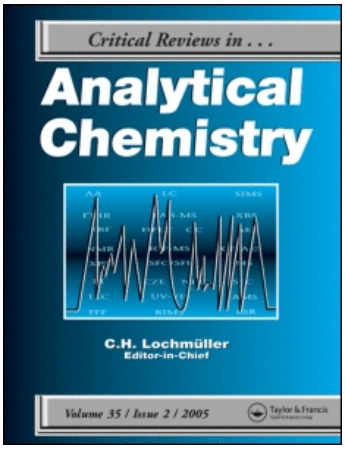

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Spectrophotometric Methods for the Determination of Fluoroquinolones: A Review

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Spectrophotometric Methods for the Determination of Fluoroquinolones: A Review

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Department of Chemistry, Punjabi University, Patiala, Punjab, India

The majority of quinolones of clinical use belong to the subset of fluoroquinolones, which have a fluoro group attached the central ring system, typically at the 6-position. Fluoroquinolones are widely used in human and veterinary medicine. In recent times there has been significant development in the field of fluoroquinolones and many new analogues have been synthesized. The clinical and pharmaceutical analysis of these drugs requires effective analytical procedures for quality control and pharmacodynamic and pharmacokinetic studies. In this review article, various spectrophotometric methods used for determination of fluoroquinolones have been covered. The methods include visible spectrophotometry, which is based on formation of ion-pair or charge transfer complexes, UV spectrophotometry and derivative spectrophotometry. The application of these methods for the determination of fluoroquinolones in pharmaceutical and real samples has also been discussed.

Keywords Review, fluoroquinolones, spectrophotometry, complexes

INTRODUCTION

General Aspects of Fluoroquinolones

Quinolones are a class of broad-spectrum antibiotics, which are active against both gram-positive and gram-negative bacteria. The parent compound of all fluoroquinolones is nalidixic acid. Modifications of nalidixic acid were made based on structure-activity relationships. A large number of new analogues have been synthesized because of a good understanding of structure activity relationship. Almost all of the recent clinically useful quinolones bear a fluorine atom in the C-6 position of the quinolone, napthyridine or benzoaxazine ring systems. Because of the presence of a fluorine atom in their molecules, these antibacterial agents are generally described as fluoroquinolones. Pharmaceutical research in fluoroquinolones has made considerable progress in expanding their spectrum of activity.

Quinolones rapidly inhibit DNA synthesis by promoting cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and type IV topoisomerase, resulting in rapid bacterial death (1, 2). As a general rule, gram-negative bacterial activity correlates with inhibition of DNA gyrase, and gram-positive bacterial activity corresponds with inhibition of DNA type IV topoisomerase (1).

The first quinolone, nalidixic acid, was introduced in 1962. Since then, structural modifications have resulted in second-, third- and fourth-generations. The quinolones are divided into generations based on their antibacterial spectrum. The earlier generation agents are generally more narrow spectrum than the later ones. First-generation agents like nalidixic acid, which are used less often today, have moderate gram-negative activity and minimal systemic distribution. Second-generation quinolones like ciprofloxacin and norfloxacin have expanded gram-negative activity and atypical pathogen coverage, but limited gram-positive activity. These agents are most active against aerobic gram-negative bacilli. Third-generation quinolones like sparfloxacin and levofloxacin retain expanded gram-negative and atypical intracellular activity but have improved gram-positive coverage. Finally, fourth-generation agents like gemifloxacin have improved gram-positive coverage, maintain gram-negative coverage, and gain anaerobic coverage (3).

Fluoroquinolones are widely used to treat human and veterinary diseases (4, 5). Fluoroquinolones can enter cells easily and therefore are often used to treat intracellular infections. They are extremely useful for the treatment of a variety of infections, including urinary tract infections, soft tissue infections, respiratory infections, bone-joint infections, typhoid fever, sexually transmitted diseases, prostatitis, community acquired pneumonia, acute bronchitis and sinusitis They are particularly used in bacterial urinary infections and also for infections whose antimicrobial agent possess great resistance .The ample spectra of antimicrobial activity, the excellent bioavailability, the good tissular penetration and long plasmatic stocking life, all have made fluoroquinolones a special group of drugs. Fluoroquinolones have few adverse effects, most notably nausea, headache, dizziness and confusion. Other adverse effects include prolongation of the corrected QT interval, phototoxicity, liver enzyme abnormalities, arthropathy and cartilage and tendon abnormalities (6). The fluoroquinolones should be employed judiciously. Inappropriate use of fluoroquinolone antibiotic agents will likely worsen current problems with antibiotic resistance.

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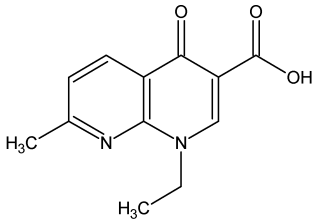
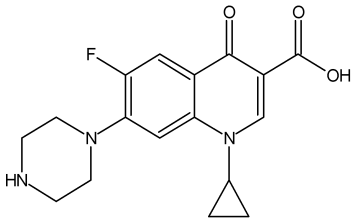
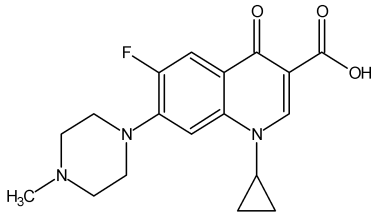
Structures of Fluoroquinolones



