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Spectrophotometric and Spectrofluorimetric Determination of Terazosin in Tablets by Eosin Y

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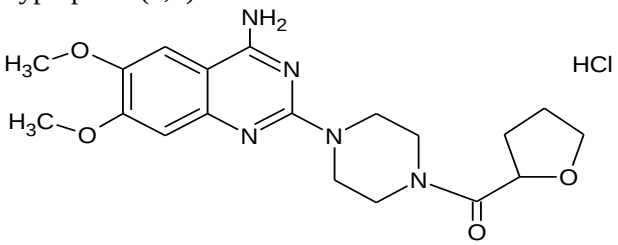
Abstract:

Simple, sensitive and accurate two methods were described for the determination of terazosin. The spectrophotometric method (A) is based on measuring the spectral absorption of the ion-pair complex formed between terazosin with eosin Y in the acetate buffer medium pH 3 at 545 nm. Method (B) is based on the quantitative quenching effect of terazosin on the native fluorescence of Eosin Y at the pH 3. The quenching of the fluorescence of Eosin Y was measured at 556 nm after excitation at 345 nm. The two methods obeyed Beer's law over the concentration ranges of 0.1-8 and 0.05-7 µg/mL for method A and B respectively. Both methods succeeded in the determination of terazosin in its tablets

Key words: EosinY dye, Ion-pair complex , Spectrofluorimetric, Spectrophotometric method, Terazosin.

Introduction:

Terazosin 1-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetrahydro-2-furanyl) carbonyl] piperazine hydrochloride (Fig.1) are one of group drugs called alpha-adrenergic blockers. It facilitates the passage of blood pass through veins and arteries by relaxation of smooth muscle in blood vessels. It also relaxes the muscles in the prostate and bladder neck, improving the urinary flow. Therefore it was indicated for the treatment of hypertension, or to improve urination in men with benign prostatic hyperplasia(1,2).



M.Wt = 423.95 g/mol
($C_{19}H_{25}N_5O_4$. HCl)

Figure 1. Chemical structure of terazosin

Analytical literature review shows a number of methods to determine trerazosin in pharmaceutical preparations and biological fluids such as: reversed phase high performance liquid chromatography, HPLC (3-5), high performance thin layer chromatography, HPTLC (4,6), Electrochemical (7-11) spectrophotometric methods (12-18), and spectroflurimetric methods (19-21)

The aim from this work is the development of two methods That are simple, accurate, sensitive and fast utilizing spectrophotometric and spectrofluorimetric and applying to pharmaceutical preparations using the eosineY dye. The present methods do not need to control the temperature or extraction process.

Material and Methods:

Apparatus

The absorption measurements were conducted using Shimadzu UV-Visible 1650 PC Double - beam spectrophotometer. The spectrofluorimetric measurements were Performed on RF-5301 PC- Spectrofluorophotometer, Xenon lamp and quartz cell (1 cm).

Eosin Y standard solution (5×10^{-4}M) was prepared by dissolving 0.0345 g from pure reagent (LOBA-Chemie) in distilled water then diluted in 100 mL volumetric flask .

Acetate buffer solution (pH 3, pH3.5) was prepared by mixing suitable volumes of 0.02 M sodium acetate (BDH) and 0.02 M acetic acid and modifying the pH to 3 and 3.5 using pH meter.

Standard solution of terazosin HCl (100 µg/mL) was prepared by dissolving 0.0100 g of pure compound (S.D.I-Iraq) in 100 mL volumetric flask with distilled water. This solution was further diluted to 40 µg/mL using distilled water

Terazosin HCl tablets

Ten tablets (each tablet contain 5 mg of terazosin HCl) were weighed precisely powdered and mixed carefully. A weighted amount of the powder equivalent to 0.005 g from pure drug was dissolved in distilled water and filtered. The filtrate was made up to mark in a 50 ml volumetric flask. This solution was further diluted as needed.

Procedures for calibration graph

The spectrophotometric method included the addition of increasing amounts 0.1-8 µg/mL of standard terazosin solution transferred into set of 10 mL standard volumetric flasks then 1.5 mL of 5×10^{-4} M eosinY solution and 1 ml of acetate buffer (pH 3) were added to each flask followed by adjustment to volume with distilled water and the absorbance value was measured against blank solution at 545 nm.

