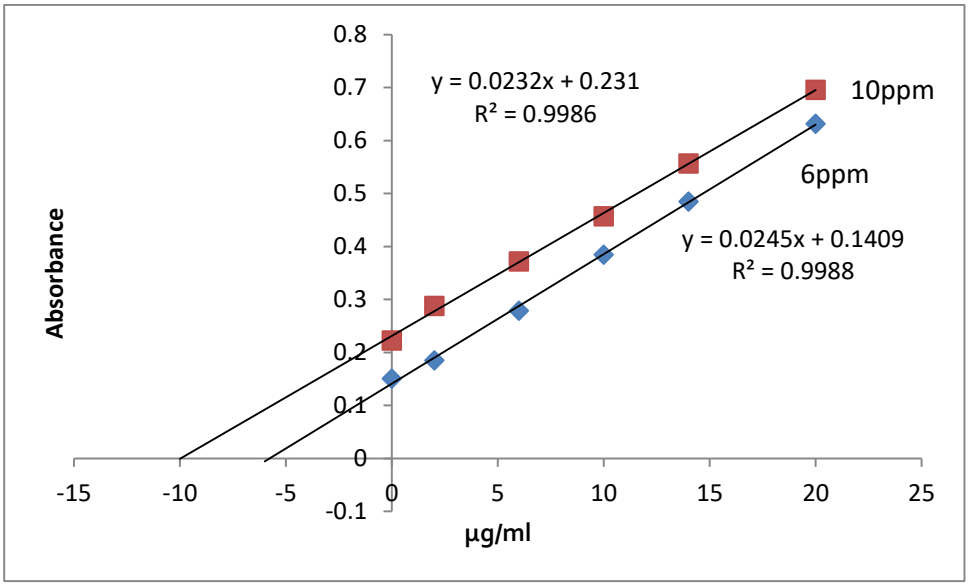


Fig. 5: Standard addition plot.

The results shown in Table 6, indicated that the proposed method has proven its success and credibility in the estimation of tetracycline and there is no interfere of additives.

Table 6: Results of the standard addition method.

Drug	Amount taken	Amount measured	Recovery	Drug content
Tetracycline capsule,250 mg (S.D.I)	6	5.75	95.83	239.57
	10	9.95	99.50	248.87

Method B

Method B included calculated the area under the peak. Peak area measurements (height or area) are very important in chromatography, and peak area measurements are sometimes also used in spectroscopy. To strictly Beer's law. A problem with measuring the peak area

from which the area is determined is that the peak start point and peak end point must be determined precisely [28].

Experimental

Apparatus

The same instruments as mentioned in method A.

Chemicals and solutions

Chemicals and solutions are the same as mentioned in method A.

Principle of the method

The principle of the reaction is the same mentioned in method A, as the formation of the product from the reaction of concentrated sulphuric acid with tetracycline with the same optimum additions specified of reagents.

Absorption spectrum

Figure 6 shows the absorption spectrum of 30 µg/ml of tetracycline solution treated according to the optimal condition in method A, which shows that the highest absorption peak was at 435 nm. Using the spectrophotometer program, the area under the peak was determined on the peak with wavelengths from 423 to 437 nm.

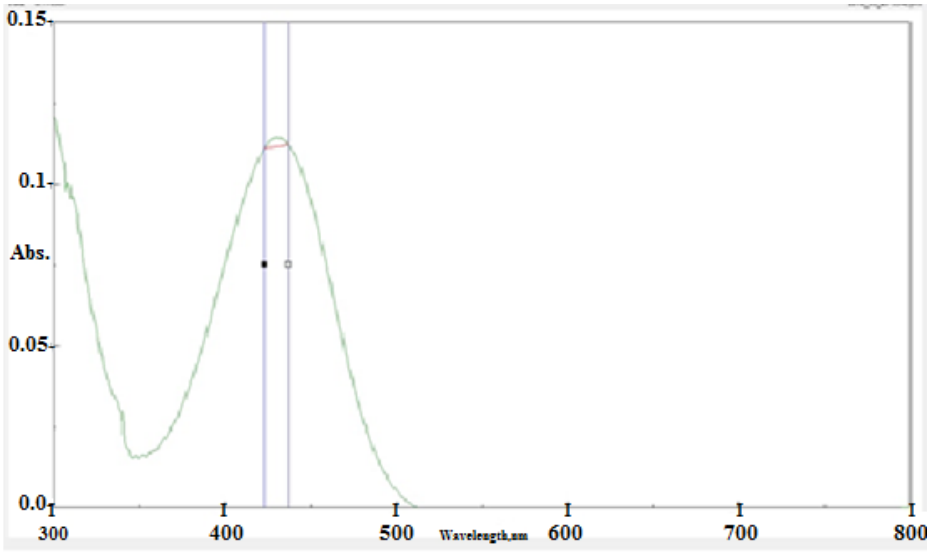


Fig. 6: The absorption spectrum of tetracycline is parameterized according to the proposed method, with the area under the peak determined.

