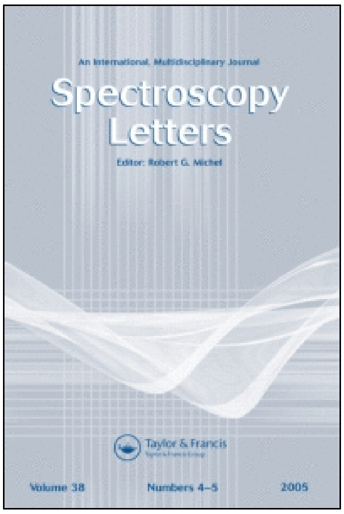

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Spectrophotometric Determination of Oxamniquine via Charge Transfer Complex Formation with Iodine

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SPECTROPHOTOMETRIC DETERMINATION OF OXAMNIQUINE VIA CHARGE TRANSFER COMPLEX FORMATION WITH IODINE

Key words: Schistosomicide - Oxamniquine - Vansil - Iodine Spectrophotometry - Charge transfer Complexes.

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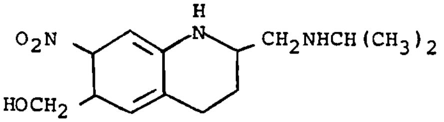
ABSTRACT

In this work the reaction between oxamniquine as n donor and iodine as sigma acceptor was studied,. Different parameters involved in the reaction were investigated such as choice of solvent, iodine concentration, time, light and temperature. Also the stoichiometry of the reaction was determined. Thus, a spectrophotometric procedure has been developed for the determination of **oxamniquine** by reaction with iodine and measurement of absorbance of the formed charge transfer complex at λ 291 and λ 360 nm. Molar absorptivities, A 1%, 1 cm and the regression equations were computed. The proposed procedure was applied for the determination of oxamniquine in its dosage forms. Accurate and precise results were obtained when compared to the manufacturer's procedure.

INTRODUCTION

Oxamniquine is 1,2,3,4-tetrahydro-2-[(isopropyl-amino) methyl]-7-nitro-6-quinolinemethanol$^{(1)}$. It has the following structural formula.



Mol. wt. 279.3

Oxamniquine is one of the powerful drugs dispensed as capsules and oral suspension recently used for treatment of schistosomiasis$^{(2-5)}$. Few methods have been reported for the analysis of this drug. Among these is a non-qaueous titrimetric method$^{(6)}$ using acetous perchloric and quinaldine red or malachite green as indicator. Serum concentration profiles of different dosage forms of the drug were studied by gas liquid chromatography$^{(7)}$. Also a high performance liquid chromatographic method was reported for the determination of oxamniquine in plasma samples$^{(8)}$. The manufacturer control laboratory uses the $A_{1cm}^{1\%}$ at 251 nm for the assay of the drug.$^{(9)}$.

This manuscript extends the application of charge transfer complex formation for the determination of pharmaceutical compounds$^{(10-14)}$. In such reactions intensification of absorption of substances was observed. Usually a new intense band appears in the electronic spectrum of the complex not found in either components of the complex$^{(15)}$. Thus oxamniquine was determined via its charge transfer complex formation with iodine.

EXPERIMENTAL:

Apparatus:

Beckman Du-7 Spectrophotometer was used throughout the study.

Reagents and materials:

- Dichloromethane; prolabo, previously distilled over calcium chloride.
- 1 x 10^{-2}M iodine solution; prepared by dissolving 0.254 g of iodine in about 40 ml of dichloromethane in a 100 ml

volumetric flask with vigorous shaking, then completing to volume with the solvent.

- 1×10^{-3} M iodine solution; prepared by diluting the above solution ten times using dichloromethane as a solvent.
- Stock oxamniquine solution; 1 ml = 280 mcg. prepared by dissolving 0.028 g of oxamniquine in about 20 ml of dichloromethane in a 100 ml volumetric flask and completing to volume with dichloromethane.
- Authentic oxamniquine, Vansil capsules; labelled 250 mg/capsule and vansil oral suspension; labelled 50 mg/ml were kindly supplied by Pfizer Egypt; Cairo under authority of Pfizer Inc. USA.

