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QUANTITATIVE DETERMINATION OF OFLOXACIN AND CIPROFLOXACIN HYDROCHLORIDE IN THE PRESENCE OF SOME RELATED SUBSTANCES IN PHARMACEUTICAL PREPARATIONS USING HPLC

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ABSTRACT

An analytical method for the determination of ofloxacin or ciprofloxacin hydrochloride in pharmaceutical preparations by high performance liquid chromatography was developed . Piperazine, triethylformate, 3-chloro-4-fluoroaniline and 1, 3-dichloro-4-fluorobenzene do not interfere with the analysis of ofloxacin. Also, cyclopropylamine, piperazine hexahydrate, ethylene diamine ciprofloxacin analog, 3- chloro-4- fluoroaniline, 1,3-dichloro-4-fluorobenzene and fluoroquinolonic acid do not interfere with the analysis of ciprofloxacin. Salicylic acid was used as internal standard and the mobile phase consisted of a mixture of 35% methanol in 0.05 M sodium dihydrogen phosphate and the pH adjusted to 2.8 at flow rate 1 ml min^{-1}.

The chromatographic separation was achieved on Lichrospher 60-RP column with ultraviolet detection at 274 nm. The isocratic system was operated at ambient temperature and required 8 min of chromatographic time . The method was applied to Tarivid® tablets and Ciprinol ® ampoules with relative standard deviation 0.75 and 1.62, respectively.

INTRODUCTION

Ofloxacin; 9-fluoro-2,3-dihydro-3- methyl-10 -(4- methyl-1- piperazinyl)-7- oxo-7H-pyrido [1,2,3 de) -1-4-benzoxazine -6- carboxylic acid , and ciprofloxacin hydrochloride; 1-cyclopropyl-6-fluro-1,4- dihydro - 4- oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid mono-hydrochloride monohydrate, are broad spectrum fluoroquinolone antibacterial agents (1).

Several methods were reported for the determination of these compounds. These methods include: non aqueous titrimetry (2), spectro-photometry(3-5) , fluorimetry (6) , polarography (7) , voltametry (8), HPLC(9-12), and HPTLC (13).

The purpose of this work was to develop a simple method for the assay of ofloxacin and ciprofloxacin hydrochloride in pharmaceutical preparations and detection of some related compounds which may be present as starting materials , reagents or potential impurities identified by the manufacture (14).

EXPERIMENTAL

Apparatus and reagents :

Shimadzu, SCL-10A system controller , LC-10 AS liquid chromatograph SPD-10A UV Spectro-photometric detector, C-R6-A chromatopac.

Ofloxacin I; 0.1 mg ml^{-1} , from Sigma Chem - Co, USA; Ciprofloxacin hydrochloride II; 0.1 mg ml^{-1}, from Bayer, Germany; Salicylic acid III; 0.2 mg ml^{-1}, from Bayer, Germany. Ethylenediamine ciprofloxacin analog VI and fluroquinolonic acid X, from Bayer, Germany.

Cycloproply amine IV, piperazine hexahydrate V, triethylformate VII, 3-chloro-4- fluoroaniline VIII and 1,3 - dichloro -4- fluorobenzene IX from Aldrich Chem- Co, USA.

Ciprinol ampoules from KRKA, Novo mesto, Slovenia, labeled to contain 100 mg/10 ml ciprofloxacin as hydrochloride BN. 2430. Tarivid tablets from Hoechst labelled to contain 200 mg ofloxacin BN: 118.

All standard solutions were prepared by dissolving in the mobile phase.

Chromatographic conditions :

Column : Lichrospher 60-RP, Select , B, 5 μm, 120 x 4.0 mm id.

Mobile phase : 35% methanol in 0.05M sodium dihydrogen phosphate adjusted to pH 2.8.

Detector : 274 nm, 0.01 aufs. ; **Flow rate :** 1 ml min^{-1}. **Pressure :** 135 PSIG. ; **Temperature :** Ambient.

Procedure :

A-Preparation of calibration curves :

Different aliquots of ofloxacin (0.1-1ml) or ciprofloxacin hydrochloride (0.05 - 0.5ml) standard solution were transferred to 10 ml volumetric flask. 1 ml aliquot of salicylic acid standard solution was added to each flask, then completed to volumes with the mobile phase. 10μl of each sample was injected and all measurements were repeated three times at each concentration. The calibration curve was based on peak area ratio of each component to the internal standard against concentration.

