ELSEVIER

Journal of Pharmaceutical and Biomedical Analysis
27 (2002) 133–142

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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# Spectrophotometric determination of ciprofloxacin, enrofloxacin and pefloxacin through charge transfer complex formation

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Received 4 April 2001; received in revised form 23 May 2001; accepted 30 May 2001

**Abstract**

A spectrophotometric method was described for the determination of the antibacterial quinolone derivatives, *ciprofloxacin*, *enrofloxacin* and *pefloxacin* through charge transfer complex formation with three different acceptors. Chloranilic acid (CL) was utilized for their determination, forming charge transfer complex with $\lambda$max 520 nm. The proposed method was applied for determination of *Ciprocin tablets*, *Enroxil oral solution*, *Peflacin* ampoules and *Peflacin* tablets, with mean percentage accuracies, $99.58 \pm 1.25$, $99.94 \pm 0.96$, $100.91 \pm 1.59$ and $99.86 \pm 1.003$. Also, tetracyanoethylene (TCNE) was utilized in the determination of the concerned compounds forming charge transfer complexes with maximum absorbances at $\lambda$max 335 nm for *ciprofloxacin* and at $\lambda$max 290 nm for both *enrofloxacin* and *pefloxacin*. The procedure was applied for determination of *Ciprocin tablets*, *Enroxil* 10% oral solution, *Peflacine tablets* and *Peflacine ampoules* with mean percentage accuracies $99.40 \pm 1.27$, $99.95 \pm 0.90$, $98.98 \pm 1.565$ and $99.88 \pm 0.998$, respectively. Also, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) was utilized for determination of pefloxacin forming charge transfer complex with maximum absorbance at $\lambda$max 460 nm. The procedure was applied for determination of peflacine tablets and peflacine ampoules with mean percentage accuracies $100.40 \pm 0.76$ and $99.91 \pm 0.623$, respectively. Statistical analysis of the obtained results showed no significant difference between the proposed method and other official and reported methods as evident from the *t*-test and variance ratio. 

*Keywords:* Ciprofloxacin; Enrofloxacin; Pefloxacin; Spectrophotometry; Charge transfer complexes

## 1. Introduction

Fluoroquinolones are broad spectrum antibacterial agents, they are effective against most Gram-negative and -positive aerobic bacteria, also they have some activity against mycobacteria, mycoplasmas, rickettsias and the protozoan *Plasmodium falciparm* [1]. Ciprofloxacin, enrofloxacin and pefloxacin are member of this group.

Several chromatographic methods have been reported for determination of these compounds.

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0731-7085/02/$ - see front matter 
PII: S0731-7085(01)00524-6

Ciprofloxacin hydrochloride was determined by high performance capillary electrophoresis and high performance CZE [2], reversed phase ion pair-high performance liquid chromatography [3], a fully automated HPLC [4] and also HPLC method described by U.S.P. [5]. Enrofloxacin was determined in tablets by reversed phase MPLC [6] and also in presence of some related materials, synthetic intermediates by another HPLC method [7]. HPLC method was described for determination of pefloxacin in its dosage form [8] and also by reversed phase HPLC [9]. Titrimetric procedures have been described for determination of ciprofloxacin [10] and also for pefloxacin [11]. Various spectrophotometric methods were described for determination of ciprofloxacin by complex formation with eosin and palladium [12], through charge transfer complex formation with tetrachlorobenzoquinone, *p*-benzoquinone, *p*-nitrophenol, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone, *p*-chloranil, tetracyanoquinodimethane [13–16], and through ion-pair complex formation with bromocresol purple and bromophenol blue [17], and methyl orange, bromothymol blue [18].

Enrofloxacin was determined spectrophotometry in its dosage forms through formation of complex with Fe (III), charge transfer complex with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone, ion-pair complex with bromocresol purple [19] also pefloxacin by treating with 3-methylbenzothiazolin-2-one hydrazone and Ce (IV) [20].

However, no spectrophotometric method for determination of ciprofloxacin, enrofloxacin and pefloxacin through charge-transfer complexation with chloranilic acid or tetracyanoethylene, has been reported. Also no method for determination of pefloxacin through complexation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone, has been described.