PROCEDURES:

A- Determination of Authentic Oxamniquine By Reaction With Iodine:

Two sets; A and B of 10 ml volumetric flasks protected from light using aluminium foil, were prepared. 2 ml of 1×10^{-3}M iodine solution were delivered into each flask, followed by accurately measured aliquots of oxamniquine solution in dichloromethane (14-140 mcg) for set A and (14-196 mcg) for set B. Solutions were completed to volume with solvent, mixed well and allowed to stand in the dark for about two hours. Absorbances of solutions were measured at 291 nm for set A and at 360 nm for set B against a blank experiment similarly prepared; excluding oxamniquine. Two calibration curves were constructed at 291 and 360 nm for set A and B respectively. Concentration of unknown samples of oxamniquine could be calculated using these calibration curves or from the following regression equations:

$$A = 0.0703\ C + 0.0147 \qquad \text{at } 291 \text{ nm}$$

or

$$A = 0.0402\ C + 0.0119 \qquad \text{at } 360 \text{ nm}$$

where A is absorbance and C is concentration in mcg/ml.

B- Determination of Oxamniquine in Vansil Capsules:

The contents of not less than twenty capsules were weighed and mixed well. An accurately weighed portion of the capsule contents equivalent to 0.028 g of oxamniquine was transferred into a 100 ml volumetric flask using dichloromethane as a solvent. The solution was completed to volume, stirred for thirty minutes using a magnetic stirrer and filtered; rejecting the first few mullilitres. Concentration of this solution is claimed to contain 280 mcg/ml. This filtrate was used for analysis of oxamniquine content as detailed under authentic drug.

C- Determination of Oxamniquine in Vansil Oral suspension:

An accurately measured volume of vansil oral suspension, previously well shaken, equivalent to 0.028 g of oxamniquine was delivered into a 250 ml separating funnel containing 15 ml of dichloromethane. 20 ml of water were added and the mixture was shaken vigorously. Oxamniquine was extracted in the organic phase, while other suspension vehicles e.g. glycerol, sorbitol...etc which are water soluble were extrated into water. Extraction was repeated four times each with 15 ml of solvent. The organic extract was collected and washed with distilled water, then filtered over anhydrous sodium sulphate into a 100 ml volumetric flask.