Calibration curve

To a series of 5 ml volumetric flasks, increasing volumes of pure tetracycline solution at a concentration of 100 µg/ml to cover the range (50 µg/ml) were added to 0.5 ml of concentrated sulphuric acid and stand for 5 minutes, then complemented with distilled water to the mark. The area was calculated between wavelengths 423-437 nm (Figure 7).

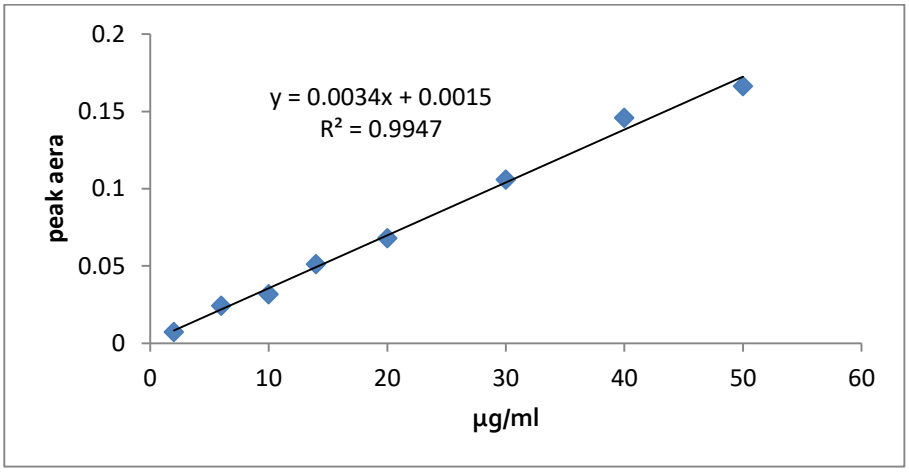


Fig. 7: Calibration curve for the determination of tetracycline.

Accuracy and precession

Under the optimal conditions mentioned before, the accuracy and precession of the method were checked by calculating the recovery percentage (expressive of accuracy) and calculating the relative standard deviation (RSD%, expressive of precession) of two different concentrations of tetracycline 6 and 10 µg / ml. The results obtained are summarized in Table 7, which indicates that the method is accurate according to the value of recovery (98.3%) and good precession (RSD% not more than 0.142 %).

Table 7: Accuracy and precession of the method.

Pharmaceutical preparation	Certified Value (mg)	Amount present (µg/ml)	Amount measured	Rec.* %	RSD%
Tetracycline	250 mg	6	6.00	100	0.142
		10	9.66	96.6	0.033

*Average of three determinations.

Application of the method

The method was applied to the estimation of tetracycline in its pharmaceutical preparation (capsule). The method was applied by taking two different amounts of standard solution of capsules 6 and 10 µg/ml and they were treated according to the suggested and the obtained results are summarized in Table 8.

Table 8: Application of the proposed method.

Pharmaceutical preparation	Certified Value (mg)	Amount present (µg/ml)	Recovery%	Drug content found (mg)
Tetracycline capsule / S.D.I	250 mg	6	99.98	249.95
		10	100.10	250.25
Tetracycline capsule / India	250 mg	6	98.50	246.25
		10	97.20	243.00

Methods comparison

A number of analytical variables for the proposed method were compared with the same variables from two spectrophotometric methods from the literature in Table 9.

Table 9: Comparison of the analytical variables for the proposed method with other methods.

Parameter	Method A	Method* B	Literature method (27)	Literature method(25)
Type of reaction	Sulphonation	Sulphonation	Oxidation	Oxidative Coupling
Reagent used	Sulphuric acid	Sulphuric acid	Sodium hypochlorite	N-N – Diethyl p-phenylene diamine
Maximum wavelength, nm	435	423-437	400	552
Medium of reaction	Acidic	Acidic	Alkaline	Alkaline
Beer's law µg /ml	2-40	2-50	2-24	10-32
ε, l/mol.cm.	$8.31x\ 10^3$	……..	1.346×10^4	1.0579×10^4

* Via estimation of area under the peak.