In the present work, attempts were made to determine ciprofloxacin, enrofloxacin and pefloxacin (*n* donors) through charge transfer complexation with ($\pi$ acceptors), chloranilic acid (CL), tetracyanoethylene (TCNE) and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ). The proposed methods are simple and suitable for routine determination of the drugs. Also this methods provide economic procedures, less time consuming and more sensitive compared with other reported spectrophotometric methods.

## 2. Experimental

### 2.1. Instrumentation

A double-beam Schimadzu (Japan) 160 IPC UV–Visible spectrophotometer connected to an IBM compatible fitted with UVPC personal spectroscopy software version 3.7 (Shimadzu) was used.

### 2.2. Materials and reagents

All solvents used were of analytical grade. Acetonitrile (Aldrich, England), methanol and chloroform (BDH, England). Chloranilic acid (Merck, Germany), was prepared as 1 mg $ml^{-1}$ in acetonitrile. Tetracyanoethylene, (Merck, Schuchardt) was prepared as 0.128 mg $ml^{-1}$ in chloroform. 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), (sigma) was prepared as 1 mg $ml^{-1}$ in acetonitrile. Pharmaceutical grade ciprofloacin hydrochloride was obtained from Eipico, Egypt and its standard solution was prepared as 0.8 mg $ml^{-1}$ in methanol for (CL method) and as 0.05 mg $ml^{-1}$ for (TCNE method). Enrofloxacin base and pefloxacin mesylate dihydrate were obtained from (Amriya, Alexandria, Egypt). Standard enrofloxacin solution was prepared as 0.2 mg $ml^{-1}$ in acetonitrile for (CL method), 0.02 mg $ml^{-1}$ in chloroform for (TCNE method). Pefloxacin standard solution was prepared as 0.2 mg $ml^{-1}$ in acetonitrile for (CL method), 0.02 mg $ml^{-1}$ in chloroform for (TCNE) and 0.25 mg $ml^{-1}$ in acetonitrile for (DDQ method). Ciprocin tablets used was manufactured by Eipico, Egypt. Each tablet contain 500 mg ciprofloxacin hydrochloride. Enroxil 10% oral solution, was obtained from (KRKA, Novomesto, Slovenia), labelled to contain 100 mg enrofloxacin per ml. Peflacine tablets and peflacine ampoules were manufactured by Amriya, Alexandria, Egypt and labelled to contain 400 mg pefloxacin mesylate dihydrate per tablet and per ampoule, respectively.

### 2.3. Methods

#### 2.3.1. Chloranilic acid (CL method)

*2.3.1.1. General procedure*. Aliquots containing (0.16–0.96 mg) *ciprofloxacin*, (0.2–1.6 mg) *enrofloxacin* or *pefloxacin* were transferred to 10 ml calibrated flasks. One millilitre of chloranilic acid solution was added. The reaction mixture was mixed and the volume was completed to 10 ml with acetonitrile. The immediately formed purple colour was measured at $\lambda$max 520 nm against a blank prepared in the same manner except addition of drug, as shown in Fig. 1.

*2.3.1.2. Procedure for ciprocin tablets*. Twenty tablets of *ciprocin* were accurately weighed and the average weight of one tablet was determined. The tablets were triturated and an amount equivalent to 80 mg of *ciprofloxacin* was taken then dissolved in 4 ml distilled water by heating in a water bath at 60 °C for 3 min, then filtered. To the filtrate containing *Ciprofloxacin hydrochloride*, three drops of concentrated ammonia solution was added then filtered. The residue was washed with distilled water, dried, then dissolved in methanol, transfered to 100 ml calibrated flask, the volume completed with methanol, and procedure followed as mentioned under general procedure.

*2.3.1.3. Procedure for enroxil oral solution*. 0.2 millilitre of the solution was transfered to a 100 ml calibrated flask, completed to volume with acetonitrile, then procedure followed as mentioned under general procedure.