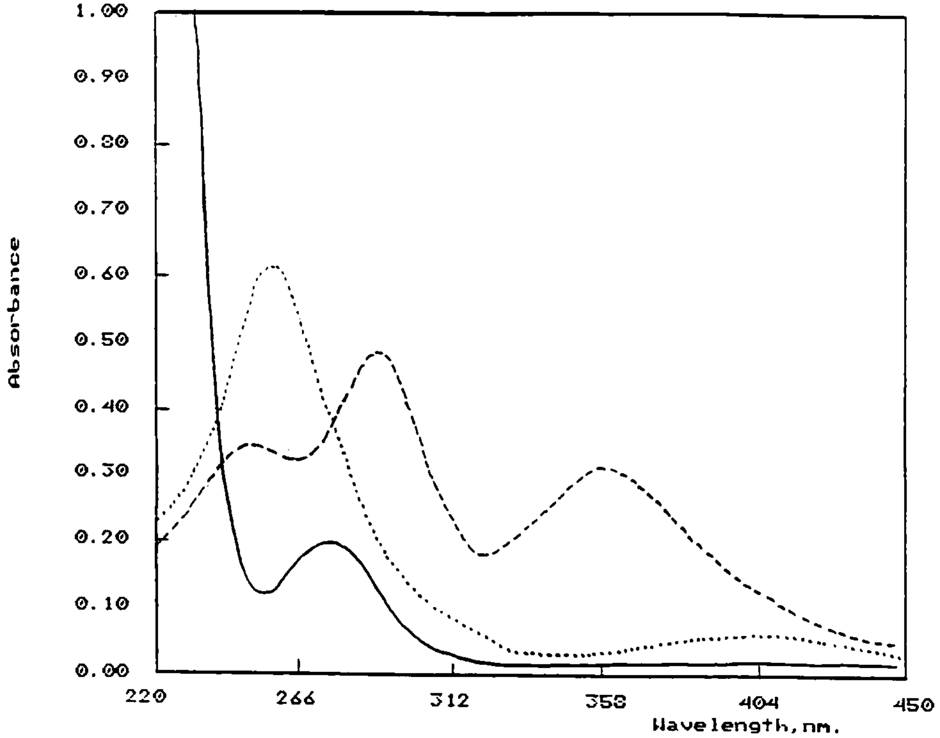


Fig.(1) : UV-Visible Absorption Spectra Of Oxamniquine (......) , Iodine (——) and Their Reaction Product (– – –) in Dichloromethane.

The solution was completed to volume with dichloromethane and mixed well. Concentration of this solution is claimed to be 280 mcg/ml. It was used for analysis of oxamniquine content as detailed under authentic drug.

RESULTS AND DISCUSSION:

The absorption spectra of oxamniquine, iodine and their reaction product in dichloromethane are shown in Fig. (1). The spectra reveal that the reaction product has two newly formed absorption bands having their λ_{max} at 291 &

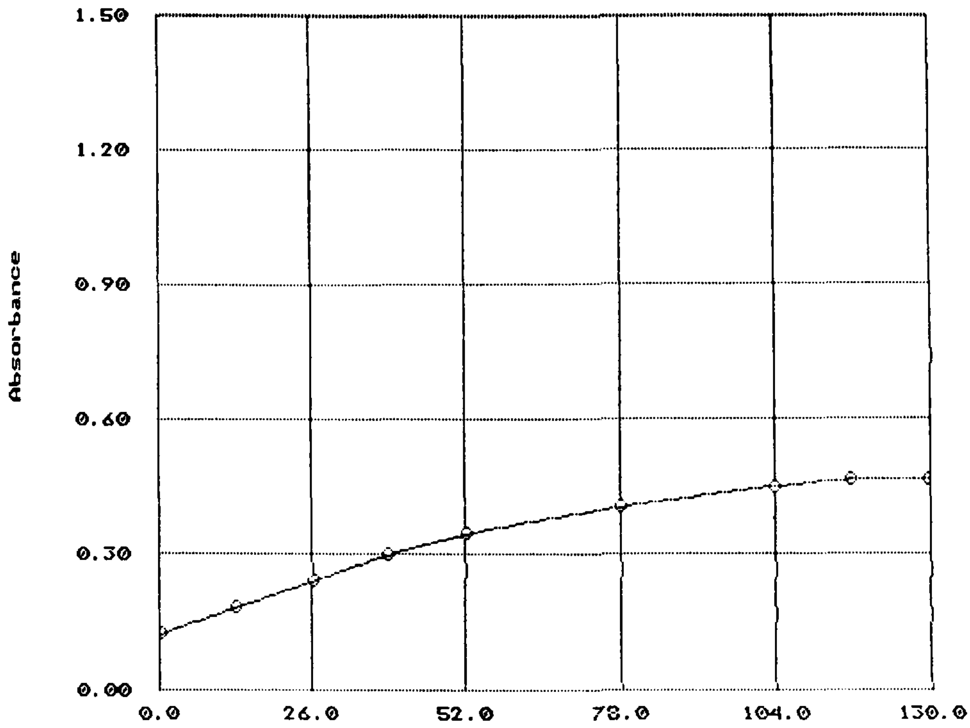


Fig.(2) : Effect of time on the Reaction Between Oxamniquine and Iodine in Dichloromethane.

360 nm. These are accountable as intermolecular charge transfer transitions(15-17). In order to find a linear relationship between absorbance and concentration of the drug, different experimental parameters are to be studied.

Facotrs Affecting the Reaction:

As regards the solvent, it should be well chosen, as solvent affects the kinetics and thermodynamics of complex formation. From the donor side, the solvent should be able to dissolve it to a sufficient degree and if possible extract it from buffered aqueous media when the solvent is water immiscible It must show minimal interaction with the acceptor. Also solvent is preferred to have a low cut off in order to allow the examination of a wider segment of the spectrum. Considering all the above factors dichloromethane was used as a solvent in the assay.