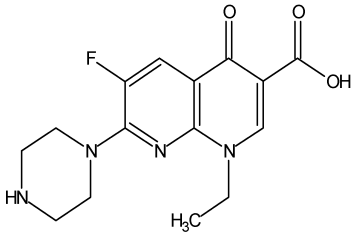
Nalidixic acid



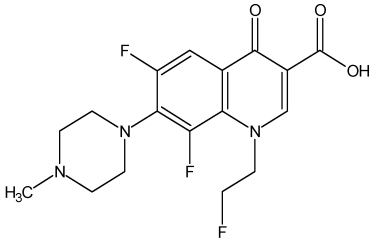
Ciprofloxacin



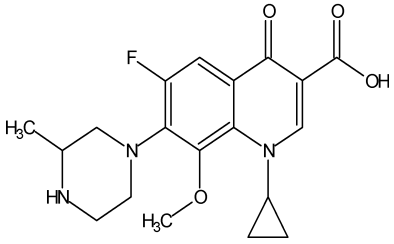
Enrofloxacin



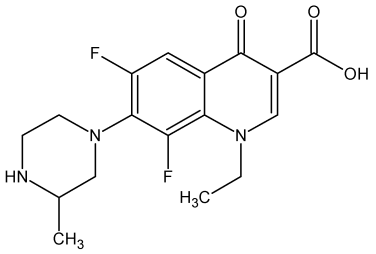
Enoxacin



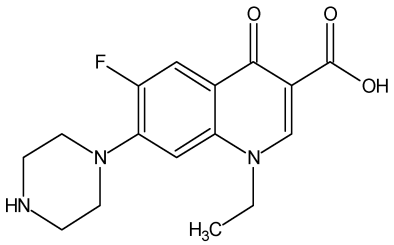
Fleroxacin



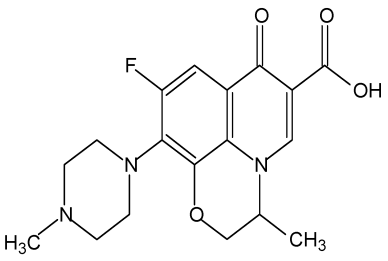
Gatifloxacin



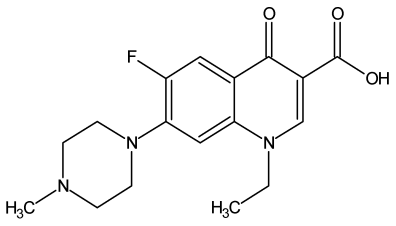
Lomefloxacin



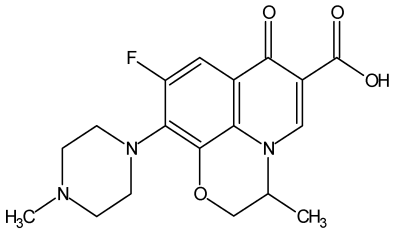
Norfloxacin



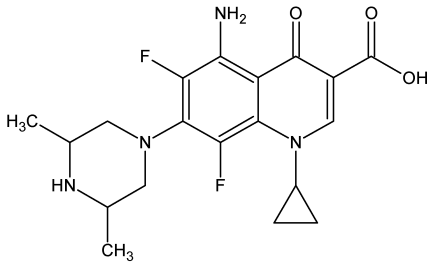
Ofloxacin



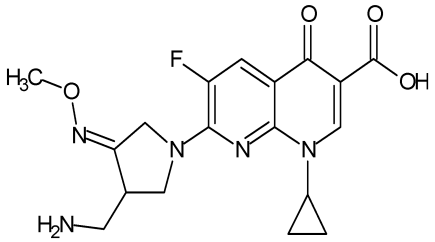
Pefloxacin



Levofloxacin



Sparfloxacin



Moxifloxacin

Analytical Methods for Determination of Fluoroquinolones

Development and validation of analytical methods is of basic importance to optimize the analysis of drugs in the pharmaceutical industry and to guarantee quality of the commercialized product. Several techniques like atomic absorption spectrometry (7), CE (8, 9), flow injection analysis (10), spectrofluorimetry (11, 12), HPLC (13, 14), LC (15, 16), SPE-LC (17), mass spectrometry (18–20), tandem mass spectrometry (21), luminescence (22), voltametry and polarography (23, 24), and titrimetric methods (25, 26) have been used for the determination of quinolones. Chromatographic methods have been extensively used and recommended. However these methods generally require complex and expensive equipment, provision for use and disposal of solvents, labor-intensive sample preparation procedures and personal skills in chromatographic techniques. Spectrophotometric methods have several advantages such as low interference level, good analytical selectivity, easy and less expensive and less time consuming compared with most of the other methods. Spectrophotometric methods are simple and rapid so these methods can be successfully used for pharmaceutical analysis, involving quality control of commercialized product and pharmacodynamic studies. These methods are mostly based on the formation of colored complexes between fluoroquinolone drug and the reagent which can be determined by visible spectrophotometry. The complexes formed are mostly due to charge transfer reaction between the drug and the reagent or due to formation of ion-pair complexes. The spectrophotometric methods based on charge-transfer or ion-pair complex formation are simple and rapid but less sensitive. UV spectrophotometric and derivative spectrophotometric methods have also been widely used for fluoroquinolones and are covered under this review.

SPECTROPHOTOMETRIC METHODS FOR DETERMINATION OF FLUOROQUINOLONES

Nalidixic Acid

Determination of nalidixic acid has been reported by derivative spectrophotometric methods involving peak-zero and peak-peak techniques. The linear range of the method was determined to be 2–12 μg/mL (27). A UV spectrophotometric method reported for nalidixic acid involves extraction of the drug with hydrotropic solutions sodium benzoate and niacinamide and then measuring the absorbance of the drug at 330 nm, where

hydrotropic solvents do not show any interference. The method is simple, rapid and precludes the use of costly organic solvents (28). A spectrophotometric method for the determination of nalidixic acid by reaction with Cd (II) and rose bengal has been reported (29). The method involves formation of ion-pair complexes, which were extracted with chloroform and quantitated spectrophotometrically at 564 nm. The relative standard deviation (RSD) was found to be less than 2%.

Ciprofloxacin

Several methods including charge transfer complexes, ion-pair complexes and derivative spectrophotometric methods have been used for determination of ciprofloxacin. Ciprofloxacin has been determined by reaction with cobalt (II) tetrathiocyanate at pH 2.5 which resulted in the formation of blue-colored ion-pair associates between the drug and cobalt (II) tetrathiocyanate. The complex was extracted into a n-butanol-dichloromethane solvent (3.5:6.5) mixture and determined at 623 nm. The results obtained by this method were found to be in good agreement with reference methods (30). El-Brashy *et al*. (31) repoted that ciprofloxacin can be determined by reaction with bismuth (III) tetraiodide, which results in the formation of orange-red ion-pair associates between ciprofloxacin and bismuth (III) tetraiodide. The reaction occurs in an acidic medium and the ion-pair associates can be filtered off and determined spectrophotometrically at 453 nm. The results were found to be satisfactory. Xanthene dyes like eosin Y and merbromin have been used for the determination of ciprofloxacin. These dyes form colored complexes with ciprofloxacin in an aqueous buffered medium which can be determined spectrophotometrically at 547 nm for eosin Y and at 545 nm for merbromin. The linear range was found to be 2–8 μg/mL and 2–15 μg/mL for eosin Y and merbromin, respectively. A mean percentage recovery of about 100.011 $\pm$ 0.606 and of 99.980 $\pm$ 0.506 was obtained for eosin Y and merbromin, respectively. The methods have the advantage of being applicable for the determination of the drug without prior extraction. The results obtained for the above reported method were comparable to those reported for the reference methods (32).

A spectrophotometric method for the determination of ciprofloxacin has been developed by treating it with a dye, bromocresol green (BCG), in dichloromethane in presence of aqueous acidic medium. The yellow-colored complex formed was extracted into dichloromethane and quantified spectrophotometrically at 412 nm. The method was found to be applicable in the linear range of 1–20 μg/mL and a mean percentage recovery of 100.23 $\pm$ 0.91 was obtained (33). Mostafa *et al.* (34) reported the use of two different pi-electron acceptors, chloranilic acid (CL) and tetracyanoethylene (TCNE), for the determination of ciprofloxacin, which forms charge transfer complexes with maximum absorbance at 520 nm for CL and 335 nm for TCNE. When analyzed by t-test and variance ratio, the results obtained by the above-reported method showed no significant difference from other reference methods. El-Walily *et al*. (35) has reported a spectrophotometric method based on the formation of a ternary complex between palladium (II), eosin and ciprofloxacin in the presence of methylcellulose as a surfactant and with maximum absorbance at 545 nm. Sandell's sensitivity for the method was found to be 1.01×10^{-2} μg/cm^2. The apparent molar absorptivity of the complex was found to be 3.4×10^4 L.mol^{-1}cm^{-1} and the linear concentration range was determined to be 3–10 μg/mL. Ciprofloxacin has also been estimated by complexation reaction with iron (III) in sulphuric acid media and spectrophotometric measurement of absorbance of the corresponding complex at 447 nm. Sequential injection spectrophotometric technique (36) was used.