*2.3.1.4. Procedure for peflacine tablets*. Twenty tablets were accurately weighed and the average weight of one tablet was determined. The tablets were treated as ciprocin tablets, then the residue was dissolved in 70 ml acetonitrile by heating in a water bath at 60 °C for 3 min and completed to 100 ml with acetonitrile in a 100 ml calibrated flask, 25 ml of the above solution were transfered into a 100 ml calibrated flask, completed to volume with acetonitrile, and procedure followed as mentioned under general procedure.

*2.3.1.5. Procedure for peflacine ampoules*. To 1 ml of ampoules, three drops of concentrated ammonia solution was added. The precipitated *pefloxacin* was filtered, washed with distilled water, dried, dissolved in 70 ml acetonitrile, and procedure completed as mentioned under peflacine tables.

#### 2.3.2. Tetracyanoethylene (TCNE method)

*2.3.2.1. General procedure*. Accurate aliquots containing (0.025–0.15 mg) *ciprofloxacin*, (0.002–0.01

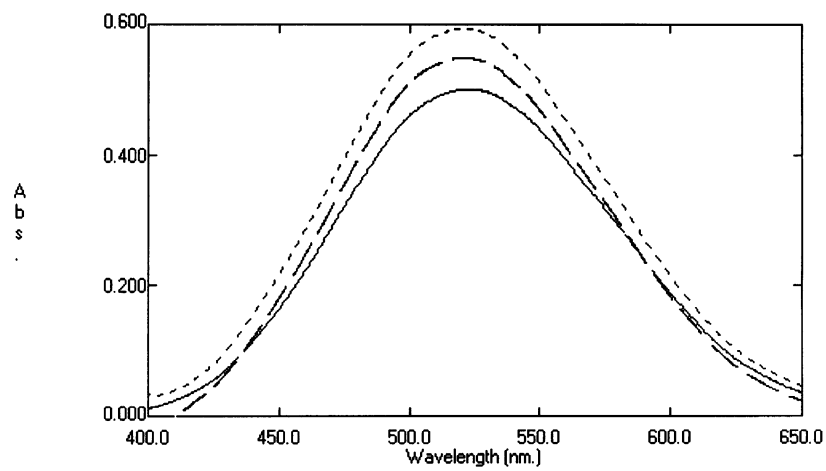



Fig. 1. Absorption curves of ciprofloxacin (—), enrofloxacin (- - -) and perfloxacin (. . . .) chloranilic acid (CT) complexes.

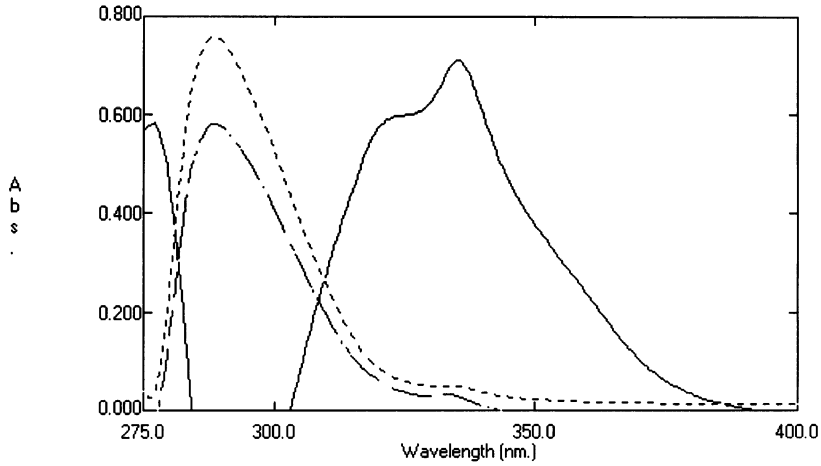



Fig. 2. Absorption curves of ciprofloxacin (—), enrofloxacin (- - -) and perfloxacin (. . . .) TCNE (CT) complexes.

mg) *enrofloxacin* or *pefloxacin* were transfered to 10 ml calibrated flask. One millilitre of tetracyanoethylene solution was added for *ciprofloxacin* while 2 ml was added for both *enrofloxacin* and *pefloxacin*. For *ciprofloxacin*, the reaction mixture was mixed and the volume was made up to 10 ml with chloroform, while for *enrofloxacin* and *pefloxacin*, the reaction mixture was allowed to stand for 15 and 25 min, respectively before dilution to volume. The absorbance was measured at $\lambda$max 335 nm for *ciprofloxacin* and at $\lambda$max 290 nm for both *enrofloxacin* and *pefloxacin* against a reagent blank prepared in the same manner except addition of drug, as shown in Fig. 2.

