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DETERMINATION OF NORFLOXACIN AND OFLOXACIN THROUGH CHARGE TRANSFER COMPLEXATION

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ABSTRACT

A spectrophotometric method was described for the determination of the antibacterial quinolone derivative, norfloxacin and ofloxacin. Chloranilic acid was utilized for their determination, forming charge transfer complex with λmax. 517 and 520 for norfloxacin and ofloxacin, respectively. The optimum conditions of the reaction were discussed. The proposed method was applied for the determination of Noroxin and Tarivid tablets with means percentage accuracies, 100.7 ± 2.08 and 102.13 ± 2.08, respectively. Statistical analysis showed no significant difference between the proposed and official methods.

INTRODUCTION

Certainly, some fluoroquinolone derivatives have shown potent antibacterial action; Norfloxacin and ofloxacin are member of this group which are related to nalidixic acid.

Obviously, several methods were reported for determination of these compounds. These methods include direct spectrophotometry [1,2] or after reaction with ferric ions[3,4] or after reaction with β-naphthol[5]. Titimetric determination of norfloxacin with conductometric measurment after addition of NaOH as titrant was also described[6].

The USP XXII described non aqueous titration of norfloxacin by perchloric acid. In addition, fluorometric determination after TLC separation was reported[8,9]. Also chromatographic methods using reversed phase HPLC was described[10,14].

In the present work, attempts were made to determine norfloxacin and ofloxacin (n donor) using π acceptor chloranilic acid in acetonitril through charge transfer complexation.

EXPERIMENTAL

Apparatus :

Shimadzu UV - Visible recording spectrophotometer UV-260.

Chemicals and Reagents :

All chemical and reagents are of analytical grade quality.

i-Acetonitril; Aldrich, England.

ii-Chloranilic acid (from Merck, Germany) solution, 100 mg % acetonitril.

iii-Standard norfloxacin solution; 20 mg % in acetonitril (from Hoechst orient, Egypt).

iv-Noroxin tablets; from Epico, Egypt.(Batch No. 942249), labeled to contain 400 mg norfloxacin per tablet. Average weight of one tablet is 0.517 g.

v-Tarivid tablets; from Hoechst orient, Egypt.(Batch No. 054), labeled to contain 200 mg ofloxacin per tablet. Average weight of one tablet is 0.4065 g.

Procedure A:

Aliquot (5 ml) containing 0.2-1.0 mg of norfloxacin or 0.2-1.2 mg of ofloxacin was transferred to 10 ml calibrated flask. One ml of chloranilic acid was added and the contents were mixed and completed to volume with acetonitril. The immidiately formed purple colour was measured against blank prepared by the same manner without addition of drug at λmax 517 and 520 nm for norfloxacin and ofloxacin, respectively.

Procedure B:

Twenty tablets of Noroxin or Tarivid were accurately weighed and the average weight of one tablet was determined. The tablets were triturated and amount equivalent to 20 mg of norfloxacin or ofloxacin was taken and dissolved in about 80 ml hot acetontril, filtered in a 100 ml volumetric flask and completed to volume with acetonitril then completed as mentioned under procedure A.

Stoichiometric balance:

The molar ratio of norfloxacin-Chloranilic acid and ofloxacin-chloranilic acid was determined as shown in the following procedure :

In 10 ml calibrated flask, 0.5-4.5 ml of $2\times55.4\times10^{-5}$ M of ofloxacin or $2 \times 62.7 \times 10^{-5}$ M of norfloxacin (V_M) were added to the complementary volumes of $2\times55.4\times10^{-5}$ M or $2 \times 62.7 \times 10^{-5}$ M chloranilic acid (V_L) for ofloxacin or norfloxacin, respectively, to make the total 5 ml and the flask was completed) to volume with acetonitril and the absorbance was measured at the corresponding λmax. The results are shown in table (1).

DISCUSSION

Norfloxacin and ofloxacin are nitrogenous compounds that act as n donor to the π acceptor Chloranilic acid. The purple colour obtained showed maximum absorbance at λ 517 and 520 nm for norfloxacin and ofloxacin, respectively(Fig. 1).

The colour immediately reachs its maximum intensity at room temperature and remains stable up to 25 min for both compounds. High concentrations showed marked decrease in the colour by time (Fig. 2,3). The colour intensity decreases by heating time (Fig. 4) norfloxacin shows marked stability relative to ofloxacin.