The intensity of absorption was found to decrease by rising the temperature. However, working in a non-fluctuating room temperature was found quite adequate in order to obtain fairly sensitive and precise results.

Studying the effect of light it was found that light affects greatly absorbance readings. Very high and non reproducible results were obtained upon carrying out the experiment in light. Thus the experiment should be carried out in complete darkness by covering the flasks with aluminium foil and keeping them in the dark for the specified time.

The effect of time on the reaction was studied as shown in Fig. (2). It indicates that the optimum time required to reach a steady absorbance readings is about two hours. Changes in absorbance with time are common to n-donor complexes with iodine due to the tendency of the complex species for transformation from outer to inner form. Such a transformation is not instantaneous.

Stoichiometry of the Reaction:

To determine the complexation ratio, both Job's method of continuous variation(18) and the mole ratio method(19) were carried out. Both procedures revealed a 1:1 molar ratio as shown in Fig. (3) and Fig. (4) respectively.

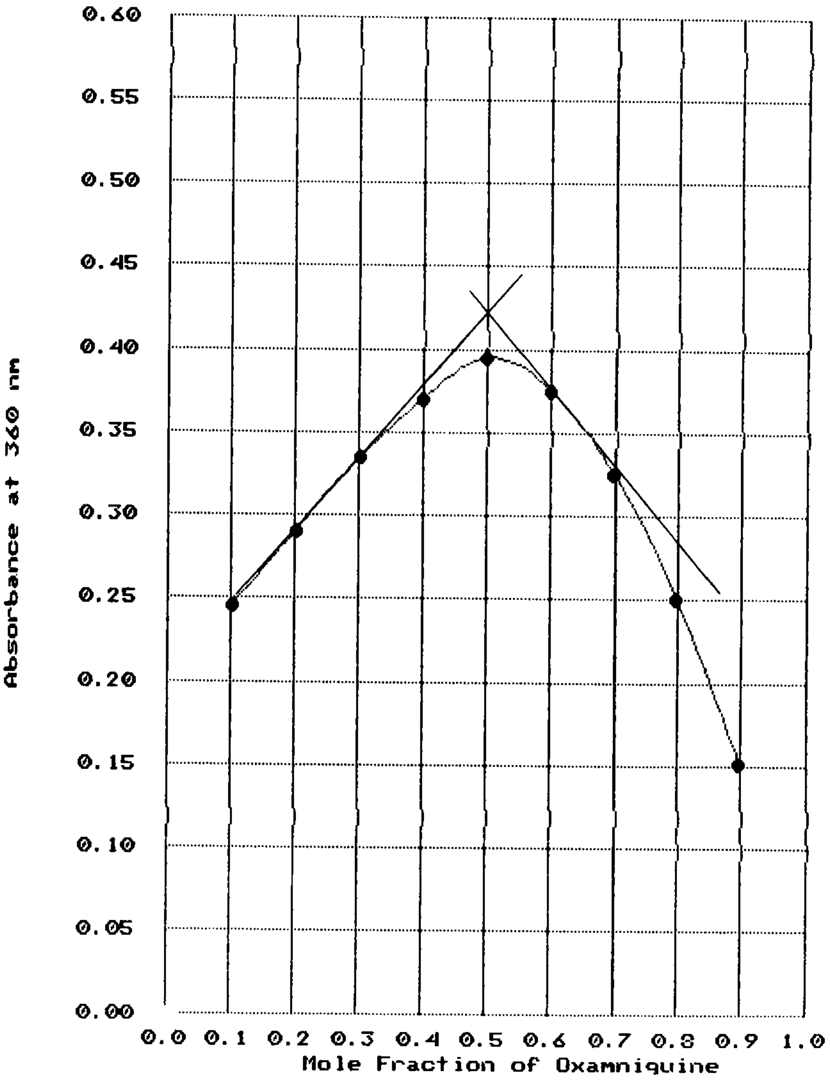


Fig.(3): Determination of the Stoichiometry of the Reaction of Oxamniquine and Iodine by the Continuous Variation Method.