Spectroflurimetric calibration curve, the same procedure was adopted for the spectrophotometric method to serial concentration (0.05- 7 µg/mL) of standard terazosin solution transferred into a set of 10 mL volumetric flasks, 2 mL of 5×10^{-4} M eosinY solution and 1 mL of acetate buffer (pH 3.5) was added and then completed to the mark with distilled water and was well mixed. The fluorescence intensity was measured at 556 nm after excitation at 345 nm.

Results and Discussion:

The proposed methods described in this study are based on the interaction of terazosin and eosin Y at acid pH The formed complex is mainly due to the electrostatic interaction between the tertiary amino groups in terazosin and the anionic functional group of eosin under acidic medium. The formed ion pair associate has a red color and shows maximum absorption at 545 nm (Fig. 2). Both terazosin and the ion pair complex of formed are not fluorescent. Consequently, complex formation is followed by a decrease in the native eosin Y fluorescence at 556 nm after excitation at 345 nm. The Fluorescence quenching is caused by the transformation of fluorescent free eosin Y into a complex, non-fluorescent form (Fig. 3).

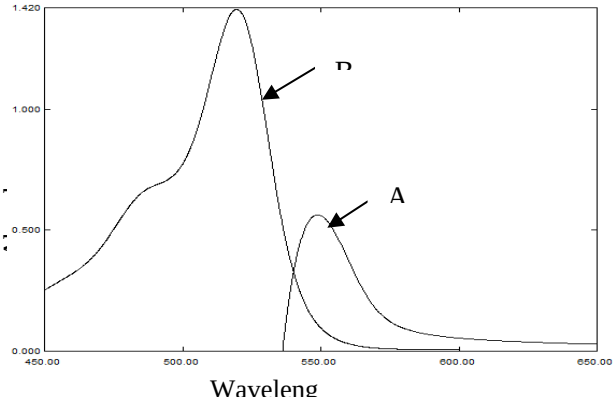


Figure 2. Absorption spectra of: A reaction product of terazosine (4µmL $^{-1}$) with eosin Y of blank, B absorption of blank

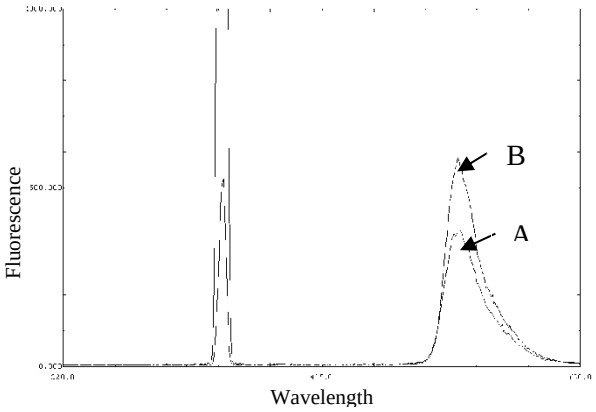


Figure 3. Fluorescence spectra: A` emission product of terazosine (4µmL$^{-1}$) with eosin Yof blank, B`emission spectra of blank

Optimization conditions

All the conditions affecting the color intensity and ΔF (difference between the intensity of fluorescent eosin Y alone (F°) and after its interaction with the drug compound (F)) were studied using a concentration of 4 µg/mL from terazosin understudy in all subsequent experiments..

Effect of pH

The effect of pH is important on the reaction between the drug compound and the eosinY dye because of its effect on the ionization of the dye. The effect of the pH on the absorption of the complex and extent of its effect on the quenching amount of eosin Y fluorescence in its reaction with terazosin were studied. Therefore, different buffers as acetate, citrate, formate, and phthalate of pH 2.5- 4.5 were prepared to obtain maximum absorption of the colored complexes and high ΔF. a fixed amount 1.0 mL of each buffer added to a volumetric flask containing 4µg/mL terazosin and 1.0ml of eosinY solution at a concentration of 5×10^{-4} M and complete with distilled water to 10 mL (Fig. 4).