*2.3.2.2. Procedure for ciprocin tablets*. Twenty tablets were accurately weighed and the average weight of one tablet was determined. The tablets were triturated and an amount equivalent to 100 mg of *ciprofloxacin* was taken, treated as mentioned under chloranilic acid method, but the residue was dissolved in chloroform and diluted to 100 ml, 5 ml of the above solution were transfered to 100 ml calibrated flask, completed to volume with chloroform and followed as mentioned under general procedure.

*2.3.2.3. Procedure for enroxil oral solution*. 0.2 millilitre of the solution was transfered to 100 ml calibrated flask, completed to volume with chloroform, 10 ml of the diluted solution was transfered to a 100 ml calibrated flask, completed to volume with chloroform and followed as mentioned under general procedure.

*2.3.2.4. Procedure for peflacine tablets*. Twenty tablets were accurately weighed, and the average weight of one tablet was determined. The tablets were triturated and an amount equivalent to 80 mg of *pefloxacin* was taken, dissolved in 1 ml distilled water, then filtered. To the filtrate containing *pefloxacin* mesylate dihydrate, three drops of concentrated ammonia solution was added and completed as mentioned under *ciprocen* tablets except that 2.5 ml of the above solution were transfered into a 100 ml calibrated flask.

*2.3.2.5. Procedure for peflacine ampoules*. To 1 ml, three drops of concentrated ammonia solution was added. The precipitated *pefloxacin* was filtered, washed with distilled water, dried, dissolved in chloroform and diluted to 100 ml. 2.5 millilitre of the above solution were transfered to a 100 ml calibrated flask, completed to volume with chloroform, then general procedure was followed.

*2.3.3. Dichloro-dicyano-p-benzoquinone (DDQ method)*

*2.3.3.1. General procedure*. Accurate aliquots containing 0.05–0.5 mg *pefloxacin* were transfered to 10 ml calibrated flasks. Two millilitre of (DDQ) solution were added. The reaction mixture was allowed to stand for 15 min at $25 \pm 2$ °C. The volume was made up to 10 ml with acetonitrile. The absorbance was measured at $\lambda$max 460 nm against a reagent blank prepared in the same manner except addition of drug as shown in Fig. 3.

*2.3.3.2. Procedure for peflacin tablets*. Twenty tablets were accurately weighed and the average weight of one tablet was determined. The tablets were triturated and an amount equivalent to 100 mg of *pefloxacin* was taken, treated as mentioned under chloranilic acid method, and then followed as the general procedure.

*2.3.3.3. Procedure for peflacine ampoules*. To 1.25 ml, three drops of concentrated ammonia solution was added. The preciptated *pefloxacin* was filtered, washed with distilled water, dried, dissolved in 70 ml acetonitrile and completed as mentioned under *peflacine* tablets.

## 3. Results and discussion

*Ciprofloxacin*, *enrofloxacin* and *pefloxacin* are nitrogenous compounds that act as *n* donors to the $\pi$ acceptors, as chloranilic acid, tetracyanoethylene (TCNE) and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ). They form complexes absorbing maximally at wavelengths 520 nm for the three drugs, 335 nm for ciprofloxacin and 290 nm for both enrofloxacin and pefloxacin and at 460 nm for pefloxacin with CL, TCNE and DDQ, respectively, Table 1, Figs. 1–3.

Using CL, the purple colour immediately reaches its maximum intensity at room temperature and remains stable up to 30 min. No change in colour intensity upon heating till 50 °C for 15 min, heating at longer time lead to decrease in intensity, 0.6 ml of CL solution was found to be sufficient for production of maximum absorbance.

With TCNE, heating of the complexes till 50 °C, shows no change in absorbance. One and 1.5 ml of TCNE solution were sufficient for maximum absorbance with ciprofloxacin and both enrofloxacin and pefloxacin, respectively.