Ciprofloxacin has been determined by reaction with excess of cerium (IV) sulphate and the determination of residual oxidant by treatment with methyl orange (MO) and measuring the absorbance at 520 nm or with indigo carmine and measuring the absorbance at 610 nm. MO and indigo carmine dyes serve as chromogenic agents. The amount of cerium sulphate reacted corresponds to the amount of the drug. The method was successfully applied for quantitative determination of the drug (37). Another method reported for the determination of ciprofloxacin spectrophotometrically involves cerium (IV) oxidation of the drug in acidic media. The yellowish-orange product obtained was extracted with chloroform and the product showed maximum absorbance at 345 nm. The method gave results comparable to reference methods (38). Two simple and sensitive extractive spectrophotometric methods for the determination of ciprofloxacin have been developed by Sastry *et al*. (39). The methods are based on the formation of ion-association complexes of ciprofloxacin with two dyes, supracene violet 3B and tropaeolin 000. The ion-pair complexes were extracted into chloroform and these showed maximum absorbance at 575 nm and 485 nm, respectively. The methods were compared to the reference methods and favorable results were obtained. Some simple spectrophotometric methods involving reaction of the drug with pi-electron acceptors have been reported (40). Pi-electron acceptors, 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ), 7,7,8,8-tetracyanoquinodimethane (TCNQ) and p-chloranil form colored complexes with ciprofloxacin, which can be quantitated spectrophotometrically at 460, 843 and 550 nm, respectively, and form the basis for spectrophotometric determination of ciprofloxacin. RSD was reported to be $<$1.5% (40). Another method reported for the determination of ciprofloxacin (41) involves reaction of the drug with tris (o-phenanthroline) iron (II) and tris (bipyridyl) iron (II). The complexes have been determined spectrophotometrically at 510 nm and 522 nm. The results obtained by the two methods have been favorably compared with the reference methods.

Ciprofloxacin has also been estimated by treatment with an ammonium reineckate reagent solution in hydrochloric or sulphuric acid media and measurement of the absorbance of the formed precipitates at 524 nm after dissolving them in aqueous 50% acetone. The RSD was reported to be 0.3–0.55% (42). A simple spectrophotometric method reported for the

determination of ciprofloxacin is based on reaction of the drug with brilliant blue G (BBG) in a sodium acetate-acetic acid buffer of pH 4.0 and measurement of the absorbance of the complex formed at 610 nm. The linear range of the method was reported to be 500–6000 μg/mL (43). Ciprofloxacin has been determined by complexation with Cu (II) in an aqueous medium and then applying third order UV derivative spectrophotometry. A linear correlation was established between amplitude of the peak and concentration of the drug in the range of 0.035–0.120 μg/mL. The results obtained by the above method were favorably compared with those of the reference methods. The results obtained were satisfactory, accurate and precise (44). Another method reported (45) for the determination of the drug is based on the reaction of the drug in acidic media (0.1 M HCl) with 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) in the presence of cerium (IV) ammonium sulphate as an oxidant and measuring the absorbance of the product at 630 nm. The results obtained were found to be comparable to the reference methods (45). A method based on the formation of an ion pair with Sudan III in an aqueous acetone medium has been reported for ciprofloxacin (46). The absorbance of the colored product formed was measured at 566 nm. Beer's law was obeyed in the range of 0.4–10.4 μg/mL. The results obtained showed good recoveries of $\pm$ 1.7% with a RSD of 1.08% for ciprofloxacin. Ciprofloxacin has been determined by reaction with p-nitrophenol resulting in the formation of charge-transfer complex with maximum absorbance at 403 nm. The results were found to be in good agreement with official methods (47). A simple and inexpensive method for the determination of ciprofloxacin has been developed using solid-phase spectrophotometry (48). The intrinsic absorbance of ciprofloxacin fixed on a dextran-type cation-exchange resin, Sephadex SP C-25, was measured directly at 277 and 380 nm after packing the gel beads in a 1-mm cell. The calibration graph was linear over the range 0.05–0.3 μg/mL with a RSD of 1.11%. A simple, rapid and reliable derivative UV-spectrophotometric method involving first, second, third and fourth derivative methods with the use of peak-zero and peak-peak technique has been developed for ciprofloxacin. The calibration curve obtained was linear in the concentration range of 2–12 μg/mL (49). Ammonium vandate has been used for spectrophotometric determination of the drug. The method involves oxidation of the drug by ammonium vandate in sulphuric acid (H_2SO_4) medium resulting in the development of greenish-blue color at 766 nm, which was due to Vanadium (IV) (V) produced by reduction of V (V) by the drug. Beer's law was obeyed in the range of 10–40 μg/mL with correlation coefficient of about 0.9994 (50). A flow injection spectrophotometric method has been reported for the determination of the drug (51). The reactants were passed through a reaction coil and the absorbance of the brown-red complex was measured at 447 nm. The method has been successfully used for quantitative estimation of the drug.

Enrofloxacin

Two different pi-electron acceptors, CL and TCNE, have been used for the determination of enrofloxacin. These pi-acceptors and the drug form charge transfer complexes with maximum absorbance at 520 and 290 nm, respectively. The methods were successfully applied for the determination of the drug in pharmaceutical samples giving mean percentage accuracy of 99.94 $\pm$ 0.96 in the case of CL and 99.95 $\pm$ 0.90 in the case of TCNE (34). Enrofloxacin forms colored ion-association complexes with two dyes, supracene violet 3B and tropaeolin 000. These complexes after extraction into chloroform show absorption maxima at 575 nm and 485 nm, respectively. These methods have been used for spectrophotometric determination of the drug. Detection limit was found to be 2.5 μg/mL for both the methods (39). Ammonium reineckate reagent has been used for the determination of enrofloxacin. The complex formed between drug and reagent showed maximum absorbance at 524 nm. Relative standard deviation (RSD) was found to be 0.46–0.8% (42).

Enrofloxacin has been determined by reacting with MBTH in the presence of cerium (IV) ammonium sulphate as an oxidant and the absorbance of the product was measured at 630 nm (45). Ammonium vandate has been used for spectrophotometric determination of the drug according to the method reported above (50). Enrofloxacin has been determined spectrophotometrically by reaction with BPB in an aqueous buffered medium at pH 2.3–2.5 and with MO at pH 3.6 to form colored complexes. The complexes were extracted with chloroform and determined spectrophotometrically at 420 and 424 nm for bromophenol blue (BPB) and MO, respectively. The method was reported to be quick, sensitive and accurate (52). El-Sherif (53) has reported three simple and accurate spectrophotometric methods for determination of enrofloxacin. The first method is based on the reaction of enrofloxacin with iron (III). The drug forms a water-soluble yellow complex with Fe (III), which can be determined spectrophotometrically at 434 nm. The method allows the determination of the drug in the range of 25–140 μg/mL. The second method is based on the formation of an ion-pair complex with bromocrescol purple (BCP) in the presence of a phthalate buffer; the complex shows maximum absorbance at 410 nm after extraction with chloroform. The third method for the determination of the drug is based on the reaction of the drug with DDQ as pi-acceptor in methanol as medium to form charge-transfer complex with maximum absorbance at 460 nm. The method has been applied successfully to commercial samples and RSD was found to be less than 2%.

Two spectrophotometric methods for determination of enrofloxacin have been reported by Sastry *et al.* (54). The first method involves reaction of the drug with Folin-Ciocalteau's (F-C) reagent in alkaline media to form a colored product having maximum absorbance at 770 nm. Beer's law was obeyed in the concentration range of 2.5–12.5 μg/mL. The second method involves a reaction with $FeCl_3$ in acidic medium. The drug forms

a yellow-orange chromogen which shows maximum absorbance at 440 nm. Beer's law was obeyed in the concentration range of 100–120 μg/mL^{-1}.

Enoxacin

A fourth order derivative spectrophotometric method involving peak-zero and peak-peak techniques of measurement has been used for the determination of enoxacin by Hopkala *et al*. The linear range of the method has been determined to be 2.0–12 μg/mL (27). Enoxacin has also been determined by ammonium vandate according to the method reported above at wavelength of 766 nm (50). Enoxacin has been determined spectrophotometrically as ion-pairs with BPB and BCP. The complexes showed maximum absorbance at 412 nm and 410 nm respectively. Beer's law was obeyed in the range of 2.0–20 μg/mL^{-1} for BPB and 0.77–1762 μg/mL for BCP, respectively (55).