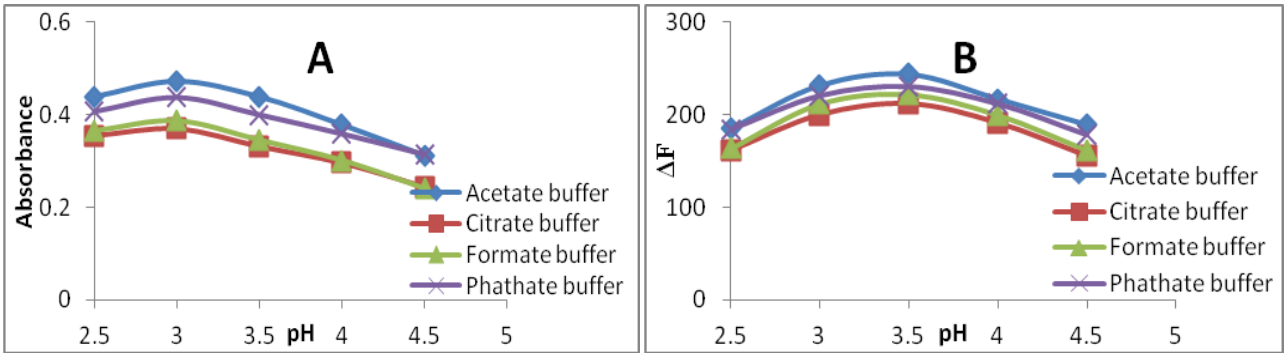


Figure 4. Effect of buffer solution in the estimation of terazosin in spectrophotometric method (A) and spectroflurimetric method (B)

The results in Fig.4 indicate that the acetate buffer was the best medium as it gives maximum absorption at pH 3 and the highest value of ΔF at pH 3.5.

Effect of volume of acetate buffer solution

Varying volumes 0.25 -2 mL of the acetate buffer solution pH 3 and pH 3.5 in methods A and B respectively were added to study their effect on the sensitivity of the developed spectrophotometric and spectrofluorimetric methods. The results of the study are shown in Fig.5, the highest absorption and highest value of ΔF were obtained when adding 1 ml of the buffer solution, so the volume was adopted in subsequent experiments.

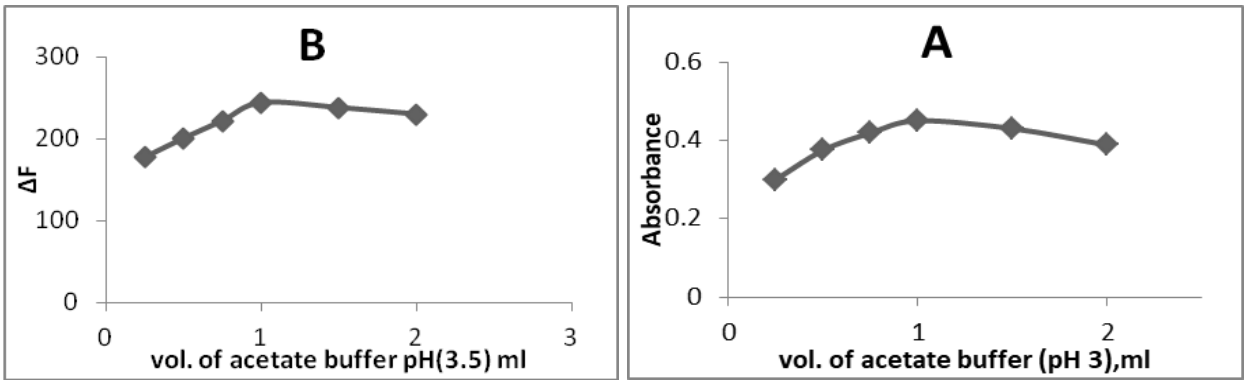


Figure 5. The effect of acetate buffer volume on spectrophotometric method (A) and spectroflurimetric method (B)

Effect volume of EosinY dye additions

The effect of eosin Y (5×10^{-4} M) amount on the absorbance and fluorescence quenching (ΔF) of the reaction products was studied. It was found that by increasing the reagent volumes, the absorbance and ΔF were gradually increased. Maximum values were obtained when eosin Y was 1.5 mL for absorbance and 2.0 mL for ΔF. Figure 6 shows that higher or lower volume decreases the obtained results. Therefore these volumes from eosin Y were chosen in subsequent experiments.