B-Commercial dosage forms :

Ciprinol ampoules :

The contents of 10 ampoules were mixed , an accurately measured volume equivalent to 50 mg of ciprofloxacin was transferred to a 500 ml volumetric flask, diluted with the mobile phase to volume Different aliquots from this solution were transferred to 10 ml volumetric flask and completed as described under procedure A.

Tarivid Tablets :

Twenty tablets were weighed and the average weight of one tablet was determined The tablets were powdered and mixed. An accurately weighed portion equivalent to 25 mg of ofloxacin was dissolved in 250ml of the mobile phase with the aid of ultrasonic bath, filtered in 250 ml volumetric flask and completed to volume Different aliquots from this solution were transferred to 10 ml volumetric flask and completed as described under procedure A.

RESULTS AND DISCUSSION

The chromatogram shown in Fig. 1. indicates the possibility of separating I and II from the internal standard III on Lichrospher 60-RP column with 35% methanol in phosphate buffer adjusted to pH 2.8 at 274 nm. The selected compounds were determined at flow rate 1 ml min^{-1} and retention time 3.4, 4.2 and 8 min for I, II and III, respectively, without the interference of IV, V, VII, VIII, IX and X which may be present as starting materials, synthetic intermediate or potential impurities identified by the manufacture.

Due to the great differences in polarity among I or II and IX, X it was necessary to increase the flow rate to 1.5 ml min^{-1} after 10 min. Fig 2, shows chromatogram of I and its related substances at retention time 1.5, 3.4, 4.4, 5.2, 8 and 28 min for V, I, VII, VIII, III and IX, respectively. Fig. 3, shows the separation of II from its related compounds at retention time 1.6 , 3.4, 4.2, 5.2, 8, 28 min for IV (and V) , VI, II, VIII, III and IX (and X) , respectively.

The peak area ratio (Y) to concentration X in mg% were found to be linear within the concentration range 0.1 - 0.9 and 0.05 - 0.5 mg% for I and II, respectively.

Fig. 4 and 5 show different concentration of I or II with the same concentration of III.

Regression analysis of the data for each component gave the slope, intercept and correlation coefficient for each calibration curve , as shown in Table I. The proposed method was applied to assay Tarivid tablets for I and Ciprinol ampoules for II, the results show good accuracy and precision as shown from the percentage recovery and relative standard deviation in Tables (2 and 3) moreover from the aforementioned , it is obvious that the method is highly sensitive , time saving and could be used in quality control of pharmaceutical preparations containing these substances .

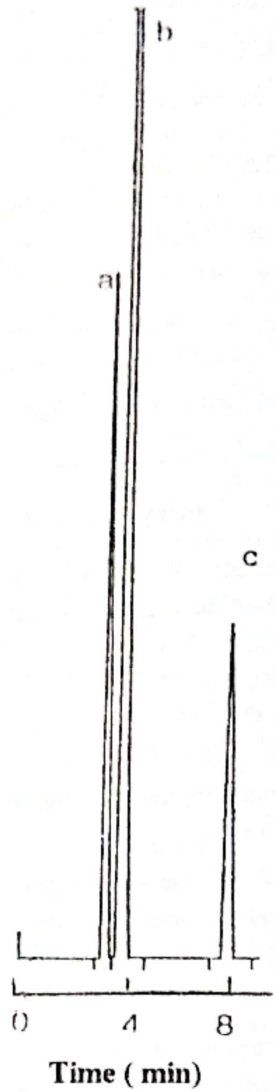

Fig. (1) : Chromatogram of ofloxacin ; **a** , ciprofloxacin hydrochloride ; **b** and salicylic acid; **c** on lichrospher 60-RP column and 35% methanol in phosphate buffer pH 2.8 at 274 nm.

Table (1) : Regression Analysis of the Data .

Compound	Regression equation	Correlation coefficient
Ofloxacin	Y= -0.0147 + 2.327 X	0.9998
Ciprofloxacin hydrochloride	Y= 0.1399 + 7.287 X	0.999