From the results of Table 9 the proposed methods are sensitive and have a wide range of estimation.

Conclusion

A simple, economic and very easy two spectrophotometric methods were suggested for the determination of tetracycline. Method A relied on the formation of a coloured reaction between tetracycline and concentrated sulphuric acid, the product gave the highest absorption, at a wavelength of 435 nm. Method B a developed for method A on the determination of tetracycline in capsules preparation on measuring the area under the peak between two wavelengths 423 to 437 nm. The methods were successfully applied for the determination of tetracycline in capsules with satisfactory results.

Acknowledgement

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References

1. Chopra, I., Roberts, M., 2001. Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. *Microbiol. Mol. Biol. Rev*. 65 (2), 232–260.
2. Daghrir, R., Drogui, P., 2013. Tetracycline antibiotics in the environment: a review. *Environ. Chem. Lett*. 11 (3), 209–227.
3. The Japanese Pharmacopoeia, (2016). 17th edn., English Version, The Ministry of Health, Labor and Welfare ,p1670.
4. British Pharmacopeia on CD-ROM. System Simulation Ltd, the Stationary Office Ltd, London, 2009.

5. Morrison ,R.T. and Boyd, R.N.(1972). Organic Chemistry, 2 Ed., Alyn and Bacon ,Inc. New York, pp80.
6. Abed, H. H., Shebeeb, A. H., & Badea, R. A. (2018). Chromatographic estimation of tetracycline in saliva. *Mustansiriya Dental Journal*, 5(1), 47-52.
7. Saleh, S. M. K., Mussaed, A. M., & Al-Hariri, F. M. (2016). Determination of tetracycline and oxytetracycline residues in honey by high performance liquid chromatography. *Journal of Agricultural Science and Technology B*, 6(2), 135-139.
8. Alanazi, F., Almugbel, R., Maher, H. M., Alodaib, F. M., & Alzoman, N. Z. (2021). Determination of tetracycline, oxytetracycline and chlortetracycline residues in seafood products of Saudi Arabia using high performance liquid chromatography–Photo diode array detection. *Saudi Pharmaceutical Journal*,6 (9),566-575.
9. Saridal, K., & Ulusoy, H. I. (2019). A simple methodology based on cloud point extraction prior to HPLC-PDA analysis for tetracycline residues in food samples. *Microchemical Journal*, 150, 104170.
10. Singh, S. P., Pundhir, A., & Ghosh, S. (2015). Validation of an analytical methodology for determination of tetracyclines residues in honey by UPLC-MS/MS detection. *Indian Journal of Natural Products and Resources (IJNPR)[Formerly Natural Product Radiance (NPR)]*, 6(4), 293-298.
11. Patyra, E., & Kwiatek, K. (2016). Analytical procedure for the determination of tetracyclines in medicated feeding stuffs by liquid chromatography-mass spectrometry. *J Vet Res,* 60(1), 35-41.
12. Guidi, L. R., Santos, F. A., Ribeiro, A. C. S., Fernandes, C., Silva, L. H., & Gloria, M. B. A. (2018). Quinolones and tetracyclines in aquaculture fish by a simple and rapid LC-MS/MS method. *Food Chemistry*, 245, 1232-1238.
13. Dizavandi, Z. R., Aliakbar, A., & Sheykhan, M. (2017). A novel Pb-poly aminophenol glassy carbon electrode for determination of tetracycline by adsorptive differential pulse cathodic stripping voltammetry. *Electrochimica Acta*, 227, 345-356.
14. Abass, A. M. (2018). Preparation and Application of Tetracycline Hydrochloride Liquid membrane Electrodes. *Al-Nahrain Journal of Science*, 21(2), 73-80.
15. Sultana, A., Sazawa, K., Islam, M. S., Sugawara, K., & Kuramitz, H. (2019). Determination of tetracycline by microdroplet hydrodynamic adsorptive voltammetry using a multiwalled carbon nanotube paste rotating disk electrode. *Analytical Letters*, 52(7), 1153-1164.
16. Arabsorkhi, B., & Sereshti, H. (2018). Determination of tetracycline and cefotaxime residues in honey by micro-solid phase extraction based on electro-spun nanofibers coupled with HPLC. *Microchemical Journal*, 140, 241-247.
17. Turbale, M., Moges, A., Dawit, M., & Amare, M. (2020). Adsorptive stripping voltammetric determination of Tetracycline in pharmaceutical capsule formulation using Poly (Malachite green) modified glassy carbon electrode. *Heliyon,* 6(12), e05782.
18. Risheed, C. M. (2013). Application of factorial design for optimization of flow-injection spectrophotometric determination of tetracycline in some pharmaceutical formulations. *Tikrit Journal of Pure Science*, 18(3),56-62.
19. Namegabe, L. M., Sarr, S. O., & Diop, Y. M. (2018). Development and validation of a spectrofluorimetric method for the assay of tetracycline in capsules. *American Journal of Analytical Chemistry,* 9(03), 162-170.