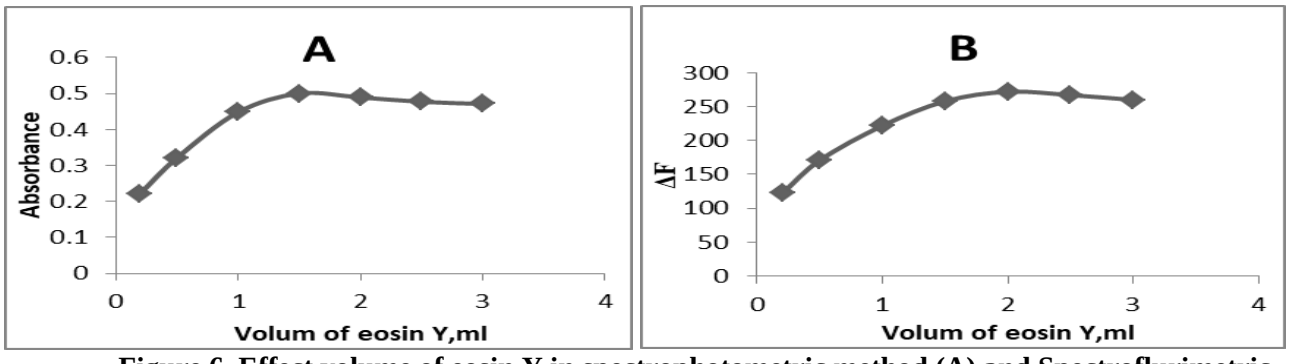


Figure 6. Effect volume of eosin Y in spectrophotometric method (A) and Spectroflurimetric method (B)

Temperature - time effect on reaction and stability

To obtain the optimum temperature to the reaction, different temperatures (0-50° C) were studied in the spectrophotometric method and spectroflurimetric method (Fig.7).

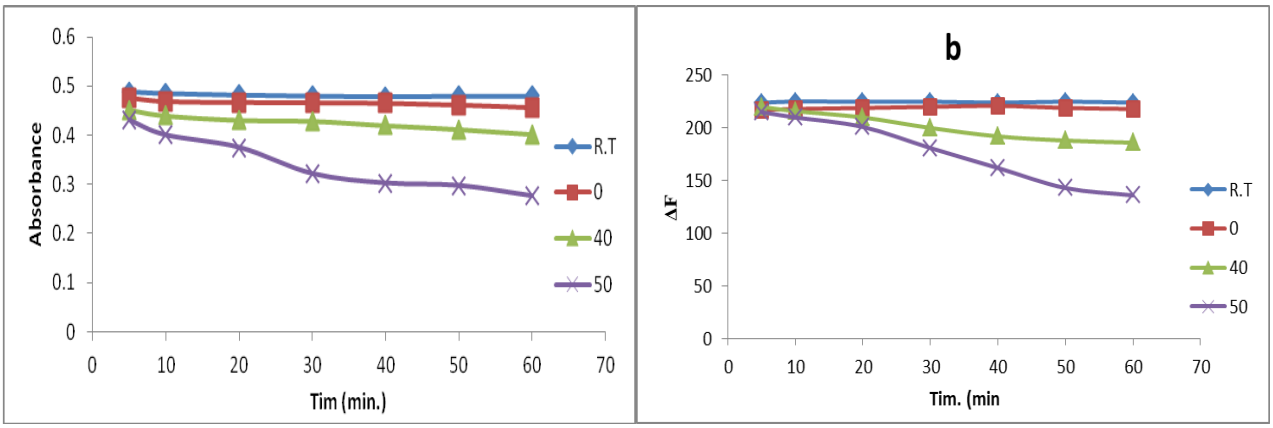


Figure 7 Effect of temperature on the reaction in spectrophotometric method (a) and spectroflurimetric metod (b).

The results in Fig.7 showed that the complex was formed immediately after the addition of the dye to the drug compound in acetate buffer and that the highest absorption intensity and ΔF were obtained 5 minutes after the reaction at room temperature (23 ± 2 C) and absorbance and florescent intensity was stable for at least 55 minutes.

Table 1 presents a summary of the optimum conditions obtained from the spectophotometric and spectroflurimetric methods used to estimate the drug compound.

Table 1. Summary of optimal conditions

Experimental conditions	Spectrophotometric method	spectroflurimetric method
Wavelength (nm)	λ_{max} 545	λ_{em} 556 λ_{ex} 345
pH of acetate buffer solution	pH 3.0	pH 3.5
Buffer volume (ml)	1.0	1.0
Eosin Y (5×10^{-4} M) amount (ml)	1.5	2.0
Standing time (min)	5	5
Stability period (min)	55	55

Calibration curves for analysis

Following optimal conditions the calibration for spectrophotometric and spectrofluorimetric methods were linear over the concentrations extent (0.1-8 µg/mL), and (0.05- 7 µg/mL), respectively. The two correlation coefficient values were greater than 0.9986 in Fig. 8, which statistically indicates that the two calibrations curves possess excellent linear specifications, (Table 2).