Y= peak area ratio X = Concentration mg%

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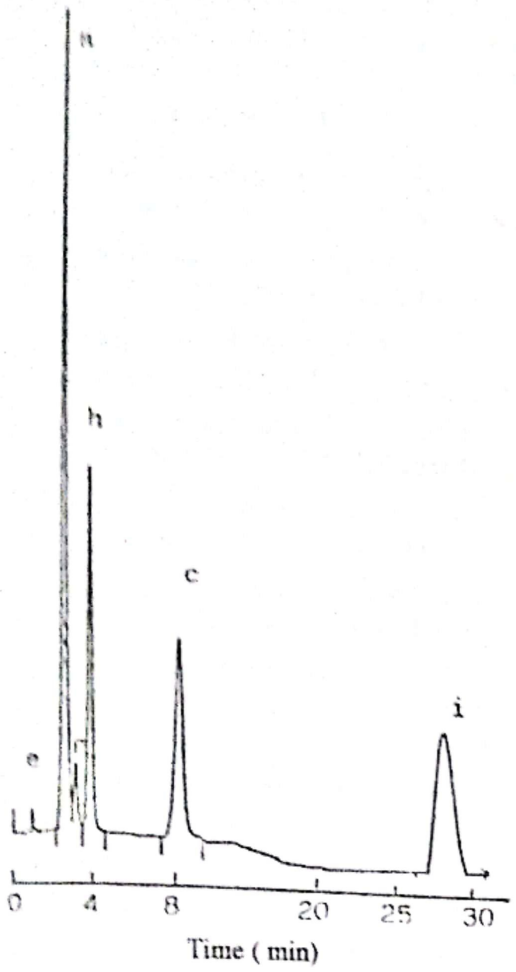

Fig. (2) :Chromatogram of ofloxacin ; **a** spiked by piperazin; **e** triethylformate; **g** 3-chloro -4-flouro aniline; **h** , salicylic acid; **c** and 1,3 - dichloro -4- flourobenzen ; **i** at 274 nm.

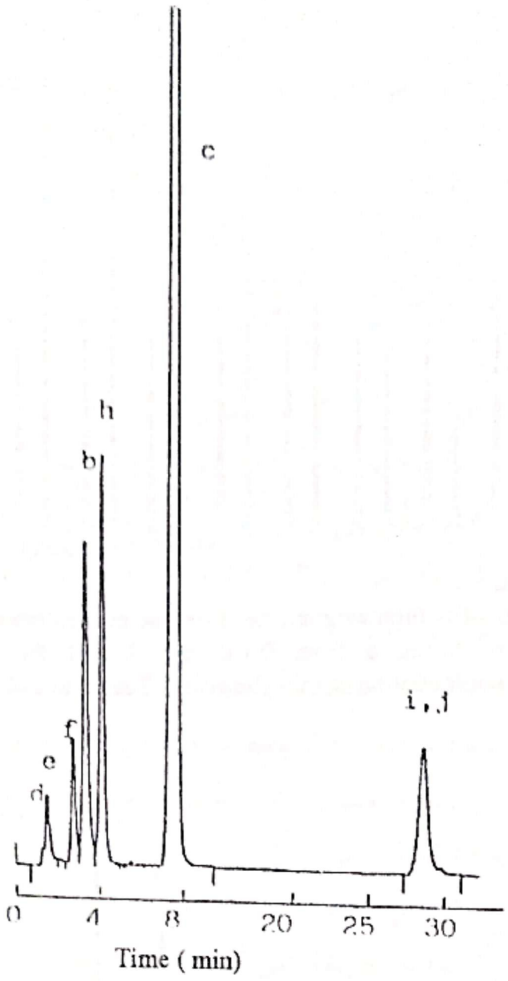

Fig. (3):Chromatogram of ciprofloxacin hydrochloride ; **b** spiked with cyclopropylamine ; **d** , piperazin; **e** , ethylene acid; **c**, 1,3 - dichloro -4- flourobenzen : **i** , and flouro quinolonic acid ; **i** at 274 nm.

Table (2): Determination of ofloxacin in Tarivid tablets.

Concentration claimed	Concentration found mg%	Recovery %
0.2	0.199	99.85
0.3	0.292	98.08
0.4	0.393	98.27
0.5	0.492	98.38
0.6	0.595	99.18
Mean		98.75
SD		0.74
RSD		0.75

Table (3): Determination of ciprofloxacin hydrochloride in ciprinol ampoules

Concentration claimed	Concentration found mg%	Recovery %
0.1	0.101	101.56
0.2	0.196	98.13
0.3	0.297	99.04
0.4	0.406	101.55
0.5	0.507	101.40
Mean		100.34
SD		1.63
RSD		1.62