The effect of volume of chloranilic acid was studied and 5 ml was found to be the optimum and excess chloranilic does not affect the absorbance (Fig.5)

Acetonitrile was found to be the most satisfactory solvent, other solvents as ethanol or methanol were unsuitable due to limited solubility of the [illegible] drugs

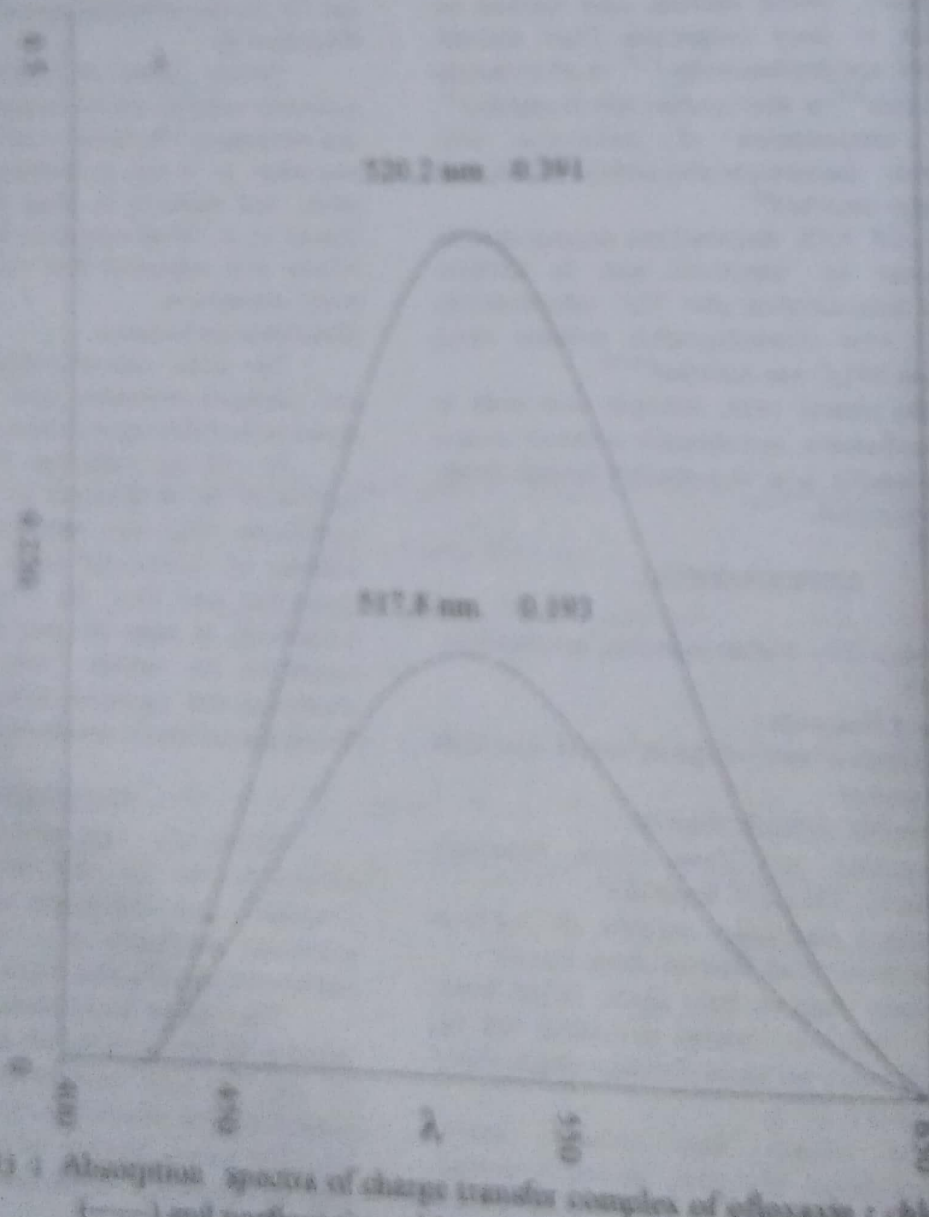

Fig. (1) : Absorption spectra of charge transfer complex of ofloxacin : chloranilic acid (——) and norfloxacin : chloranilic acid (——)

