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PROPERTIES AND ANALYTICAL METHOD FOR DETERMINATION FLOURO QUINOLONES: A REVIEW

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ABSTRACT

Fluroquinolone is a broad-spectrum antibiotic that has gained significant attention in the medical field due to its efficacy in treating a wide range of bacterial infections. This review article aims to provide a comprehensive overview ofloxacin, covering its properties, analytical methods for determination, and its clinical significance. We explore the chemical structure, pharmacokinetics, and pharmacodynamics of levofloxacin, along with the various analytical techniques used for its quantification and quality control. Furthermore, we discuss the clinical applications and significance of levofloxacin in modern healthcare, high lighting its therapeutic benefits and potential concerns.

Keywords: Analytical method, fluroquinolone, levofloxacin, ciprofloxacin, nalidixic acid, moxifloxacin quality control

1. INTRODUCTION

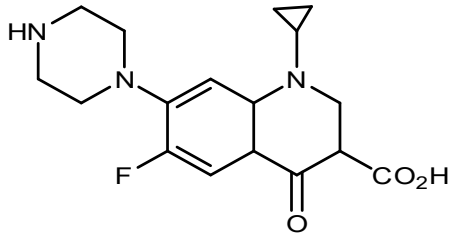
1.1 brief overview of fluoroquinolone as widely used antibiotic

A fluoroquinolone antibacterial drug with a broad spectrum of activity is levofloxacin, ciprofloxacin, nalidixic acid, moxifloxacin. Fluoroquinolone is an oral broad-spectrum antibiotic of the fluoroquinolone drug widely used in the treatment of certain bacterial infections including pneumonia, urinary tract infections and abdominal infections **[1-4]**. Against both Gram positive and Gram-negative bacteria. It works by preventing DNA gyrase, a type II topoisomerase enzyme required for its action. to segregate DNA that has been copied, preventing cell division **[5]**.

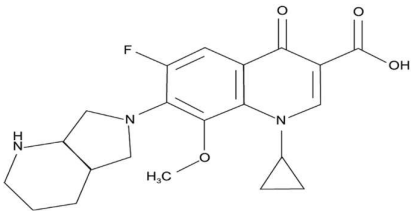
Fluoroquinolones is the L-isomer of the quinolone antibacterial drug acetate ofloxacin. Floroquinolone, a chiral fluorinated carboxyquinolone, is the exact enantiomer of the antibiotic ofloxacin, a racemic compound. Infections caused by susceptible strains of bacteria such Hemophilus influenzae, Klebsiella pneumoniae, Legionella pneumophila, Moraxella catarrhalis, Streptococcus pneumoniae, Chlamydia pneumoniae, and Mycoplasma pneumoniae are treated with levofloxacin on a global scale. Fluoroquinolones is prized for its wide range of therapeutic effects, superior tissue penetration, and accessibility in both oral and intravenous preparations **[6]**.