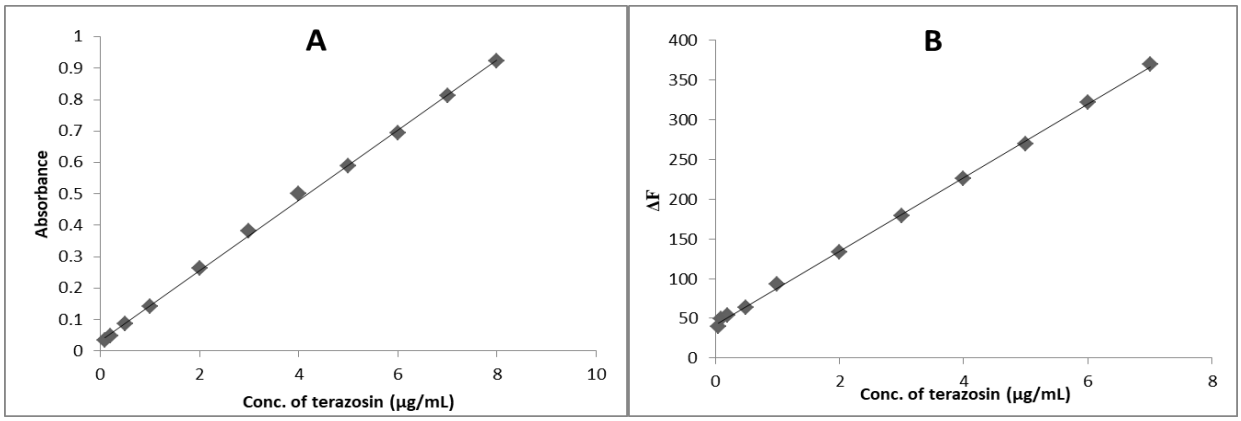


Figure 8. Calibration curves to determination of terazosin in spectrophotometric method (A) and spectroflurimetric method (B)

Table 2. Analytical values of statistical treatments of calibration curves for terazosin

Parameters	Value	
	Spectrophotometric method	Spectroflurimetric method
Linearity range (µg/mL)	0.1 - 8.0	0.05 - 7
Intercept	0.031	41.87
Slope	0.112	46.42
Correlation coefficient (r^2)	0.9987	0.9993
Standard deviation of intercept	0.0053	1.432
Standard deviation of slope	0.0014	0.401
LOD* (µg/ml)	0.031	0.019
LOQ* (µg/ml)	0.102	0.063
Molar absorptivity (l. $mol^{-1}.cm^{-1}$)	4.52×10^4	------

* Average for ten determination of C_{low} of drug

Sensitivity

The detection limit (LOD) and the quantitation limit (LOQ) for the presented methods were calculated using the following equations (22).

$LOD= 3.3\sigma C_{low}/S$

$LOQ= 10\sigma C_{low}/S$

σ :standard deviation of low concentration, S: slop of calibration curve.

LOQ and LOD for terazosin are listed in (Table 2).

Accuracy and precision of the method

To find accuracy and precision of the presented methods, recovery% , and RSD% were calculated using four different concentrations. Table 3 shows the results obtained indicate that the two methods have good accuracy and precision.

Table 3. Accuracy and precision of the presented methods

Method	Amount added (µg/ml)	Recovery* (%)	Average recovery (%)	RSD* (%)
Spectrophotometric	0.2	100.37	100.08	1.09
	1	99.31		0.90
	4	99.88		0.69
	6	100.75		0.43
Spectrofluorimetric	0.2	96.00	98.81	3.67
	1	99.28		1.45
	4	99.82		1.04
	6	100.15		0.76

*Average of five determinations.

Interferences

The effect of some foreign substances which often accompanied with pharmaceutical preparations were studied, it is found that the studied foreign species didn't interfere in the present methods (Table 4).