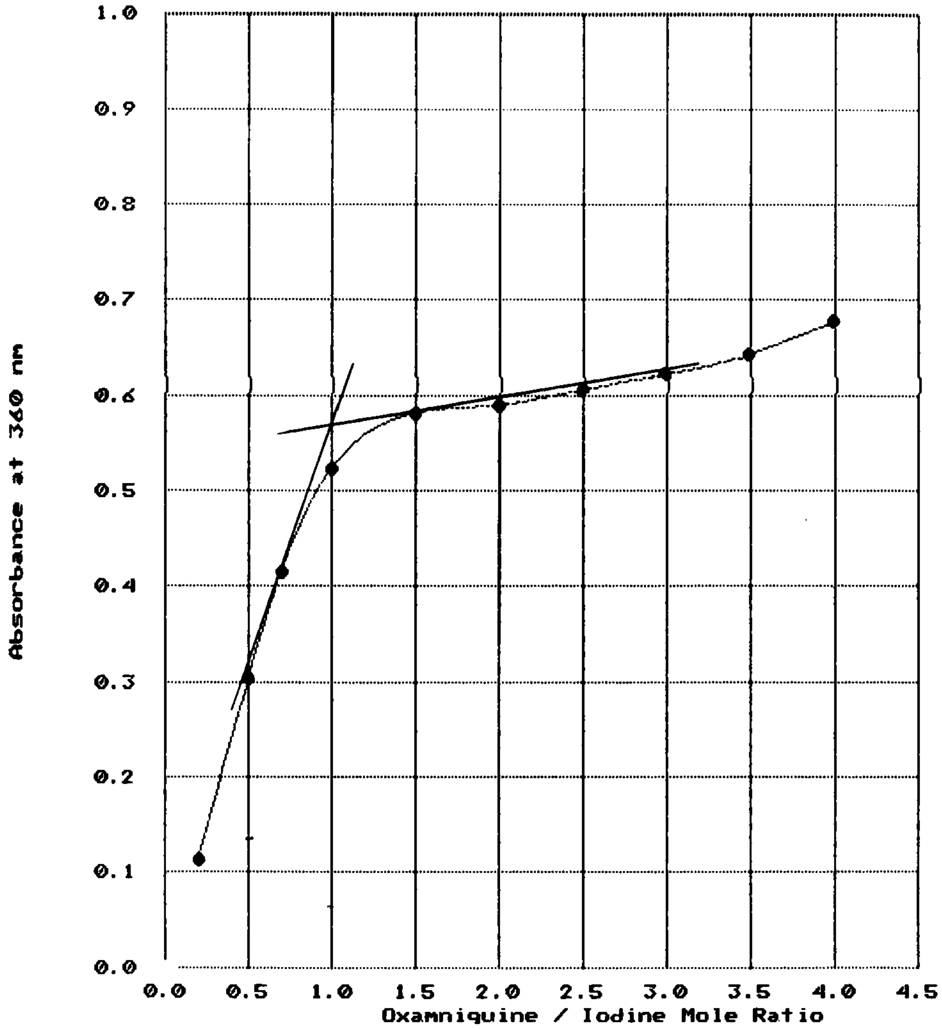


Fig.(4): Determination of the Stoichiometry of the Reaction of Oxamniquine and Iodine by the Mole Ratio Method.