For DDQ method, heating the complex of pefloxacin at different temperatures till 50 °C, showed no change in colour intensity. Complete colour development was attained at room temper-

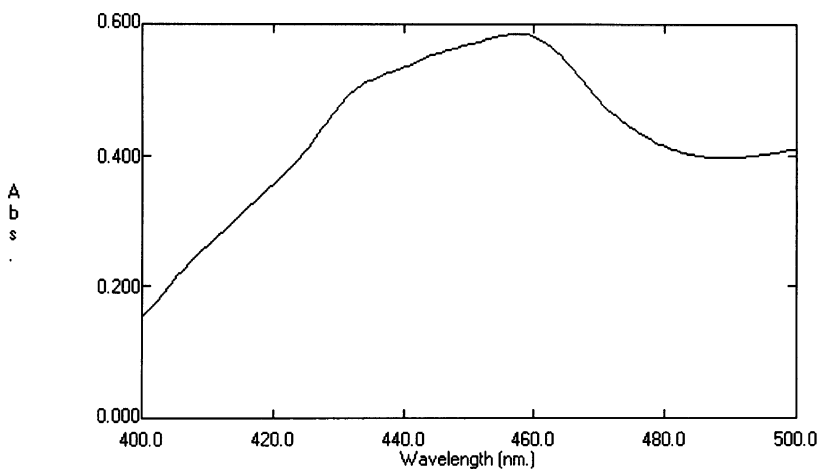



Fig. 3. Absorption curves of perfloxacin-DDQ (CT) complexes.

Table 1
Characteristic parameters for complexation of ciprofloxacin, enrofloxacin and pefloxacin with CL, TCNE and DDQ

| Parameters | Ciprofloxacin method | | Enrofloxacin method | | Pefloxacin method | | |
|---|---|---|---|---|---|---|---|
| | CL | TCNE | CL | TCNE | CL | TCNE | DDQ |
| $\lambda$max (nm) | 520 | 335 | 520 | 290 | 520 | 290 | 460 |
| Beer's law limits (μg ml$^{-1}$) | 16–96 | 2.5–15 | 20–160 | 0.2–1.0 | 20–160 | 0.2–1.0 | 5–50 |
| Regression equation | | | | | | | |
| Slope | 0.0318 | 0.669 | 0.0344 | −11.56 | 0.0373 | 10.445 | 0.1504 |
| RSD (%) | 0.7 | 1.3 | 0.8 | 1.4 | 1.0 | 1.3 | 0.9 |
| Intercept | 0.02 | 0.0059 | 0.0008 | −0.0872 | 0.0271 | −0.1157 | −0.0113 |
| RSD (%) | 1.0 | 1.2 | 1.1 | 0.9 | 1.3 | 1.3 | 1.1 |
| Correlation coefficients ($r$) | 0.9998 | 0.9992 | 0.9977 | 0.9983 | 0.9929 | 0.9925 | 0.9991 |

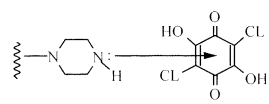
Spiked placebos were prepared according to the manufacturing formula. The spiked placebos were tested at five levels: 50, 75, 100, 125 and 150% of label claim for each individual drug.

ature (25 ± 2 °C) after 15 min, and showed stability for 2 h. 1.5 millilitre of (DDQ) solution was sufficient for maximum absorbance, higher volumes did not affect the colour intensity.

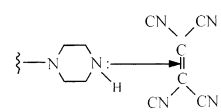
Acetonitrile was found to be the best solvent for CL and DDQ methods, other solvents as ethanol or methanol were unsuitable due to limited solubility of the concerned drugs. Chloroform was unsuitable, as CL and DDQ have limited solubility in it. Also, acetone was unsuitable as the complexes formed show limited solubility in it. Chloroform, was found to be the best solvent for TNCE method, other solvents as dichloromethane, 1,2-dichloroethane, benzene and acetonitrile were unsuitable owing to the limited solubility of TCNE in these solvents.

No interferences were observed in the determination of ciprofloxacin and pefloxacin in the presence of the common excipients of the tablets, i.e. talc, magnesium stearate, starch, lactose, glucose and sucrose.