20. Al-Ashow, R., & S Othman, N. (2012). Spectrophotometric determination of tetracycline by coupling with diazotised 4-aminoantipyrine in presence of cetylpyridinium chloride. *Rafidain Journal of Science*, 23(3), 72-84.
21. Abd, M. M., Dikran, S. B., & Mahmood, A. K. (2017). Spectrophotometric determination of tetracycline hydrochloride in pure form and pharmaceutical preparation by coupling with diazotized anthranilic acid. *Ibn AL-Haitham Journal For Pure and Applied Science*, 30(1), 400-412.
22. Alassaf, N. A., Zankanah, F. H., Hamody, A. S., & Dikran, S. B. (2019). Kinetic-Spectrophotometric Estimation of Tetracycline in Bulk and Pharmaceutical Forms. *International Journal of Drug Delivery Technology*, 9(02), 197-201.DIAZ
23. Ali, R. J., Hawezy, H. J. S., & Abdullah, M. S. (2018). Spectrophotometric determination of tetracycline hydrochloride through coupling with sulphanilic acid. *Diyala Journal of Medicine*, 15(2), 15-22
24. Hadi, H., & Fadhil, G. (2014). Sensitive spectrophotometric determination of tetracycline hydrochloride in dosage forms using sodium nitroprusside and hydroxylamine hydrochloride. *Al-Nahrain Journal of Science*, 17(3), 53-58.
25. Bakir, L. F. M. M. H., & Aziz, M. S. A. (2016). Spectrophotometric determination of tetracycline, in pharmaceutical formulations by oxidative coupling. *Kirkuk university journal for scientific studies*, 11(4). 159-183. 10.32894/Kujss.2016.131071.
26. Khaleel, R. M., & Mohammed, D. H. (2020). Spectrophotometric determination of tetracycline hydrochloride using 2, 4–dinitrophenyl hydrazine as coupling reagent. *In Journal of Physics*: Conference Series (Vol. 1664, No. 1, p. 012084). IOP Publishing.
27. Ahmed, N. R., Edress, S. B., & Yaseen, H. W. (2018). Assay of tetracycline in pharmaceutical preparations, spiked industrial wastewater and chicken meat samples using visible spectrophotometer technique. *J. Vet. Res*, 17(2), 173-185.
28. Mahdi, N. I. (2021). Simple two spectrophotometric methods for estimation of cephalexin in pure and pharmaceutical dosage form. *Samarra Journal of Pure and Applied Science,* 3(1).37-45.

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تطوير طريقتين طيفيتين لتقدير التتراسايكلين

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الخلاصة:

تم تطوير طريقتين طيفين لتقدير التتراسايكلين بصورته النقية وفي مستحضراته الصيدلانية .تضمنت الطريقة (A) تفاعل التتراسايكلين مع حامض الكبريتيك المركز ليتكون محلول بلون أصفر من التتراسايكلين – حامض السلفونيك يمتلك أقصى امتصاص عند الطول الموجي 435 نانومتر مع امتصاص مولاري 8.31×10^3 لتر / مول.سم .وحساسية ساندل وحد الكشف وحد التقدير الكمي يساوي 0.0534 مايكروغرام /سم^2 و0.108 و0.360 مايكروغرام /مل. ينطبق قانون بير على مدى التركيز من 2 الى 40 ميكروغرام / مل، تضمنت الطريقة B نفس مبدأ التفاعل كما في الطريقة A، باستثناء التقدير عن طريق حساب المنطقة الواقعة تحت المنحنى بدلاً من الامتصاصية. الخطية من 2 إلى 50 ميكروغرام / مل مع RSD٪ لا تزيد عن 0.142٪ وRE ٪ لا تزيد عن % 3.4-. امتازت الطريقتين بالبساطة والسهولة وانهما اقتصاديتان ولم نحتج الا كاشف واحد وهو حامض الكبريتيك وبذلك نقلل من احتمالية التلوث بالمواد والكواشف العضوية. تم تطبيق الطريقتين بنجاح لتقدير التتراسايكلين في المستحضرات الصيدلانية لنوعين من الكبسولات.