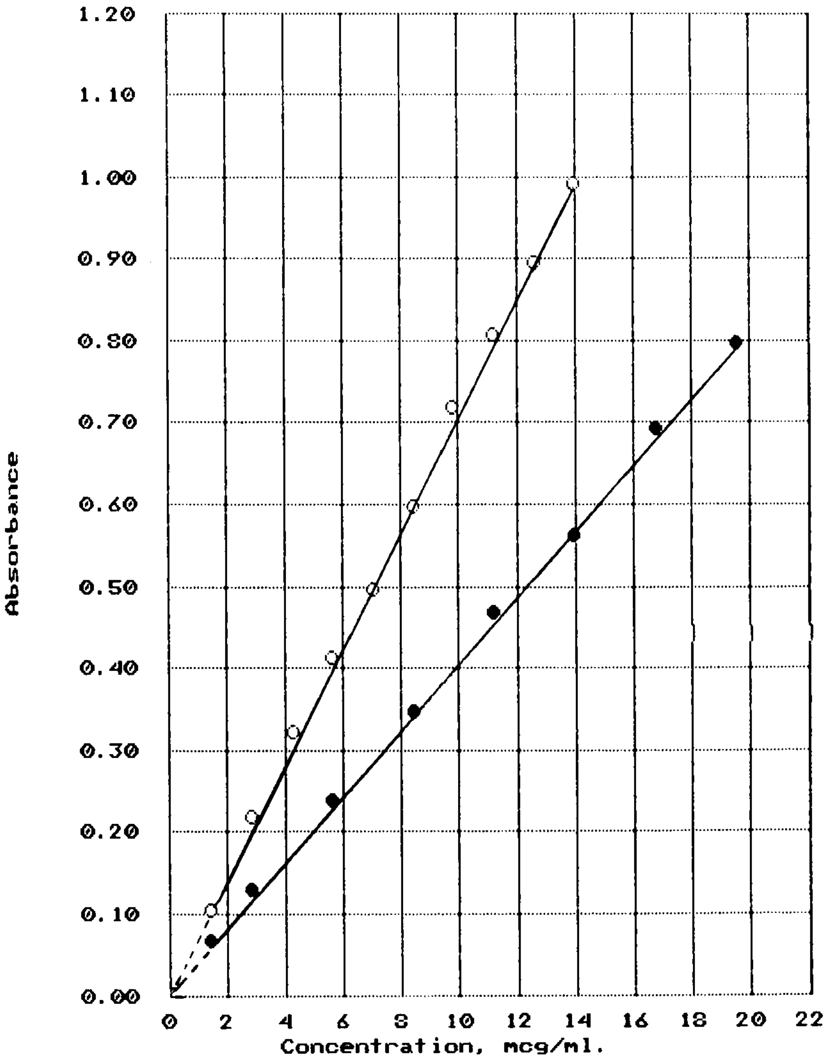


Fig.(5): Linearity of Absorbance to Concentration of Oxamniquine via Reaction with Iodine at :
1- λ max 291 nm.(o——o)
2- λ max 360 nm.(●——●)

TABLE (1)

The Range , A 1% , 1cm , and Regression Equations Obtained on Using Both λ 291 and λ 360 nm for the Determination of oxamniquine via Charge Transfer Complex Formation with Iodine.

Item	at λ 291 nm.	at λ 360 nm.
Range	1.4 - 14 mcg/ml	1.4 - 19.6 mcg/ml
n	8	8
$A^{1\%}_{1cm}$	730	428
	2×10^{5}	1.2×10^{4}
Regression Equation	A = 0.0703 C + 0.0147	A = 0.0402 C + 0.0119

A is absorbance at the corresponding λ max .

C is concentration in mcg/ml.

Linearity of Absorbance to Concentration and Reproducibility of the Results:

Calibration graphs for the drugs at λ 291 and λ 360 nm were prepared as mentioned under procedure A. Linear relationships were obtained in the concentration ranges of 1.4-14 mcg/ml and 1.4-19.6 mcg/ml at 291 and 360 nm respectively as shown in Fig. (5).Table (1) illustrates the ranges, $A^{1\%}_{1cm}$, and regression equations upon using both $\lambda_{max.}$.

TABLE (2)

Determination of Authentic Samples of Oxamniquine via Charge Transfer Complex Formation with Iodine at λ 291 and λ 360 nm.

Exp. No.	At λ 291 nm.			At λ 360 nm.		
	Taken mcg/ml	* Found mcg/ml	Accuracy %	Taken mcg/ml	* Found mcg/ml	Accuracy %
1	1.4	1.40	100.00	1.4	1.41	100.71
2	2.8	2.76	98.57	4.2	4.14	98.57
3	5.6	5.66	101.07	8.4	8.49	101.07
4	7.0	7.07	101.00	12.6	12.83	101.83
5	9.8	9.87	100.71	14.0	13.92	99.43
6	12.6	12.47	98.97	16.8	17.08	101.67
7	14.0	13.75	98.21	19.6	19.67	100.36
Mean			99.79			100.52
F.L (p = 0.05)			± 1.111			± 1.094

* Average of at least three experiments .