Fleroxacin

MBTH has also been used for the determination of fleroxacin according to the method reported above (45). Fleroxacin has been determined by a simple and rapid UV spectrophotometric assay at 286 nm in 0.1 M HCl at pH $<$ 3.5 by different workers. The method was found to be successful and gave satisfactory results when applied to real samples (56, 57). Derivative spectrophotometry involving first, second, third and fourth order measurements with the use of peak-zero and peak-peak techniques has also been used for determination of fleroxacin. The linear range obtained was 2.0–12 μg/mL^{-1}. The method was found to be accurate and precise with mean recovery of about 100% and RSD $<$ 1% (58).

Gatifloxacin

Gatifloxacin has been determined by treating the drug with sulphonphthalein acid dyes BCG, BCP, BPB and bromothymol blue (BTB). Yellow-colored ion-pair complexes were formed in a phthalate buffer at pH 3.0, 3.4, 3.2 and 3.2: the complexes after extraction into chloroform showed maximum absorbance at 415 nm, 412 nm, 417 nm, and 414 nm, respectively (59). Gatifloxacin has been estimated with a ferric nitrate reagent at 470 nm. The drug forms an orange-colored chromogen due to reaction with the ferric nitrate solution having a maximum absorbance at 470 nm. The linear range was determined to be 20–200 μg/mL^{-1} (60). A method reported for gatifloxacin involves estimation of the drug by UV spectrophotometry at 289 and 292 nm by dissolving in sodium hydroxide (NaOH) and hydrochloric acid (HCl), respectively (61). Another method reported for gatifloxacin is based on the formation of yellow-colored chromogen with ferric chloride and potassium dichromate, which shows maximum absorbance at 352 nm. Beer's law was obeyed in the concentration range of 5–30 μg/mL^{-1}. Results of analysis of the method were validated statistically and by recovery studies (61). A simple and sensitive method has been reported for the determination of gatifloxacin in pure and dosage form. The method is based on the oxidative coupling reaction of gatifloxacin with MBTH in the presence of an oxidizing agent like ceric ammonium sulphate. The chromogen attained a green color and exhibited absorption maxima at 630 nm. Good agreement with Beer's law was found in the range of 2–10 μg/mL^{-1}. The results obtained were found to be reproducible with a coefficient of variation less than 1.0% (62). Gatifloxacin has been estimated at 286 nm in 100 mM phosphate buffer (pH 7.4) and at 292 nm in 100 mM HCl (pH 1.2) by Venugopal and Saha (63). The quantitation limit was found to be 0.312 and 0.3 μg/mL in phosphate buffer and HCL media, respectively. The method was found to be simple, precise and reproducible with standard deviation $<$ 2%. Another UV spectrophotometric method developed for gatifloxacin involves determination of the drug at 287 nm. The linearity range was found to be 4.0–14 μg/mL. The method gave good results when applied to pharmaceutical samples (64).

Lomefloxacin

Ammonium reineckate reagent has been used for the determination of lomefloxacin according to the method reported above (42). Lomefloxacin has also been determined according to the reference method (50) reported for ciprofloxacin. Another method based on the use of ferric nitrate as a reagent has been used for lomefloxacin. The method is based on the reaction of lomefloxacin with 1% w/v ferric nitrate solution in 1% v/v nitric acid. The drug interacts with Fe (II) to form a water soluble orange-yellow colored chromogen which exhibits absorption maximum at 445 nm. Beer's law was obeyed in the concentration range of 2.0–10 μg/mL (65).

A simple and accurate method based on the reaction between the drug and dichlone, in the presence of crotonaldehyde in dimethyl sulphoxide (DMSO), which produces a blue chromogen with absorption maximum at 645 nm, has also been reported for lomefloxacin (66). Statistical comparison of the results with those of the reference methods showed no significant difference. The results were found to be reproducible and precise. Lomefloxacin has been determined spectrophotometrically by ion-pair complex formation with BCG and extraction into chloroform ($CHCl_3$) at pH 3.6. The complex showed absorption maximum at 415 nm. The linearity range was found to be 1–15 μg/mL. The detection limit was found to be 0.014 μg/mL. The percentage recovery was found to be 98.9%–101.6% (67).

An ultraviolet spectrophotometric method based on the charge-transfer complex formation between lomefloxacin as the donor and chloranil as the acceptor in a cetyl pyridinium bromide (CPB) micellar system has been reported for the determination of lomefloxacin (68). Good recoveries of about 97.8%–100.5% were obtained on application of the method to commercial samples. The RSD was calculated to be 0.9%–2.4%. A simple and reproducible UV spectrophotometric method has been reported for the assay of lomefloxacin in tablets. The method is based on the determination of the drug at 280 nm. Beer's law was obeyed

in the concentration range of 2.0–9.0 μg/mL for the drug. The results have proven the method to be as equally accurate, precise and reproducible as the official methods (69). Three spectrophotometric methods for the determination of lomefloxacin hydrochloride have been reported, which are based on formation of ion-pairs with BPB, BTB and BCP and extraction into chloroform; the calibration graphs generated were linear over the range 5–25, 2–15 and 2–20 μg/mL of the drug in chloroform, using three dyes, respectively. The described methods gave good results when applied to pharmaceutical samples (70).

Norfloxacin

A UV spectrophotometric method reported for norfloxacin involves extraction of the drug with hydrotropic solvents like sodium benzoate and niacinamide and then measuring absorbance of the drug at 324 nm. These hydrotropic solvents were successful in extracting the drug from their dosage forms precluding the use of organic solvents (28). Norfloxacin has been determined by complex formation with Co (II) tetrathiocyanate at pH 2.5. The ion-pair complex formed shows maximum absorbance at 623 nm (30). Another method reported for the spectrophotometric determination of norfloxacin and bismuth (III) tetraiodide resulted in the formation of orange-red ion-pair associates with maximum absorbance at 453 nm (31). Two xanthene dyes, eosin Y and merbromin, have also been used by El-Brashy *et al*. (32) for the determination of norfloxacin. These dyes form colored binary complexes with norfloxacin, which showed absorption maxima at 547 nm for eosin Y and 545 nm for merbromin, and give results comparable to reference methods. A dye, BCG, when allowed to react with norfloxacin in dichloromethane forms highly yellow-colored complex instataneously with maximum absorbance at 412 nm. The method has been successfully applied for spectrophotometric determination of norfloxacin and a mean percentage recovery of 99.99 $\pm$ 0.54 was obtained (33). Norfloxacin has also been determined by reaction with pi-electron acceptor TCNE in acetonitrile to form a complex with maximum absorbance at 333 nm. The results obtained by the above method compared favorably with the reference methods and gave mean percentage recovery of 100.26 $\pm$ 0.68 (33). A method developed by El-Walily *et al*. involves the formation of a ternary complex between palladium (II), eosin and norfloxacin in the presence of methyl cellulose as surfactant. The ternary complex showed absorption maxima at 545 nm and can be determined spectrophotometrically at this wavelength (35).