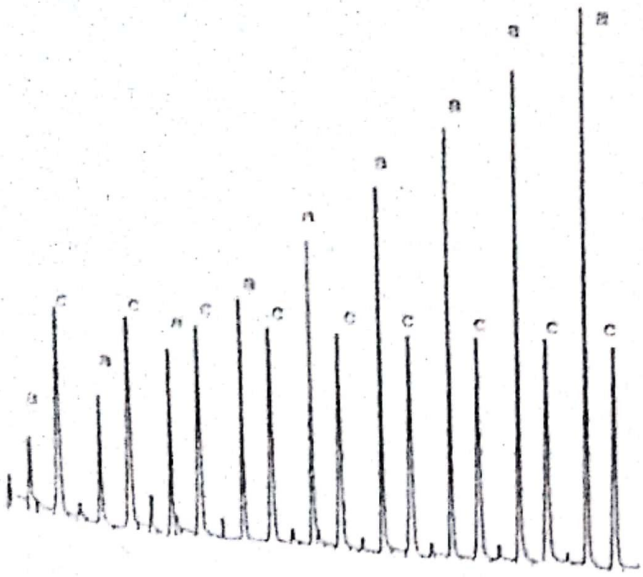

Fig. (4): Chromatogram of different concentrations of ofloxacin; a from 0.1-0.9mg % and the same concentration of salicylic acid; e 2 mg% at 274 nm.

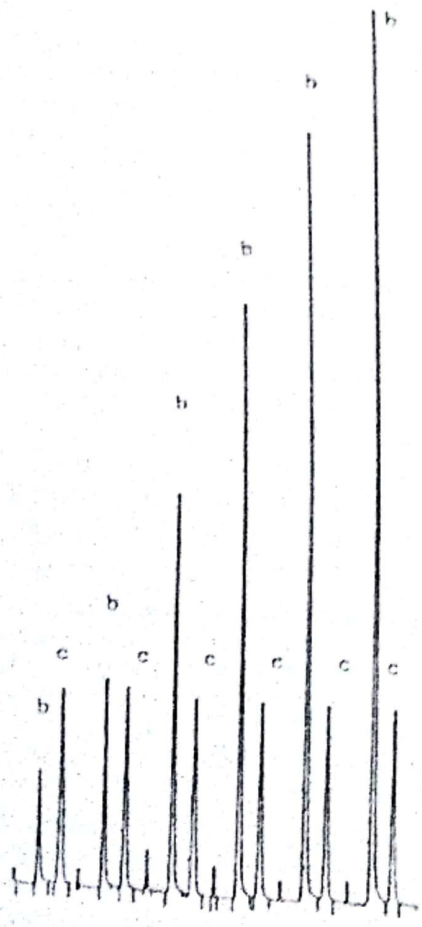

Fig. (5): Chromatogram of different concentrations of ciprofloxacin hydrochloride ; b from 0.05 - 0.5 mg% and the same concentration of salicylic acid ; e 2 mg% at 274 nm.

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التقدير الكمى لكل من أوفلوكساسين وسبروفلوكساسين هيدروكلورايد مع بعض المواد المشابهة وذلك فى مستحضرات صيدلية بإستخدام كروماتوجرافيا السائلة ذات الضغط العالى

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فى هذا البحث تم تطوير طريقة تحليلية لتعيين كل من اوفلوكساسين وسبروفلوكساسين هيدروكلورايد فى مستحضرات صيدلية بطريقة كروماتوجرافيا السائلة ذات الضغط العالى .

وقد وجد أن سيكوبروبيل أمين ، بيبرازين هسكاهيدرات ، ايثلين داى أمين سبروفلوكساسين ومشابهاتها تراى ايثيل أورثوفورمات ، ٣ - كلورو - ٤ - فلورو ، حمض فلوروكينولينيك ١ ، ٣ ثنائى كلورو - ٤ - فلوروبنزين . هذه المركبات لاتتداخل فى تعيين المركبان المختاران.

ولقد تم استخدام حمض السالبسيليك كمادة قياسية داخلية وخليط من ٣٥٪ كحول ايثيلى فى ٠,٥ مولار صوديوم داى هيدروجين فوسفات عند اس هيدروجينى ٢,٨ ومعدل سريان ١ مل فى دقيقة .

ولقد تم الفصل الكروماتوجرافى باستخدام عمود ٦٠ ذو الوسط المعكوس وباستخدام كاشف فوق بنفسجى عند طول موجة ٢٧٤ نانوميتر.

ولقد تم استخدام نسبة ثابته من المذيبات عند درجة الحرارة العادية وتطلب الفصل ثمانى دقائق .

وطبقت الطريقة على اقراص التاريفيد وحقن السبرينول مع انحراف قياسى نسبى يقدر بـ ٠,٧٥ ، ١,٦٢ لكل منهما على التوالى .