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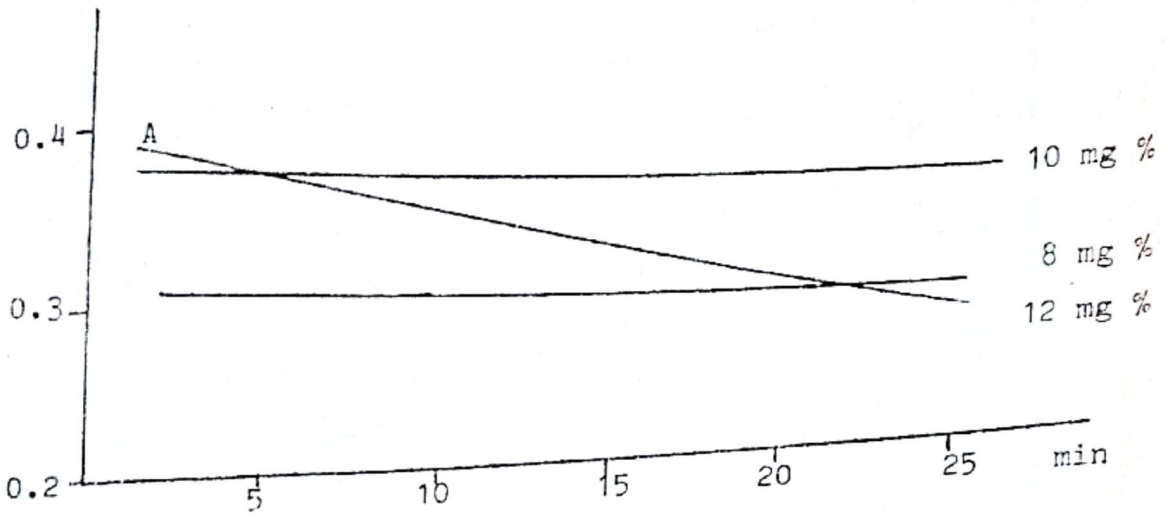

Fig. (2) : Effect of time on stability of charge transfer complex of different concentrations of norfloxacin at λ max 517 nm.

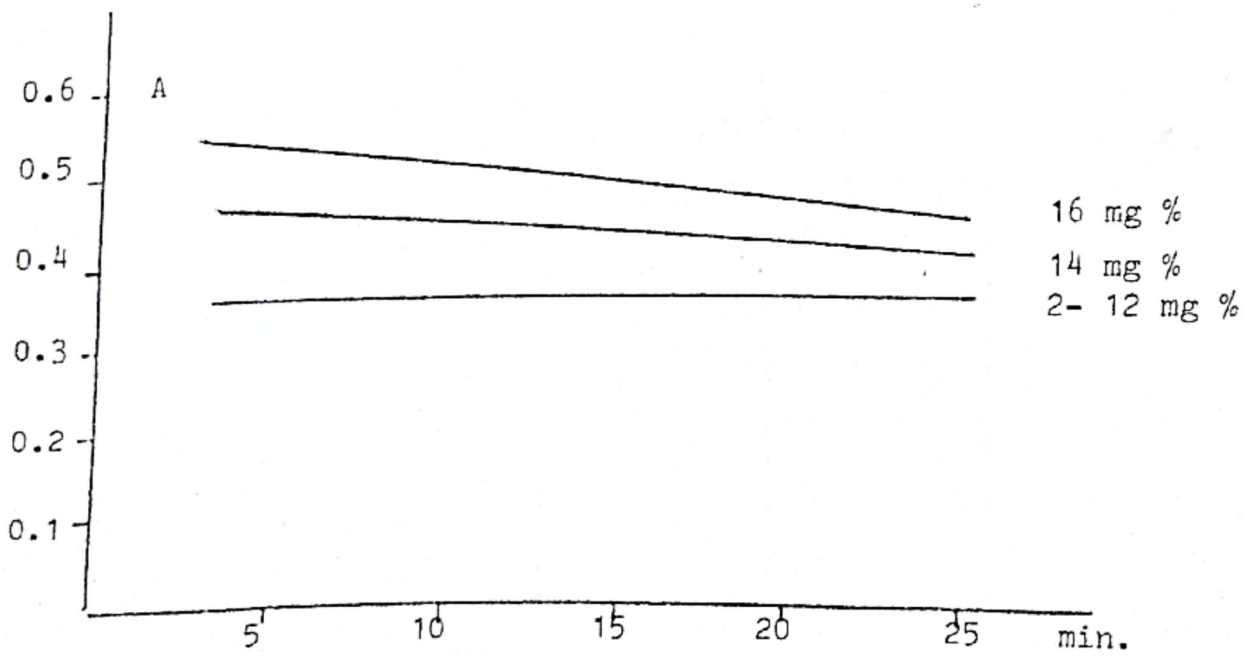

Fig. (3) : Effect of time on stability of charge transfer complex of different concentrations of ofloxacin at λ max 520 nm.