A sequential injection spectrophotometric method based on the complexation of norfloxacin with iron (III) in sulphuric acid media and spectrophotometric measurement of absorbance of the complex at 430 nm has been reported for norfloxacin. The technique has been used for quantitative estimation of the drug (36). Norfloxacin has been determined by formation of ion-pair complexes with Supracene Violet 3B and tropaeolin 000 and subsequent extraction of the complexes with chloroform. The complexes showed maximum absorbance at 575 nm and 485 nm, respectively (39). Norfloxacin has been determined by reaction with ammonium reineckate reagent and measuring the absorbance of the complex at 524 nm. The RSD has been reported to be 0.02–0.7% (42). A simple spectrophotometric method reported for determination of norfloxacin is based on reaction of the drug with BBG in sodium acetate-acetic acid (NaOAc-AcOH) buffer of pH 4.0. The ion-association complexes formed were soluble in chloroform and exhibited absorption maxima at 614 nm (43). Norfloxacin has been determined by complexation with Cu (II) in an aqueous medium and then applying third order UV derivative spectrophotometry for quantification of the drug. (44). Norfloxacin has also been determined by reacting with MBTH in the presence of cerium (IV) ammonium sulphate, which acts as an oxidant. The absorbance of the resulting complex formed was measured at 630 nm (45). A method based on the formation of ion-pair complexes with Sudan III in an aqueous-acetone medium has been used for spectrophotometric determination of norfloxacin at 567 nm. The method has given satisfactory results when compared with reference methods (46). Norfloxacin has been determined by reaction with p-nitrophenol. The resulting charge-transfer complex formed showed maximum absorbance at 407 nm. The results were found to be in good agreement with the official methods (47). The first, second, third and fourth order derivative spectrophotometric method by using peak-zero and peak-peak technique of measurement have been developed for the determination of norfloxacin by Hopkala *et al*. (49). The linear range has been reported to be 1–10 μg/mL. Ammonium vandate has been used for spectrophotometric determination of the drug according to the method reported above (50). Two spectrophotometric methods for the determination of norfloxacin in the presence of decarboxylated degradants are described in literature (71). The first method is based upon measurement of the pH-induced absorbance difference of the drug solution between 0.1 N HCl and 0.1 N NaOH at 280 nm. The second method involves chelation of the intact drug with iron (II) in an acetate buffer solution at pH 5.7 to form a yellow-colored chelate which absorbs at 358 nm; the two methods retain their accuracy in the presence of upto 62 and 76% degradates, respectively. A rapid and accurate spectrophotometric method involving a charge transfer reaction between norfloxacin as electron donor and TCNQ as electron acceptor has been used for the spectrophotometric determination of norfloxacin. A blue-colored charge transfer complex formed showed maximum absorbance at 743 nm. Beer's law was obeyed in the range 4.0–32 μg/mL. The method gave satisfactory results and the RSD was observed to be less than 3% (72). A method based on chloroform extraction of yellow color product obtained by ceric (IV) oxidation of the drug in an acidic medium has been reported for norfloxacin. The linear range of the method has been reported to be 10–100 μg/mL (73). A simple and sensitive kinetic spectrophotometric method for the determination of norfloxacin has been described by Rahman. *et al*. (74). The method is based on the oxidation of norfloxacin

with alkaline potassium permanganate. The reaction was followed spectrophotometrically by measuring the rate of change of absorbance at 603 nm. The calibration graphs were found to be linear in the concentration ranges 2.0–20 μg/mL and 1.0–20 μg/mL using the initial rate (Method 1) and fixed time methods (Method 2), respectively. Two simple and rapid spectrophotometric methods are described for the determination of norfloxacin. The methods are based on the reaction of this drug as a π-electron donor with DDQ, TCNQ, p-chloranil or chloranilic acid as π-acceptors to give highly colored complex species. The colored products were formed in non-aqueous medium and absorbance was measured spectrophotometrically at 460, 843, 550 and 531 nm for DDQ, TCNQ, p-chloranil and chloroanilic acid, respectively. Beer's law was obeyed in the range 10–400 μg/mL. The results were found to be comparable to the official methods (75).

Ofloxacin

Two extractive spectophotometric methods for the determination of ofloxacin have been reported. The first method involves formation of ion-pair complexes with supracene violet 3B and tropaeolin 000, extraction of the complexes with chloroform and spectrophotometric determination of the extracted complexes at 575 nm and 485 nm respectively. The detection limit was reported to be 2.5 μg/mL (39). Ofloxacin has also been determined at 630 nm by reacting with MBTH in the presence of cerium (IV) ammonium sulphate (45). A method based on the formation of an ion-pair with Sudan III in aqueous-acetone medium has been used for the spectrophotometric determination of ofloxacin at 565 nm. Beer's law was obeyed in the range 0.4–8.8 μg/mL (46). The first, second, third and fourth order derivative spectrophotometric methods by using peak-zero and peak-peak techniques of measurement have been developed for the determination of ofloxacin by Hopkala *et al*. (49). The linearity range was observed to be 2–15 μg/mL for ofloxacin. Ammonium vandate has been used for the spectrophotometric determination of ofloxacin according to the method reported above (50). Three sulphonphthalein dyes for the spectrophotometric determination of the drug, BPB, BTB and BCP, have been used by Issa *et al*. (69). The linearity range was observed to be 5–25, 2–15 and 2–20 μg/mL for the drugs with three dyes, respectively. Two sulphonphthalein dyes, BPB and BCP, have also been used for the determination of ofloxacin by Suslu *et al*. (76) in phthalate buffer of pH 3.0 and 3.1, repectively. The two dyes formed complexes with with the drug which were extracted into chloroform and measured at 414 and 408 nm for BPB and BCP, respectively. The results obtained were comparable to the reference methods. The charge transfer (CT) complex formed between ofloxacin as the donor and TCNQ as the acceptor in methanol-acetone medium has been reported as the basis for the spectrophotometric estimation of the drug. RSD has been observed to be less than 3%. The method has given satisfactory results (77). Ofloxacin has also been determined by complex formation with cerium. The yellow-colored complex formed has a λmax at 243 nm and obeys Beer's law in the concentration range 0–22000 μg/mL (78). A sensitive and fast flow-injection spectrophotometric method for the determination of ofloxacin, based on the formation of a yellow complex between the drug and Fe (III), in a sulphuric medium has been reported by Garcia *et al*. (79) The calibration graph at 420 nm was found to be linear over the range 1.80–289 μg/mL with a detection limit of 0.72 μg/mL. The method gave comparable results to the official methods.

Pefloxacin

Mostafa *et al*. has used three different pi-electron acceptors, CL, TCNE and DDQ, for the determination of the drug forming charge transfer complexes with maximum absorbance at 520, 290 and 460 nm, respectively (34). The methods have been reported to be comparable in results to the reference methods. Pefloxacin has been determined by reaction with ammonium reineckate reagent in hydrochloric acid or sulphuric acid media. The precipitates formed were filtered and dissolved in 50% aqueous acetone and the absorbance of the resulting complex was measured at 524 nm. RSD was reported to be 0.13–0.28% (42). Pefloxacin has been determined at 630 nm by reacting with MBTH in the presence of cerium (IV) ammonium sulphate at room temperature. The absorbance-concentration plot was found to be linear over the range of 8–40 μg/mL (45). Pefloxacin has also been determined with ammonium vandate according to the method reported above (50). Pefloxacin has been determined by reaction with BPB at pH 2.3–2.5 and MO at pH 3.6 to give highly colored species extractable with chloroform, which were quantitated spectrophotometically at 420 and 424 nm, respectively. The results obtained from the application of the method to real samples were found to be precise and accurate (51). A spectrophotometric method reported for the estimation of pefloxacin in its dosage forms involves using 0.2% solution of ferric chloride as reagent. A yellowish orange chromogen is formed which has an absorption maximum at 440 nm. Beer's law was obeyed in the concentration range of 8.0–140.0 mcg/mL. The reproducibility of the method was found to be 99.8–100.1% (80). When the drug solution was reacted with F-C reagent in the presence of sodium carbonate solution a blue-colored chromogen was formed with absorption maximum at 760 nm; the method has been used for spectrophotometric estimation of pefloxacin. Beer's law was obeyed in the range of 10–45 μg/mL, the molar absorptivity and Sandell sensitivity being 2.79×10^3 L/mol^{-1}cm^{-1} and 119.03 ng/cm^2, respectively (81). A simple extractive spectrophotometric method reported for the estimation of pefloxacin in both pure and pharmaceutical dosage forms is based on the formation of ion-pair complexes of the drug with four dyes, namely BTB, BCG, BPB, and BCP, in acidic buffer solutions followed by their extraction in any organic solvent like chloroform. The absorbance of the organic layer was measured at their respective wavelength of maximum absorbance against the corresponding reagent blank. The method was found to be precise and accurate when evaluated statistically (82). Pefloxacin also forms a complex with Fe (III) at pH 1.00–8.00,