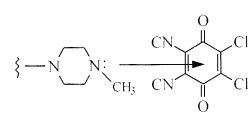
Molar ratio of the reactants (drug:reagent) in the charge transfer complex was determined by the continuous variation method (Job's method) [21,22] and it was found to be 1:1 for the three drugs: CL, TCNE and pefloxacin:DDQ (Figs. 4 and 5). These ratios may be due to the presence of donating center, the aliphatic nitrogen number 4 of piperazine moiety as it is less sterically hindered and the most basic one as shown in the following scheme:




Ciprofloxacin – CL (CT) complex




Ciprofloxacin – TCNE (CT) complex




Pefloxacin – DDQ (CT) complex

### 3.1. Method validation

Under the experimental conditions described, standard calibration curves for ciprofloxacin, enrofloxacin and pefloxacin with different reagents

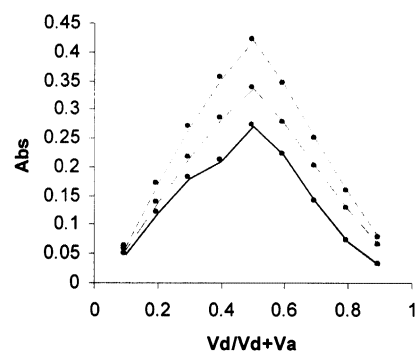



Fig. 4. Continuous variation plot for ciprofloxacin (—), enrofloxacin (- - -) and perfloxacin (. . . .) with chloranilic acid.

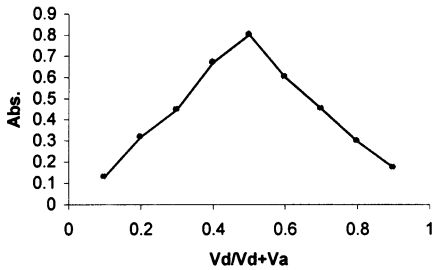



Fig. 5. Continuous variation plot for perfloxacin with DDQ.

were constructed by plotting absorbance versus concentration. Conformity with Beer's law was evident in the concentration range of the final dilution cited in (Table 1). The linear regression equation for each method are listed in Table 1. The correlation coefficients were 0.9925–0.9998 indicating good linearity.

Assays were performed in duplicate on two samples at the five levels. This was repeated with a second instrument, standard and sample preparation and analyst on different days. The complete set of validation assays was performed for each drug, determined by the proposed methods.

Spiked placebo assays were used to determine accuracy and precision of the proposed methods for determination of each drug. The recoveries ranging from 98.1 to 101.6, 98.5 to 101.7 and 98.6 to 101.5 with average 99.6, 99.84 and 100.02, RSD = 1.1, 1.09 and 0.99%, $N = 10$ for ciprofloxacin, enrofloxacin and pefloxacin, respectively, with (CL method), Table 2. With (TCNE method), the recoveries ranging from 98.2 to 100.7, 98.4 to 100.8 and 98.1 to 99.5 with average 99.31, 99.32 and 98.66, RSD = 0.82, 0.56 and 0.52%, $N = 10$, for ciprofloxacin, enrofloxacin and pefloxacin, respectively, Table 3. For DDQ method, the recoveries ranging from 98.9 to 100.3) with average 99.67, RSD = 0.5 %, $N = 10$, Table 4.

The measurement precision was determined by performing 10 replicate measurements of the methods concentration. The RSD were found to be 0.822, 0.892 and 0.896% for ciprofloxacin, enrofloxacin and pefloxacin using (CL method), Table 5. These results of accuracy and precision show that the proposed methods have good repeatability, reproducibility. Also the assay results are unaffected by the presence of excipients, this establish specificity of the methods. To ensure the validity of analytical procedure whenever used, the stability of analytical solutions of ciprofloxacin, enrofloxacin and pefloxacin during the analytical procedures were studied and the three analytes were stable for at least 24 h. Also different parameters affecting the procedures are studied, this to evaluate robustness and show reliability of the analytical procedure. The pro-