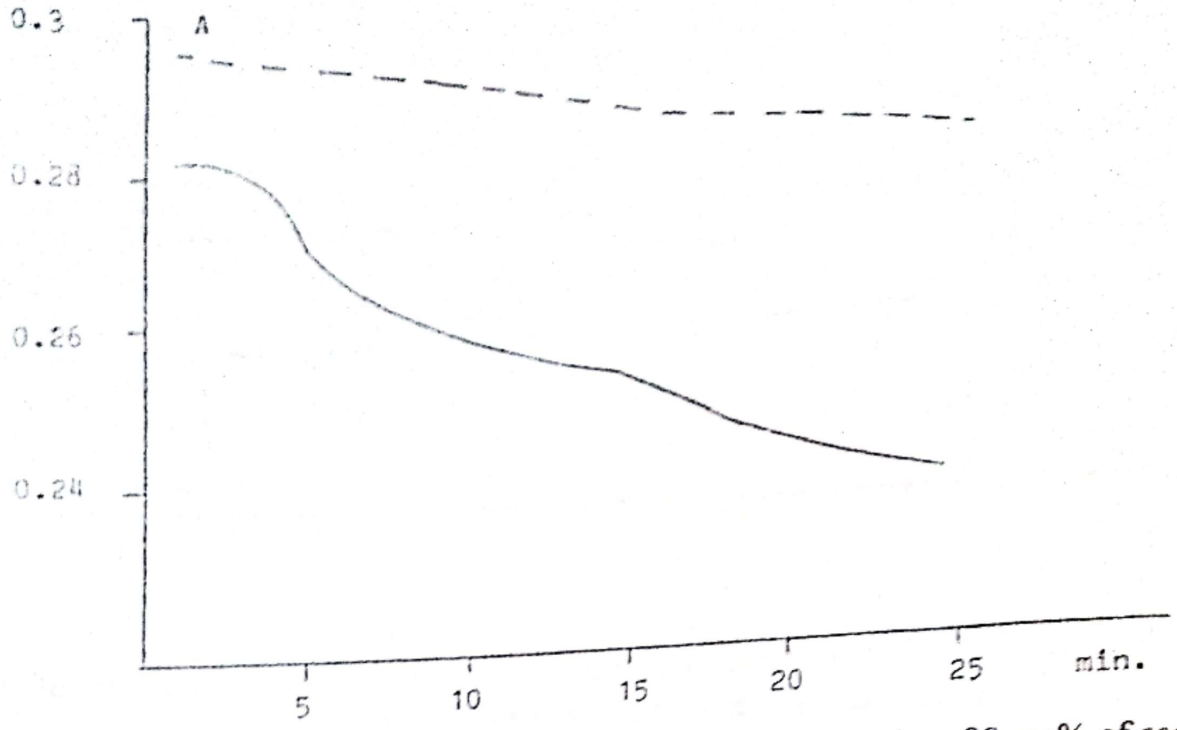

Fig. (4) : Effect of heating time at 50°C on colour intensity of 8 mg% of each ofloxacin (——) and norfloxacin (------) with chloranilic acid.

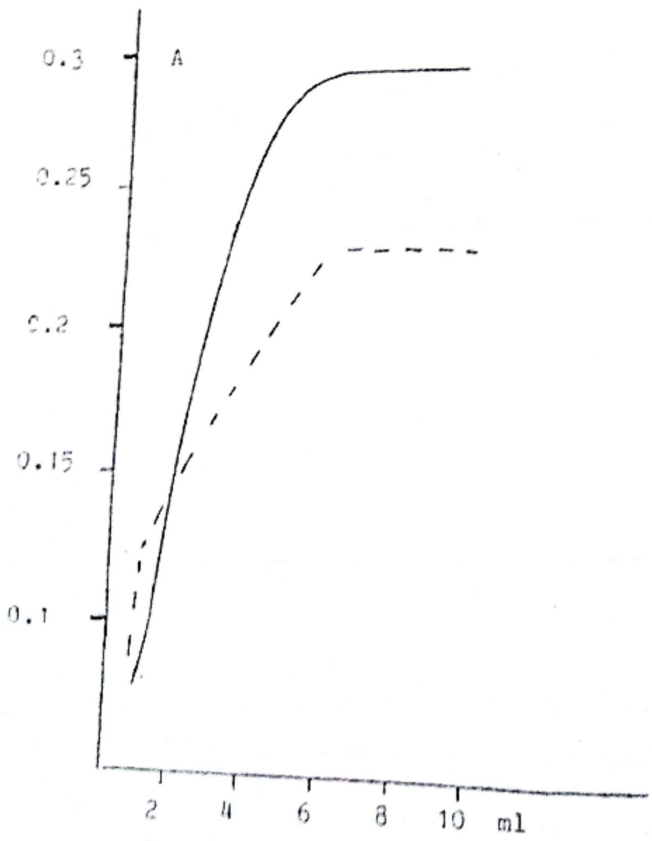

Fig. (5) : Effect of volume of chloranilic acid solution on colour intensity of ofloxacin (——) and norfloxacin (------).