which shows maximum absorbance at 360 nm. Beer's law was obeyed in the range of 2.15–85.88 μg/mL. The lower sensitivity limit of the method was 2.15 μg/mL. The RSD was 0.57–1.07% (83). Second order derivative spectrophotometry has been used for the determination of pefloxacin. Spectrophotometric assay of pefloxacin was carried out in 0.1 M/L NaOH in the case of pharmaceutical samples: in serum it was performed with 0.1 M/L NaOH with the addition of sodium dodecyl sulfate in the wavelength range of 337–347 nm. Beer's law was obeyed in the concentration range of 2–30 μg/mL. The relative error of determination, as criterion for accuracy, was less than 1%, while the precision was better than 0.004 μg/mL (84). A UV spectrophotometric method developed for the determination of the pefloxacin is based on measuring the absorbance of the drug in 0.1 N H_2SO_4 at 276 nm. Concentrations adhering to Beer's law were from 2.0–10.0 μg/mL, the mean percentage recovery $\pm$ SD was found to be 99.87 $\pm$ 0.96 (85).

Levofloxacin

Levofloxacin has been determined by complex formation with Co (II) tetrathiocyanate. The drug forms blue-colored ion-pair associates with the inorganic complex of Co (II) tetrathiocyanate at pH 2.5. The ion-pair associates formed have maximum absorbance at 623 nm and can be determined spectrophotometrically at this wavelength (30). The drug has also been determined by complex formation with bismuth (III) tetraiodide and determination of the resulting complex at 453 nm. (31). Levofloxacin, when treated with xanthene dyes eosin Y and merbromin, form colored complexes having maximum absorbance at 547 and 545 nm, respectively. Both the methods have the advantage of being applicable for the determination of the drug without prior extraction (32). A method based on direct treatment of the drug with BCG in dichloromethane has been reported for the spectrophotometric determination of levofloxacin. The highly yellow-colored complex formed was quantified spectrophotometrically at 411 nm (33). Another spectrophotometric method developed for the determination of levofloxacin is based on the reaction of levofloxacin with p-chloroanilic acid forming charge transfer complex that shows maximum absorbance at 521 nm (33). Ammonium vandate has been used for the spectrophotometric determination of the drug according to the method reported above. (50). Two simple and sensitive extractive spectrophotometric methods have been described in literature for the assay of levofloxacin either in pure form or in pharmaceutical formulations. The methods involve the formation of colored, chloroform extractable, ion-pair complexes of levofloxacin with BPB and BCG in aqueous acidic medium. The extracted complexes of levofloxacin with BPB and BCG showed absorbance maxima at 424 and 428 nm, respectively. Beer's law is obeyed in the concentration ranges 1.85–31.5 and 1.85–25 μg/mL with BPB and BCG, respectively (86). A sensitive and fast flow-injection spectrophotometric method for the determination of levofloxacin based on the formation of a colored product upon oxidation with N-bromosuccinimide (NBS) in acidic medium has been reported. The calibration curve obtained was linear over the range 10–300 μg/mL, and the detection limit was reported to be 3 μg/mL. The results were found to be precise and in agreement with other reference methods. RSD was found to be <2.7% (87).

Sparfloxacin

A derivative UV spectrophotometric method based on complexation of the drug with Cu (II) and then applying a third order measurement for quantification of the drug has been reported for sparfloxacin. Average percentage recoveries of 99.22 $\pm$ 0.55 to 100.33 $\pm$ 1.60 were obtained when the method was applied to pharmaceutical samples. The results obtained were found to be satisfactory, accurate and precise (44). A spectrophotometric method for the determination of sparfloxacin based on the complexation of BTB (0.5%) and sparfloxacin to form yellow-colored complex with maximum absorbance at 385 nm was developed by Marona *et al*. (88). The linearity range of the method was reported to be 2–12 μg/mL. A number of UV spectrophotometric methods have been developed for sparfloxacin. These include determination of sparfloxacin by Marona *et al*. (89). Another UV spectrophotometric method involving measurement of the absorbance of the drug at 292 nm has been reported for the drug (90). The method gave rise to linear data in the range of 2–12 μg/mL with accuracy and precision in the range of 0.56–3.01%. A methanolic solution of the drug shows maximum absorbance at 295.2 nm, which forms the basis for spectrophotometric determination of the drug by Kumar *et al*. (91). Another method reported by the same workers is based on diazotization of the drug with nitrous acid followed by its coupling with resorcinol in an alkaline medium, to form a colored chromogen with an absorbance maximum at 350 nm. The two methods were found to be precise and accurate (91). Sparfloxacin has also been determined by treating diazotized sparfloxacin with phloroglucinol and measuring the absorbance of the resulting complex at 430 nm (92). Two spectrophotometric methods have been developed for the estimation of sparfloxacin (93). The first method involves using 0.2% w/v of cerric ammonium sulphate (CAS) in 2 N sulphuric acid. A reddish-brown chromogen was formed which has an absorption maximum at 484 nm and a linear range of 10.0–80.0 μg/mL. The reproducibility of the method was found to be 99.1–99.9%. The second method involves reaction of the drug solution with 0.3% w/v of NQS reagent, when a reddish-orange color developed. The chromogen formed showed maximum absorbance at 458 nm. Beer's law was obeyed in the concentration range of 20.0–100.0 μg/mL. The reproducibility of the method was found to be 99.4–101.1%. Sparfloxacin forms a yellowish-orange colored complex with ferric chloride having maximum absorbance at 510 nm; the method has been used for the estimation of sparfloxacin in dosage forms. Beer's law was obeyed in the concentration range of 0.7–160 μg/mL. The reproducibility of the method was reported to be 99.7–100.2% (94). The content and dissolution of sparfloxacin tablets has been determined by UV spectrophotometry in 0.1 mol/L hydrochloride solution at

TABLE 1
Methods for the spectrophotometric determination of fluoroquinolones and their applications

