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A SENSITIVE ESTIMATION OF TAMOXIFEN IN PHARMACEUTICAL PREPARATIONS AND ENVIRONMENTAL WASTEWATER SAMPLES

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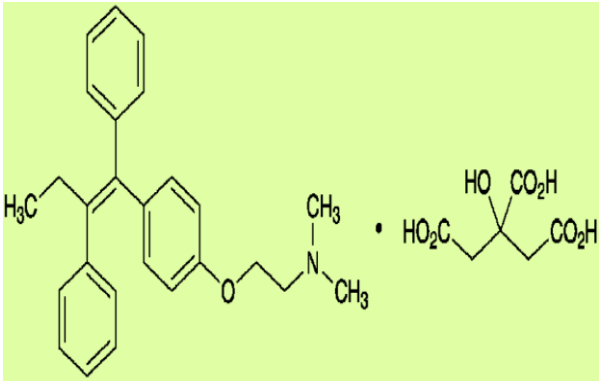
ABSTRACT

A simple, accurate, precise, rapid, economical and high sensitive ultraviolet spectrophotometric method has been developed for the determination of Tamoxifen citrate in pharmaceutical preparations and environmental wastewater samples, which shows maximum absorbance at 235 nm in distilled water. Beer's law was obeyed in the range of 2.5-40µg/ ml, with molar absorptivity of $1.324x10^4$ $L.mol^{-1}.cm^{-1}$, relative standard deviation of the method was less than 1.9%, and accuracy (average recovery %) was 100 ± 0. 8. No interference was observed from common excipients and additives often accompany with Tamoxifen citrate in pharmaceutical preparations. The method was successfully applied to the determination of Tamoxifen citrate 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 Tamoxifen citrate in true samples.

KEYWORDS: Tamoxifen, Spectrophotometry, Pharmaceutical Preparations, Environmental Samples.



C26H29NO.C6H8O7: 563.64
Figure (1): Chemical Structure of Tamoxifen citrate.

Tamoxifen citrate used for treatment of breast cancer and an ovulatory infertility. It is an anti-estrogen which induces gonadotropin release by occupying estrogen receptors in the hypothalamus, thereby interfering with feedback mechanisms; chorionic gonadotrophin is sometimes used as an adjunct in the treatment of female infertility and Indication for pre- and per menopausal women with estrogen- receptor positive breast cancer not previously treated with tamoxifen.[1-4] Treatment of infertility contraindicated if personal or family history of idiopathic venous thromboembolism or genetic predisposition to thromboembolism. There are several methods for determination of Tamoxifen citrate have been described in the literature, these include titration method[5], Potentiometric titration method[6], visible spectrophotometric[7,8], HPLC[9,10], HPTLC[11], HPLC-mass spectrometry[12,13], TLC–densitometry[14], capillary electrophoresis[15], voltammetry method.[16] The ultraviolet spectrophotometric method is the instrumental method of choice commonly used in industrial laboratories because of their simplicity, selectivity, as of our[17-19], for this reason an attempt has been made to developed new UV method for determination of Tamoxifen citrate in pharmaceutical preparations and environmental wastewater samples with high absorption value at 235 nm, result in increasing sensitivity, good accuracy, simplicity, precision and economy.

METHODOLOGY

Apparatus

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

Reagents

All chemical used were of analytical or pharmaceutical grade and Tamoxifen citrate standard material was provided from the state company for pharmaceutical industries (NDI) Mosul-Iraq.

Tamoxifen citrate standard solution 100ppm
This solution was prepared by dissolving 10 mg of Tamoxifen citrate in 100 ml of distilled water in calibrated flask.

Determination of absorption maxima
The standard solution of Tamoxifen citrate(20µg/ml) was scanned in the range of 200-400nm which show maxima located at 235 nm Figure 2. Therefore, this wavelength was used for the construction of calibration curve.

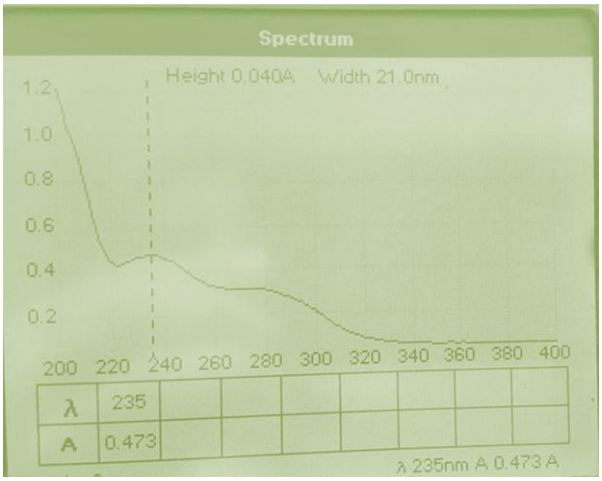


Figure 2: Absorption spectra of 20µg/ml Tamoxifen citrate against distilled water.