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Table (2) : Determination of Tarivid and Noroxin tablets using the proposed methods.

Tarivid			Noroxin		
Amount added mg%	Amount found mg%	Recovery %	Amount added mg%	Amount found mg%	Recovery %
2	2.09	104.5	2	2.21	100.5
4	3.99	99.85	4	4.12	103
6	6.15	102.5	6	5.88	98.0
8	8.14	101.7	8	8.1	101.3
Mean ± S.D.	102.13 ± 2.08			100.7 ± 2.08	

Table (3) : Statistical analysis of the data for Noroxin and Tarivid tablets obtained by the proposed and official method.

Preparation	Proposed	Official
Tarivid		
Mean ± S.D.	102.13 ± 2.08	100.3 ± 1.8
Student's t test	1.332 (2.446)	
F ratio	1.34 (9.28)	
Noroxin		
Mean ± S.D.	100.7 ± 2.08	99.4 ± 1.5
Student's t test	1.8 (2.446)	
F ratio	1.92 (9.28)	

Chloroform was unsuitable as chloranilic acid has limited solubility in it. Also, acetone was unsuitable as the complex formed shows limited solubility in it.

Calibration graphs were constructed by plotting the absorbance as function of concentration and the relation was linear in the range 2-10 mg % and 2-12 mg % for norfloxacin and ofloxacin respectively, and were described by the following regression equations :

$A = 0.0022 + 0.0358\ C$ $r = 0.998$ For norfloxacin

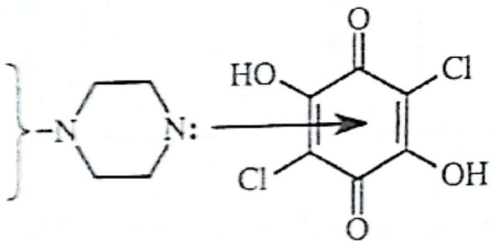
$A = -0.0016 + 0.0352\ C$ $r = 0.999$ For ofloxacin

Where : C is the concentration in mg %

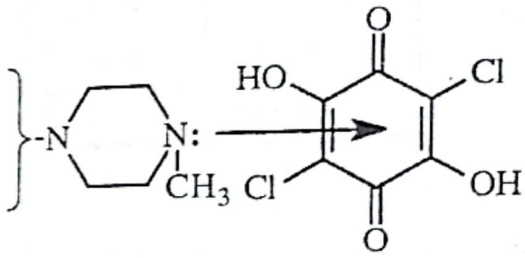
r is correlation coefficient

The molar ratio of the reaction was investigated and it was 1 : 1 for norfloxacin or ofloxacin with chloranilic acid as shown in table (1).

These ratios may be attributed to the presence of one donating center, the aliphatic nitrogen number 4 of piperazine moiety is the most basic and less sterically hindered one as shown in the following scheme :



Norfloxacin-chloranilic acid
CT complex



Ofloxacin-chloranilic acid
CT complex

The validity of the regression equation was tested by analysing Noroxin and Tarivid tablets and the results are shown in table (2).

Statistical analysis of the obtained data by the proposed and official methods showed no significant difference between them (table 3).

Finally, the proposed method is simple and selective depending upon the intact molecule and not on the hydrolytic product. Moreover no interference was observed from the tablets excipients and coloured coats.

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تقدير النورفلوكساسين واوفلوكساسين بواسطة متراكبات انتقال الشحنة

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- تحتوى هذه الدراسة على طريقة طيفية لتقدير بعض مشتقات الكينولون المضادة للبكتريا مثل النورفلوكساسين واوفلوكساسين باستخدام حمض الكلورانيلك الذى يكون متراكبات انتقال الشحنة مع هذه المركبات وقد تم دراسة أنسب الظروف لهذا التفاعل وكذلك النسب المولارية.
- كما تم تطبيق هذه الطريقة على المستحضرات الصيدلية التى تحتوى على هذه المركبات مثل أكراسن اللوركسين والتاريفيد. كما تم عمل دراسة إحصائية للمقارنة بين هذه الطريقة والطرق الدستورية الأخرى. وأوضحت النتائج عدم وجود فرق جوهرى كما أن الطريقة المقترحة تمتاز بالبساطة والسهولة فى التطبيق.