Name of drug	Reagents for complexation	λ_{max} (nm)	Linear range (μg/mL)	Applications
Nalidixic acid	1. Derivative spectrophotometry	——	2.0-12	Tablet formulations
	2. With hydrotropic solvents	330	5000–40000	Pharmaceutical formulations
	3. Cd (II) and rose bengal	564	40–56	Pharmaceutical formulations and pure drugs
Ciprofloxacin	1. Co (II) tetrathiocyanate	623	20–240	Tablet formulations
	2. Bi (III) tetraiodide	453	5–80	Tablet formulations and urine samples
	3. (a) EosinY	547	2–8	Tablet formulations and
	(b) Merbromin	545	2–15	urine samples
	4. BCG in dichloromethane	412	1–20	Tablet formulations
	5. (a) CL	520	——	Pharmaceutical
	(b) TCNE	335	——	formulations
	6. Eosin and Pd (II)	545	3–10	Tablet formulations
	7. Fe (III) in sulfuric acid media	447	50–500	Pharmaceutical formulations
	8. (a) Cerium (IV) sulphate and MO	520	0.5–3.5	Pharmaceutical formulations
	(b) Cerium (IV) sulphate and indigo carmine	610	1.0–7.0	
	9. Oxidation in acidic media with Ce (IV) and extraction in chloroform	345	12–120	Pharmaceutical formulations
	10. (a) Supracene Violet 3B	575	——	Pure and dosage
	(b) Tropaeolin 000	485	——	forms
	11. (a) DDQ	460	5–50	Pure and dosage
	(b) TCNQ	843	1.5–15	forms
	(c) CL	550	35–195	Pharmaceutical formulations
	12. (a) Tris (o-phenanthroline) iron (II)	510	0.04–7.2	Pharmaceutical formulations
	(b) Tris (bipyridyl) iron (II)	522	0.05–9.0	
	13. Ammonium reineckate reagent	524	——	Pharmaceutical formulations
	14. BBG	610	500–600	Pharmaceutical formulations
	15. Complexation with Cu (II)	630	0.035–0.120	Pharmaceutical formulations formulations, spiked human plasma and urine
	16. MBTH and cerium ammonium sulphate	630	10–50	Pharmaceutical formulations
	17. Sudan III	566	0.4–10.4	Pharmaceutical formulations
	18. p-nitrophenol	403	277—280	Tablet formulations
	19. Solid phase spectrophotometry	0.05–0.3	——	Pharmaceutical preparations
	20. Derivative spectrophotometry	——	2–12	Tablet formulations
	21. Ammonium vandate	766	10–40	Pharmaceutical formulations
	22. Flow injection spectrophotometric method	447		Pharmaceutical formulations
Enrofloxacin	1. (a) CL	520	——	Pharmaceutical formulations
	(b) TCNE	290	——	
	2. (a) Supracene violet 3B	575	——	Pure drug and dosage forms
	(b) Tropaeolin 000	485	——	
	3. Ammonium reineckate	524	——	Pharmaceutical formulations
	4. MBTH and cerium(IV) ammonium sulphate	630	10–74	Pharmaceutical formulations
	5. Ammonium vandate	766	10–40	Pharmaceutical formulations

(Continued)

TABLE 1
Methods for the spectrophotometric determination of fluoroquinolones and their applications *(Continued)*

Name of drug	Reagents for complexation	λ_{max} (nm)	Linear range (μg/mL)	Applications
	6. (a) BPB	420	2–12	Pharmaceutical
	(b) MO	424	1–12	formulations
	7. (a) Fe (III)	434	25–140	Pharmaceutical
	(b) BCP in phthalate buffer	410	4–18	formulations
	(c) DDQ in methanol	460	50–240	
	8. (a) Folin-Ciocaltaeus reagent	770	2.5–12.5	Pharmaceutical formulations
	(b) $FeCl_3$ in acidic media	440	100–120	
Enoxacin	1. Derivative spectrophotometry	—	2.0–12	Tablet formulations
	2. Ammonium vandate	766	10–40	Pharmaceutical formulations
	3. (a) BPB	412	2.0–20	Pure drug and dosage
	(b) BCP	410	0.77–1762	forms
Fleroxacin	1. MBTH and cerium ammonium sulphate	630	10–60	Pharmaceutical formulations
	2. In 0.1 M HCl at pH< 3.5	286	2—8	Tablet formulations
	3. Derivative spectrophotometry	—	2.0–12	Pure and tablet forms
Gatifloxacin	1. Sulphonphthalein dyes			
	(a) BCG	415	2–20	Pure drug and
	(b) BCP	412	2–14	pharmaceutical
	(c) BPB	417	2–16	formulations
	(d) BTB	414	2–16	Pharmaceutical
	2. Ferric nitrate reagent	470	20–200	formulations
	3. UV spectrophotometry			
	(a) In NaOH medium	289	5–30	Bulk drug,
	(b) In HCl medium	292	5–30	pharmaceutical
	(c) Ferric chloride and potassium dichromate	352	5–30	formulations and biological samples
	4. MBTH with ceric ammonium sulphate	630	2–10	Pharmaceutical preparations
	5. (a) In 100 mM phosphate buffer of pH 7.4	286	1.0–18	Pharmaceutical formulations
	(b) In 100 mM HCl at pH 1.2	292	1.0–14	
	6. UV spectrophotometry	287	4.0–14	Tablet formulations
Lomefloxacin	1. Ammonium reineckate reagent	524	—	Pharmaceutical formulations
	2. Ammonium vandate	766	10–40	Pharmaceutical formulations
	3. Ferric nitrate in nitric acid	445	2.0–10	Pharmaceutical preparations
	4. Dichlone, crotonaldehyde in DMSO	645	5.00–100	Pharmaceutical preparations
	5. BCG in $CHCl_3$	415	1–15	Pharmaceutical formulations
	6. Chloranil in CPB medium	323	0.8–54	Tablet formulations
	7. UV spectrophotometry	280	2–9	Tablet formulations
	8. (a) BPB	—	5–25	Pharmaceutical
	(b) BTB	—	2–15	preparations
	(c) BCP	—	2–20	
Norfloxacin	1. Hydrotropic solvents	324	5000–35000	Pharmaceutical formulations
	2. Co(II) tetrathiocyanate	623	20–240	Tablet formulations
	3. Bi(III) tetraiodide	453	5–80	Tablet formulations and
	4. (a) EosinY	547	2–8	urine samples
	(b) Merbromin	545	2–15	Tablet formulations and urine samples

(Continued on next page)

TABLE 1
Methods for the spectrophotometric determination of fluoroquinolones and their applications *(Continued)*

Name of drug	Reagents for complexation	λ_{max} (nm)	Linear range (μg/mL)	Applications
	5. BCG in dichloromethane	412	1–20	Tablet formulations
	6. TCNE in acetonitrile	333	0.8–16	Pharmaceutical formulations
	7. Eosin and Pd (II)	545	3–10	Tablet formulations
	8. Fe(III) in sulphuric acid media	430	50–400	Pharmaceutical formulations
	9. (a)Supracene violet 3B	575	——	Pharmaceutical
	(b) Tropaeolin 000	485	——	formulations
	10. Ammonium reineckate reagent	524	—-	Pharmaceutical formulations
	11. BBG	614	400–800	Pure and dosage forms
	12. Complexation with Cu (II)	——	0.015–0.080	Pure and dosage forms
	13. MBTH and cerium ammonium sulphate	630	20–100	Pharmaceutical formulations
	14. Sudan III	567	0.4–12	Pharmaceutical formulations
	15. p-nitrophenol	407	——	Tablet formulations
	16. Derivative spectrophotometry	——	1–10	Tablet formulations
	17. Ammonium vandate	766	10–40	Pharmaceutical formulations
	18. (a) In 0.1 N HCl and 0.1 N NaOH	280	——	Pure and dosage forms
	(b) Fe(II) in acetate buffer	358	4.0–32	
	19. TCNQ	743	——	Pharmaceutical preparations
	20. Oxidation with Ce (IV) and extraction with chloroform	——	10–100	Tablets and eye-drops
	21. Kinetic spectrophotometry by oxidation with alkaline KmnO4	603	2–20	Pharmaceutical preparations
	22. (a) DDQ		Method 1	
	(b) TCNQ		1–20	
	(c) p-Chloranil	460	Method 2	
	(d) Chloranilic acid	843	10–400	Pharmaceutical formulations
		550	10–400	
		531	10–400	
			10–400	
Ofloxacin	1. (a) Supracene violet 3B	575	——	Pharmaceutical
	(b) Tropaeolin 000	485	——	formulations
	2. MBTH	630	2–20	Pharmaceutical formulations
	3. Sudan III	565	0.4–8.8	Pharmaceutical formulations
	4. Derivative spectrophotometry	——	2.5-15	Pharmaceutical formulations
	5. Ammonium vandate	766	10–40	Pharmaceutical formulations
	6. BTB	——	2.0–15	Pharmaceutical formulations
	7. (a) BPB	414	0.87–17.35	Pharmaceutical formulations
	(b) BCP	408	0.58–14.46	
	8. TCNQ	743	0–15	Tablet formulations
	9. Cerium	243	0–22000	Pharmaceutical formulations
	10. Fe(III)	420	1.8–289	Pharmaceutical samples and human urine
Pefloxacin	1. (a) CL	520	——	Pharmaceutical
	(b) TCNE	290	——	formulations
	(c) DDQ	460	——	
	2. Ammonium reineckate reagent	524	——	Pharmaceutical formulations
	3. MBTH and cerium ammonium sulphate	630	8–40	Pharmaceutical formulations