Table 2
Accuracy of chloranilic acid method determined by recovery of ciprofloxacin (I), enrofloxacin (II) and pefloxacin (Ill) from placebo tablets

| Level (%) | mg Added | | | Recovery % | | |
|---|---|---|---|---|---|---|
| | I | II | III | I | II | III |
| 50 | 0.41 | 0.11 | 0.12 | 100.5 | 99.8 | 100.4 |
| 50 | 0.39 | 0.12 | 0.10 | 101.6 | 100.5 | 101.2 |
| 75 | 0.60 | 0.15 | 0.15 | 100.8 | 101.7 | 99.8 |
| 75 | 0.61 | 0.16 | 0.14 | 99.3 | 100.9 | 98.9 |
| 100 | 0.81 | 0.20 | 0.22 | 99.9 | 99.2 | 100.7 |
| 100 | 0.82 | 0.23 | 0.21 | 99.0 | 98.5 | 101.5 |
| 125 | 1.0 | 0.25 | 0.25 | 99.0 | 98.6 | 99.1 |
| 125 | 1.1 | 0.24 | 0.23 | 98.7 | 99.0 | 99.3 |
| 150 | 1.20 | 0.30 | 0.31 | 98.1 | 99.4 | 100.7 |
| 150 | 1.23 | 0.31 | 0.32 | 99.6 | 100.8 | 98.6 |
| Average | | | | 99.6 | 99.84 | 100.02 |
| RSD (%) | | | | 1.1 | 1.09 | 0.99 |

Table 3
Accuracy of TCNE method determined by recovery of ciprofloxacin (I), enrofloxacin (II) and pefloxacin (III) from placebo tablets

| Level (%) | μg Added | | | Recovery % | | |
|---|---|---|---|---|---|---|
| | I | II | III | I | II | III |
| 50 | 25.0 | 10.1 | 10.0 | 99.2 | 99.1 | 98.2 |
| 50 | 26.0 | 10.2 | 10.1 | 98.7 | 98.5 | 99.1 |
| 75 | 37.5 | 15.0 | 15.0 | 100.5 | 99.0 | 98.4 |
| 75 | 37.4 | 15.2 | 15.2 | 98.5 | 98.8 | 99.3 |
| 100 | 50.0 | 20.0 | 20.0 | 99.6 | 99.5 | 98.4 |
| 100 | 50.2 | 20.1 | 20.1 | 98.8 | 100.3 | 99.5 |
| 125 | 62.5 | 25.0 | 25.0 | 99.5 | 99.5 | 98.1 |
| 125 | 62.4 | 25.1 | 25.2 | 98.2 | 99.3 | 98.3 |
| 150 | 75.0 | 30.0 | 30.0 | 99.4 | 98.4 | 99.0 |
| 150 | 75.1 | 30.2 | 30.1 | 100.7 | 100.8 | 98.3 |
| Average | | | | 99.31 | 99.32 | 98.66 |
| RSD (%) | | | | 0.82 | 0.56 | 0.52 |

Table 4
Accuracy of DDQ method determined by recovery of pefloxacin from placebo tablets

| Level (%) | mg Added | Recovery % |
|---|---|---|
| 50 | 0.125 | 99.8 |
| 50 | 0.126 | 100.3 |
| 75 | 0.187 | 99.5 |
| 75 | 0.189 | 99.0 |
| 100 | 0.250 | 98.9 |
| 100 | 0.260 | 100.2 |
| 125 | 0.313 | 99.9 |
| 125 | 0.319 | 99.2 |
| 150 | 0.375 | 100.1 |
| 150 | 0.380 | 99.8 |
| Average | | 99.67 |
| RSD (%) | | 0.5 |

Table 5
Measurement precision of ciprofloxacin (I), enrofloxacin (II) and pefloxacin using CL method

| Measurements | Absorbance | | |
|---|---|---|---|
| | I | II | III |
| 1 | 0.274 | 0.274 | 0.325 |
| 2 | 0.278 | 0.273 | 0.323 |
| 3 | 0.276 | 0.271 | 0.324 |
| 4 | 0.273 | 0.277 | 0.322 |
| 5 | 0.279 | 0.275 | 0.326 |
| 6 | 0.275 | 0.270 | 0.328 |
| 7 | 0.280 | 0.276 | 0.329 |
| 8 | 0.277 | 0.274 | 0.320 |
| 9 | 0.275 | 0.272 | 0.325 |
| 10 | 0.278 | 0.270 | 0.321 |
| Average | 0.2765 | 0.2732 | 0.3243 |
| RSD (%) | 0.822 | 0.893 | 0.896 |

posed methods complied with USP [23] validation guidelines.