Recommended procedure
From the absorption maxima, calibration curve was prepared in the concentration range of 2.5-40 µg/ml. The absorbance was measured at 235 nm against distilled water as a blank. The concentration of the sample solution can be determined by using the calibration curve **Procedure for pharmaceutical preparations** For the determination of Tamoxifen citrate in tablet preparations, and to minimize a possible variation in the composition of the tablets, the composition of the[Tablets of Tamoxinan 20 mg/tab] were provided from the state company of drug industries and medical (NDI) Nineveh – Iraq. The content of ten tablets of the brand, were weighed and grounded to fine powder, then the powder equivalent to 100 mg of Tamoxifen citrate was stirred well with about 90 ml of distilled water for 20 minutes and the volume was made to 100mL with distilled water, filtered through whatman No. 41 filter paper and 20 ml of this solution was diluted to 100 ml by distilled water to get 20µg/ml solution and treated as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

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 5,20,30 µg/ml of Tamoxifen citrate. 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.

RESULTS AND DISCSSION
The method used for the determination of Tamoxifen citrate in pharmaceutical preparations and environmental wastewater samples was found to be high sensitive, simple, accurate, and reproducible. Beer s law was obeyed in the concentration range of 2.5 - 40 µg/ml Figure 3 with correlation coefficient of 0.9995, intercept of0.0024 and slope of 0.0235. The conditional molar absorptivity was found to be $1.324x10^4$ l/mol.cm. and Sandell's sensitivity was 4.26 µg/cm^2. The limit of detection and limit of quantification were evaluated as[20] : LOD = Intercept /Slopex10 and LOQ = 3.3LOD.

The limit of detection was 10.21 µg/ml and the limit of quantification 33.7µg/ml as the lowest standard concentration which could be determine with acceptable accuracy.

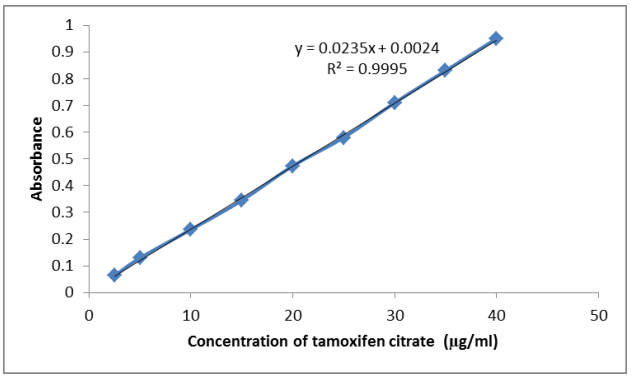


Figure 3: Calibration graph of Tamoxifen citrate.

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 (average recovery %) was 100 ± 0. 8. The RSD% value is less than1.9 indicative of accuracy of the method. the result are compiled in Table.1.

Table I: Accuracy and precision of the proposed method.

Tamoxifen citrate taken µg/ml	Er (%)[a]	RSD(%)
5	0.8	1.8
20	0.6	1.6
30	0.5	1.4

a: Mean of six determinations

Interference studies
In order to assess the possible applications of the proposed method, the effect of substance that often accompany with Tamoxifen citrate in (Tablets) were studied by adding different amount of substances to 20 µg of Tamoxifen citrate. 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 2.

Table (2): Determination of 20 µg of Tamoxifen citrate in the presence of excipients.

Interfering substances	Amount added/mg of interfering	Amount of drug found*(µg)	RSD %
Lactose	10	20.06	1.71
Microcrystalline cellulose	20	20.05	1.64
Corn starch	30	20.08	1.78
Povidene	30	20.05	1.79
Magnesium stearate	40	20.07	1.91
Hydroxyl propyl methyl cellulose	40	20.08	1.93
Poly ethylene glycol	20	5.01	0.91
Titanium dioxide	10	5.05	0.88

*Average of six determinations.

Analytical application

The proposed method was satisfactorily applied to the determination of Tamoxifen citrate 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 3, and the results of water samples Table 4 show that the recovery values obtained were closed to 100%.

Table (3): Determination of Tamoxifen citrate in pharmaceutical formulations.

Pharmaceutical formulations	Label amount (mg)	Found by proposed method * mg	Recovery%
Tablets	20mg/tab	19.97	99.85
	10mg/tab	10.02	100.2

*mean value of ten determinations.

Table (4): Determination of Tamoxifen citrate in wastewater samples.

Wastewater samples	Added µg/ml	Found* (µg/ml)	Recovery %(n=10)
Industrial wastewater	5	5.02	100.4
	20	20.09	100.45
	30	30.08	100.26

*mean value of ten determinations.

Application of the proposed method to content uniformity[21-23]

Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in table 5, indicate that the proposed method cans accurately and precisely quantitative promethazine hydrochloride in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.61 (0.98% which fall within the content uniformity limits specified by the Japanese Pharmacopoeia.[22]

Table 5: Content uniformity testing of Tamoxifen citrate tablets using the Proposed method.

Parameter	% of the label claim
Tablet No.1	100.6
Tablet No.2	100.7
Tablet No.3	100.9
Tablet No.4	100.9
Tablet No.5	99.8
Tablet No.6	100.9
Tablet No.7	100
Tablet No.8	100.8
Tablet No.9	100.4
Tablet N0.10	101.1
Mean(X)	100.61
%RSD	0.98
Max. allowed unit value[22]	±15%

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 Tamoxifen citrate in pure form, bulk, pharmaceutical formulations and environmental wastewater samples.

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