Table 4. Effect of interferences

Foreign compound	Recovery % of 40 µg terazosin/ µg of added foreign compound					
	Spectrophotometric method			Spectroflurimetric method		
	100	500	1000	100	500	1000
Glucose	98.5	98.1	97.7	99.6	98.8	98.6
Lactose	103.9	102.3	102.6	101.9	102.3	102.4
Starch	97.9	98.1	98.3	99.1	99.0	98.8
Arabic gum	102.2	101.8	101.7	102.0	101.7	102.0

Nature of the complex

Under the working condition, Job's method (23) of continuous variation was applied to estimate the stoichiometry of the reaction. Eosin Y and terazosin solutions 1x 10^{-4} M were prepared. A series of 10-ml volumetric flasks containing 3.0 ml portions of eosin Y and drug compound solutions is composed in various complimentary proportions (0:1.0, 0.1:0.9, ..., 0.9:0.1, 1.0:0). 1.0 ml of acetate buffer (pH 3) was added. The volume was completed to the mark with distilled water. In the spectrophotometric method the absorbance was measured at 545 nm against reagent blank. The same procedure was applied for the spectrofluorimetric method, but the acetate buffer (pH 3.5) and the emission of the solution was measure at 556 nm after excitation at 345 nm. The results obtained (Fig.9) show a ratio of 1:3terazosin to eosinY.

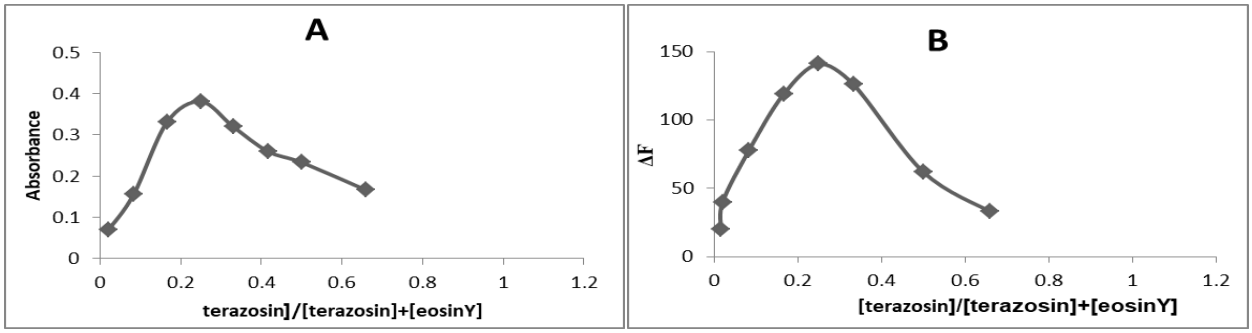
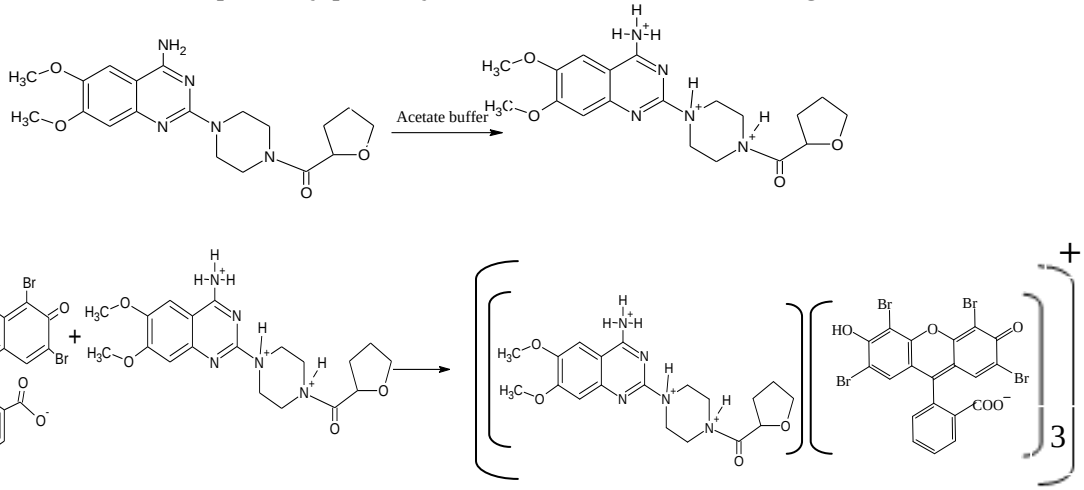


Figure 9. Draw of Job's method between terazosin and eosin Y in spectrophotometric, method (A) and spectroflurimetric method (B).

Therefore, the formation of complex may probably occur as shown in the following reaction:



Stability constant

The stability constant (K) to the ion-pair complex 1:3 (terazosin- eosin Y) was determined from the following (24):

$$K = \frac{1-\alpha}{3\alpha^4 c^3}$$

where α is degree of dissociation of the complex which is obtained by the following equation:

$$\alpha = \frac{Am-As}{Am}$$

C: Concentration of the complex
As: Absorbance of the solution contain stoichiometric.
Am: Absorbance of the solution contain excess amount.