To check the reproducibility of the results, different concentrations of an authentic sample of oxamniquine were analyzed by the proposed procedure as detailed under procedure A. Results are shown in table (2) which reveals mean percentage recoveries of 99.79±1.111 and 100.52±1.094 by using λ291 and λ360 nm respectively.

TABLE (3)

Determination of Oxamniquine in its Pharmaceutical Formulations by Charge Transfer Complex Formation with Iodine (at λ 291 nm).

Dosage Form	Reference Procedure		The Proposed Procedure				
	Found*		Found*		Standard Addition		
	mg/ unit	%	mg/ unit	%	Added mcg	Found mcg	Rec. %
Vansil Capsule 250 mg/cap	251.8	100.72	251.08	100.43			
					2.8	2.83	101.07
					4.2	4.19	99.76
					5.6	5.63	100.54
					8.4	8.46	100.71
Mean							100.52
F.L (p = 0.5)							± 0.880
Vansil Oral Suspension 50 mg/ml	50.1	100.20	50.09	100.18			
					2.8	2.79	99.64
					4.2	4.24	100.95
					5.6	5.61	100.18
					8.4	8.48	100.95
Mean							100.43
F.L (p = 0.05)							± 1.018

* Average of 5 separate determinations .

Application of the Proposed Procedure to Pharmaceutical Formulations:

Oxamniquine content in Vansil capsules and oral suspension was determined by applying the proposed procedure.

TABLE (4)

Determination of Oxamniquine in its Pharmaceutical Formulations by Charge Transfer Complex Formation with Iodine (at λ 360 nm) .

Dosage Form	Reference Procedure		The Proposed Procedure				
	* Found		* Found		Standard Addition		
	mg/ unit	%	mg/ unit	%	Added mcg	Found mcg	Rec %
Vansil Capsule 250 mg/cap.	251.8	100.72	252.17	100.87			
					2.8	2.82	100.71
					5.6	5.66	101.07
					8.4	8.29	98.69
					11.2	11.09	99.02
Mean							99.87
F.L (p = 0.05)							± 1.896
Vansil Oral Suspension 50 mg/ml	5o.1	100.20	50.18	100.36			
					2.8	2.85	101.79
					5.6	5.53	98.75
					8.4	8.45	100.60
					11.2	11.15	99.55
Mean							100.17
F.L. (p = 0.05)							± 2.097

* Average of 5 separate determinations.

Results were compared to those obtained by applying the UV procedure (direct absorbance measurement at λ 251 nm in methanol).

TABLE (5)

Statistical Comparison Between The Results Obtained by Charge Transfer Complex Formation with Iodine & The Reference Procedure For The Determination of Oxamniquine.

procedure	Reference	Charge Transfer Complex	
λ max nm.	251	291	360
Mean	100.28	99.79	100.52
F.L.(p=0.05)	± 0.675	± 1.111	± 1.094
n	7	7	7
S.D.	0.729	1.201	1.183
F { calculate		2.7	2.6
F { tabulated		4.3	4.3
t { calculated		0.923	-0.456
t { tabulated		2.179	2.179

The validity of the procedure was checked by applying the standard addition technique. Mean accuracies have been retained on using both λ_{max} as shown in tables (3) & (4).

It is noteworthy to mention that the proposed procedure showed no interference by additives in case of capsules.

Prior extraction of oxamniquine from the suspension using dichloromethane is necessary.

Statistical Analysis of the Results:

Results of the determination of oxamniquine by charge transfer complex formation with iodine using box maxima at 291 & 360 nm were statistically compared to those obtained by adopting the UV procedure. Table (5) reveals that upon using a probability of 95%, there is no significant difference between the mean accuracies of the UV procedure and the proposed one. Also no significant difference exists between their variances. Thus results demonstrate accuracy and precision.

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