### 3.2. Tablet analysis

The proposed methods were applied to the determination of ciprofloxacin and pefloxacin in commercial tablets. Five replicate determinations were made. Satisfactory results were obtained for both drugs (Table 6).

Moreover, to check the validity of the proposed methods, the standard addition method was applied by adding ciprofloxacin and pefloxacin to the previously analysed tablets. The recovery of each drug was calculated by comparing the concentration obtained from the spiked mixtures with those of the pure drug. The results of analysis of the commercial tablets and the recovery study (standard addition method) of both drugs (Table 6) suggested that there is no interference from any excipients, which are present in tablets. The results of determination of ciprofloxacin and pefloxacin in tablets obtained from CL, TCNE

Table 6
Statistical analysis of the data for ciprocin tablets, enroxil oral solution, peflacine tablets and peflacine ampoules using chloranilic acid, TCNE and DDQ compared with official and reported methods

| Method | Values | Ciprocin tablets | | Enroxil oral solution | | Peflacine tablets | | Peflacine ampoules | |
|---|---|---|---|---|---|---|---|---|---|
| | | Proposed method | Official method | Proposed method | Reported method | Proposed method | Reported method | Proposed method | Reported method |
| CL | Mean ± S.D. | 99.58 ± 1.255 | 100.11 ± 0.81 | 99.94 ± 0.96 | 100.64 ± 0.87 | 100.915 ± 1.598 | 99.98 ± 0.78 | 99.86 ± 1.003 | 99.98 ± 0.78 |
| | *N* | 6 | 6 | 6 | 5 | 6 | 6 | 6 | 6 |
| | *t* | 0.869 (2.228)* | | 1.255 (2.262)* | | 1.286 (2.228)* | | 0.23 (2.228)* | |
| | *F* | 2.4 (5.05)* | | 1.217 (6.26)* | | 4.2 (5.05)* | | 1.65 (5.05)* | |
| TCNE | Mean ± S.D. | 99.4 ± 1.27 | 100.11 ± 0.81 | 99.95 ± 0.9 | 100.64 ± 0.87 | 98.98 ± 1.565 | 99.98 ± 0.78 | 99.88 ± 0.998 | 99.98 ± 0.78 |
| | *N* | 6 | 6 | 5 | 5 | 5 | 6 | 5 | 6 |
| | *t* | 1.154 (2.228)* | | 1.232 (2.306)* | | 1.38 (2.262)* | | | |
| | *F* | 2.458 (5.05)* | | 1.07 (6.39)* | | 4.02 (5.19)* | | | |
| DDQ | Mean ± S.D. | | | | | 100.4 ± 0.76 | 99.98 ± 0.78 | 99.91 ± 0.623 | 99.98 ± 0.78 |
| | *N* | | | | | 6 | 6 | 6 | 6 |
| | *t* | | | | | 0.94 (2.228)* | | 0.17 | |
| | *F* | | | | | 1.05 (5.05)* | | 1.56 | |

* Theoretical $t$ and $F$ values at $P = 0.05$.

and DDQ methods were compared with USP [5] and reported methods [7,24].

Statistical comparison of the results was performed with regard to accuracy and precision using Student's *t*-test and *F*-ratio at 95% confidence level (Table 6). There is no significant difference between the proposed methods with regard to accuracy and precision.

## 4. Conclusion

Statistical comparison for the results of the proposed methods with USP and other reported methods indicate that there is no significant difference with regard to accuracy and precision. However, the principal advantage of the proposed methods is their suitability for the routine quality control of the drug alone and in tablets without fear of interference caused by the excipients expected to be present in tablets. In comparison with the existing photometric methods, the proposed methods, especially that with CL and DDQ, are simpler, more rapid, cheaper and much more sensitive and accurate.

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