According to the above equations, it was found stability constant K 7.9×10^{13} l.mol^{-1}. This indicates that the complex formed has good stability

Analytical applications

The present methods were evaluated by analyzing the content of the drug compound in pharmaceutical preparations, which were in the form of tablets and from various manufacturers origins, the results illustrated in Table 5 are indicated to be highly efficient and accurate in determination.

Table 5.determination of terazosin in pharmaceutical preparation

Pharmaceutical preparation	Certified value (mg)	Amount taken (µg/mL)	Spectrophotometric method			Spectroflurimetric method		
			Drug content found* (mg)	Recovery* (%)	RSD (%)	Drug content found* (mg)	Recovery (%)	RSD (%)
Prosta-nor	5	1	5.01	100.2	±1.42	4.98	99.6	±1.28
Al-Fares		2	4.90	98.0	±1.31	5.05	101.0	±1.10
(Syria)		4	4.95	99.0	±1.23	5.01	100.2	±1.23
		6	5.00	100.0	±0.98	5.01	100.2	±1.21
Terazosin, Intas	5	1	4.98	99.4	±1.52	5.05	101.0	±1.12
Pharmaceutical		2	4.92	98.4	±1.17	5.02	100.4	±1.22
(India)		4	5.01	100.2	±1.04	4.96	99.2	±1.81
		6	5.05	101.0	±1.13	4.98	99.6	±1.18
Terazosin	5	1	5.02	100.4	±1.85	4.99	99.8	±1.30
Accord		2	5.00	100.0	±1.57	5.00	100.0	±1.22
(Brittan)		4	4.98	99.6	±1.38	5.03	100.6	±1.52
		6	4.99	99.8	±1.29	5.01	100.2	±1.11

* Average of three determinations.

Comparison of the methods

In order to demonstrate the efficacy of the proposed methods and their success in estimating of tirazosin in tablets, a standard addition method was used, no standard supply tools were available for the determination of terazosin in pharmaceutical preparations in British pharmacopeia (25). (Table 6 and Fig. 10).

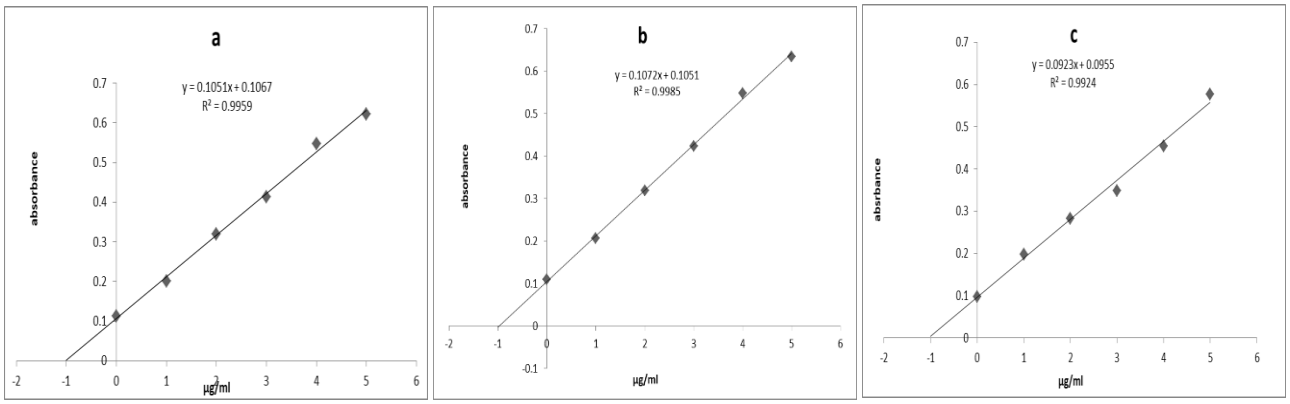


Figure 10. Calibrations standard addition graph for the spectrophotometric determination of 1 µg/mL terazosin tablets of origin (a) Syria, (b) India, (c) Brittan.