TABLE 1
Methods for the spectrophotometric determination of fluoroquinolones and their applications *(Continued)*

Name of drug	Reagents for complexation	λ_{max} (nm)	Linear range (μg/mL)	Applications
	4. Ammonium vandate	766	10–40	Pharmaceutical formulations
	5. (a)BPB	420	2–18	Pharmaceutical
	(b) MO	424	4–40	formulations
	6. Ferric chloride	440	8–140	Pharmaceutical formulations
	7. F-C reagent	760	10–45	Pharmaceutical formulations
	8. BTB, BCG, BPB, BCP in acidic buffer	——	——	Pure and dosage forms
	9. Fe (III)	360	2.15–85.88	Pharmaceutical formulations
	10. Derivative spectrophotometry	337–347	2–30 0.12–5	Tablets and serum samples
	11. In 0.1 N H_2SO_4	276	2–10	Pharmaceutical preparations
Levofloxacin	1. Co (II) tetrathiocyanate	623	20–240	Tablet formulations
	2. Bi (III) tetraiodide	453	5–80	Tablet formulations and spiked urine samples
	3. (a) EosinY	547	2–8	Tablet formulations and
	(b) Merbromin	545	2–15	spiked urine samples
	4. (a) BCG in dichloromethane	411	1–20	Tablet formulations
	(b) p-Chloroanilic acid	521	15–250	
	5. Ammonium vandate	766	10–40	Pharmaceutical formulations
	6. (a) BCG in acidic media	428	1.85–25	Pharmaceutical
	(b) BPB in acidic media	424	1.85–31.5	preparations
	7. NBS in acidic media	——	10–300	Pharmaceutical and human urine samples
Sparfloxacin	1. Complexation with Cu (II)	——	200–700	Pharmaceutical samples,human plasma and urine
	2. Bromothymol blue	385	2–12	Pharmaceutical formulations
	3. UV Spectrophotometry	292	2–12	Pharmaceutical formulations
	4. (a) In methanol	295.2	——	Pharmaceutical formulations
	(b) Nitrous acid and resorcinol	350	——	
	5. Phloroglucinol	430	—-	Pharmaceutical formulations
	6. (a) Ceric ammonium sulphate	484	10–80	Pharmaceutical formulations
	(b) NQS	458	20–100	
	7. Ferric chloride	510	0.7–160	Pharmaceutical formulations
	8. In 0.1M HCl	298	2–12	Pharmaceutical
	9. Methyl orange	390.8	——	formulations
	10. p-nitrophenol			Tablet formulations
	11. BTR buffer	298	1.8–3.0	Pharmaceutical formulations
	12. Alizarin red	530	6–160	Pharmaceutical formulations
Moxifloxacin	1. (a) In 0.1N HCl (pH 1.2)	303.4	1–12	Tablets, intravenous
	(b) In phosphate buffer of pH 7.4	296 289	1–14	infusions, eye drops and polymeric nanoparticles

the wavelength of 298 nm. The standard curve was linear over the concentration range of 2–12 μg/mL. The average recovery was 100.2% and the RSD was 0.29% (95). A method developed for the quantitative estimation of sparfloxacin in tablets is based upon the reaction of sparfloxacin with MO, forming a yellow-colored complex, which was extracted in chloroform and analyzed. The absorbance maximum was found to be at 390.8 nm. The method was found to be comparable to the official methods (96). Sparfloxacin has been determined by reaction with p-nitrophenol in water. The method gave recovery of 0.9–30% and RSD of 1.93% (97). Buffer turnover rate (BTR) found buffer of pH 3 has also been used for spectrophotometric

determination of sparfloxacin. The drug in BTR buffer showed an absorption maximum at 298 nm. The method was applicable in the linear range of 1.8–3.0 μg/mL. The method gave a recovery of 100.7%. RSD was found to be 0.23%. The results were comparable to the official methods (98). Alizarin red dye has been used for spectrophotometric determination of sparfloxacin. The dye forms a charge transfer complex with the drug in an ethanol-water medium with maximum absorbance at 530 nm. Beer's law was obeyed in the concentration range of 6–160 μg/mL. The method was found to be precise and accurate (99).

Moxifloxacin

Two simple and accurate UV spectrophotometric methods have been reported for the estimation of moxifloxacin (100). In the first method moxifloxacin was estimated at 296 nm in 0.1 N hydrochloric acid (pH 1.2) and at 289 nm in phosphate buffer (pH 7.4). Beer's law was obeyed in the concentration range of 1–12 μg/mL ($r^2 = 0.9999$) in hydrochloric acid and 1–14 μg/mL ($r^2 = 0.9998$) in the phosphate buffer medium. The detection and quantitation limits were found to be 0.0402 and 0.1217 μg/mL in hydrochloric acid and 0.0384, 0.1163 μg mL^{-1} in phosphate buffer medium, respectively. The proposed methods were successfully applied for the determination of moxifloxacin in pharmaceutical formulations. The method was found to be reproducible having a RSD $< 2\%$.

APPLICATIONS

The above mentioned methods have applications in the determination of these drugs in various pharmaceutical formulations like tablets and oral solutions. These methods give results which are comparable with other reference methods used for the determination of fluoroquinolones; hence, these methods can be successfully used for routine analysis and quality control of fluoroquinolone drugs. The methods have been used for the quantitative determination of the drug in pure form and commercial preparations. Human urine samples and serum samples have also been successfully analyzed for fluoroquinolone drugs by these methods. The commonly occurring exicipients do not interfere in the determination of the drug in the case of commercial samples. The methods have been validated statistically by applying students' t-test and f-test. The results have been found to be accurate, precise and comparable to the official methods.

ABBREVIATIONS

BBG	Brilliant blue G
BCG	Bromocresol green
BCP	Bromocresol purple
BPB	Bromophenol blue
BTB	Bromothymol blue
CE	Capillary electrophoresis
CL	Chloroanilic acid
CPB	Cetyl pyridinium bromide
DDQ	2,3-dichloro-5,6-dicyano-p-benzoquinone
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
F-C	reagent Folin-Ciocalteau's reagent
HPLC	High pressure liquid chromatography
MBTH	3-methyl-2-benzothiazolinone hydrazone hydrochloride
MO	Methyl orange
NBS	N-Bromosuccinimide
NQS	1, 2-naphtho-quinone-4-sulphonate
R.S.D	Relative standard deviation
SPE	Solid phase microextraction
TCNE	Tetracyanoethylene
TCNQ	7,7,8, 8-tetracyanoquinodimethane
UV	Ultraviolet

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