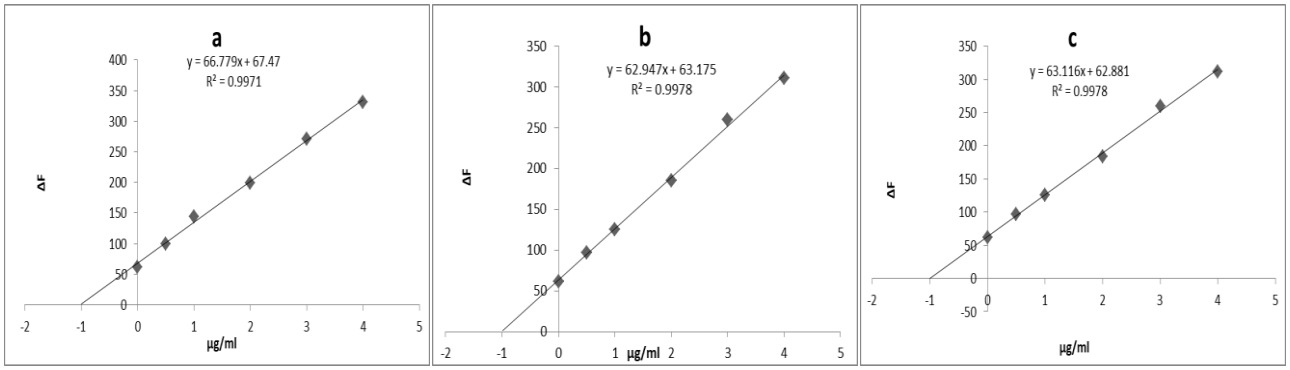


Figure 10. Calibrations standard addition graph for the spectroflurimtric determination of 1 µg/mL terazosin tablets of origin (a) Syria, (b) India, (c) Brittan.

Table6. Determination of terazosin in pharmaceutical preparations by standard addition method

Pharmaceutical preparation	Certified value (mg)	Amount present (µg/ml)	Drug content found (mg)	
			Present method*	Standard addition procedure
		Spectrophotometric method		
Prosta-nor Al-Fares (Syria)	5	1	5.01	5.08
Terazosin, Intas Pharmaceutical (India)	5	1	4.98	4.90
Terazosin Accord (Brittan)	5	1	5.02	5.17
		Spectroflurimetric method		
Prosta-nor Al-Fares (Syria)	5	1	4.98	5.05
Terazosin, Intas Pharmaceutical (India)	5	1	5.05	5.02
Terazosin Accord (Brittan)	5	1	4.99	4.98

The results obtained in Figu. 11 and Table 5 have shown that the standard addition method is in good agreement with the proposed method, indicating that the proposed method is selectively.

Conclusion:

The proposed methods for the spectrophotometric and spectroflurimetric determination of terazosin are simple, rapid and sensitive. Its advantageous over many methods with respect to its higher sensitivity, which permits the determination up 0.1 and 0.05 µg/ml for the spectrophotometric and spectroflurimetric method respectively.

Authors' declaration:

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are mine ours. Besides, the Figures and images, which are not mine ours, have been given the permission for re-publication attached with the manuscript.
- Ethical Clearance: The project was approved by the local ethical committee in Mosul University.

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التقدير الطيفي والفلورومتري للتيرازوسين في الأقراص الدوائية باستخدام الايوسين Y

زينة زهير العبدلي **ميسم حسام الفخري**

قسم الكيمياء، كلية التربية للعلوم الصرفة، جامعة الموصل، موصل، العراق

الخلاصة:

تم وصف طريقتين بسيطتين وحساستين ودقيقتين لتقدير التيرازوسين . تعتمد الطريقة الطيفية (A) على قياس امتصاص معقد التجمع الايوني الناتج من ارتباط التيرازوسين مع الايوسينY في وسط الخلات المنظم دالته الحامضية 3 عند الطول الموجي 545 نانوميتر. الطريقة (B) تعتمد على تأثير الاخماد الكمي للتيرازوسين على شدة تفلور الايوسين عند الدالة الحامضية 3.5. اذ تم قياس الاخماد في شدة تفلور الايوسينYعند 556 نانوميتر بطول موجة اثارة 345 نانوميتر، اتبعت الطريقتين قانون بير ضمن مديات التراكيز 0.1-8 مايكروغرام/مللتر و0.05-7 مايكروغرام/مللتر للطريقتين A وB على التوالي. وتم تطبيق كلتا الطريقتين بنجاح في تقدير التيرازوسين في الاقراص الدوائية..

الكلمات المفتاحية: صبغة الايوسين، معقد التجمع الايوني، الفلورومترية، الطرق الطيفية، تيرازوسين .