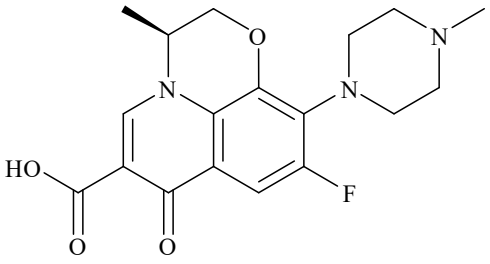
Chemical Structure of Fluoroquinolone

Levofloxacin



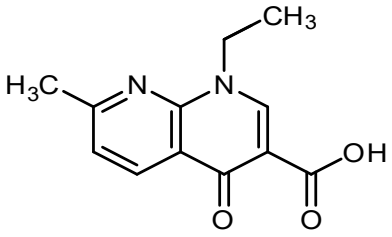
Moxifloxacin



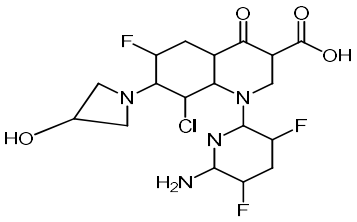


Sparflocxacin

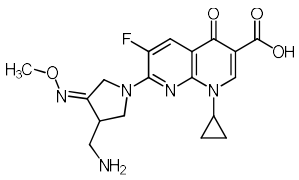
Nalidixic Acid



Delafloxacin



Gemifloxacin



2. ANALYTICAL METHODS

There are several analytical methods available to measure fluoroquinolone concentrations. One such method is liquid chromatography. A review paper published in the journal Analytical and Bioanalytical Chemistry 1 provides a thorough review of most liquid chromatographic methods reported in the literature for the separation and quantification of the novel fluoroquinolones in biological matrices and pharmaceutical formulations. The article covers a wide range of liquid chromatographic techniques, such as reversed-phase high-performance liquid chromatography (RP-HPLC), hydrophilic interaction liquid chromatography (HILIC), ion-exchange high-performance liquid chromatography (IEX-HPLC), and high-performance thin-layer chromatography (HPTLC). The study also includes a comprehensive and rigorous examination of the physicochemical properties, sample preparation methods, and chromatographic and detection settings.

2.1 High-performance liquid chromatography (HPLC)

Principle

The analytical chemistry method of high-performance liquid chromatography (HPLC), formerly known as high-pressure liquid chromatography, is used to separate, recognize, and quantify each component in a mixture. It uses pumps to move a column of solid adsorbent material through a pressured liquid solvent containing the sample combination. The adsorbent material and each component in the sample interact slightly differently, resulting in various flow rates for the various components and their separation as they exit the column.

Methodology

Chromatographic Conditions

Isocratic elution was carried out in the review. Acetonitrile, methanol, and phosphate cushion pH 3.0 (17:3:80 v/v/v) were utilized as portable stage, streaming at 1 mL/min through a Luna Phenomenex® C18 (250 4.6 mm; 5 m) segment. Per run, a volume of 20 µl of the example was infused

and uncovered with a U.V. identifier set at 295 nm.

Preparation of Standard Solution and Calibration Curve

The method used for Fluoroquinolone like levofloxacin, Ciprofloxacin, Nalidixic acid and moxifloxacin was found to as inside norm, 10 mg of LEVH and CPR were put into a 10.0 ml volumetric jar, broke up with adequate acidic corrosive, and weakened with portable stage to achieve a centralization of 1 mg/ml. The standard arrangement was weakened with the versatile stage to get LEVH centralization of 4.84; 9.68; 14.52; 19.36; 24.20; and 29.04 µg/ml. Every convergence of standard LEVH arrangement contains an interior norm as much as 20 µg/ml. Adjustment was finished by bend fitting focus to LEVH to CPR region proportion.

First, the internal standard chosen was ofloxacin. However, in the case of ofloxacin and ciprofloxacin, when both were tested together in the aforementioned conditions, they showed a retention duration of around three minutes.

To further resolve the peaks that the two compounds offered, 30% was subtracted to 26, 25, 24, and 23%. The ofloxacin retention time did not significantly change as a result of this. Next, sulfadimidine sodium was chosen in place of the internal standard since it displays similar chemical behavior under the extraction and chromatographic conditions used in this research, has strong UV absorbance at 277 nm, and has two pKa values: 2.65 ±0.2 (pKa1) and 7.40 ±0.2 (pKa2) **[7]**.

Orthophosphoric acid (0.15%) was added to phase pH 3.0. Use a gradient employing an inertsil C18 column, 250 mm × 4.0 mm, 5 µm, triethylamine, and acetonitrile software. The parameters that were utilized were the column's temperature, a flow rate of 0.7 ml/min, 10.0 µL of injection volume, and 35˚C **[7]**.

Volumetric flasks were filled with standard stock solutions containing 1500 ppm of Nalidixic acid in a 1:1 mixture of methanol and water **[9]**.

Where the HPLC for Balofloxacin After multiple experiments with different mobile phase compositions, acetonitrile and the ratio of 60:40v/v phosphate buffer pH 3.2 was selected for the mobile phase because of its resolution and symmetrical peaks. Balofloxacin's spectrophotometric data showed a discernible absorption at 293 nm, which is why that wavelength was selected as the detection wavelength. Five replicate injections of the 100% test concentration were used to assess the applicability of the system; the results showed that the number of theoretical plates, HETP, and resolution were all satisfactory. A clean chromatogram shows that Balofloxacin is present at 2.0 min. 0.999 is the concentration range. The procedure's accuracy was verified by

conducting recovery experiments using the standard addition approach. It was found that the standard's recovery percentage added to the pre was 99.0-99.66%. It was found that the detection limit was 0.055 µg/ml and the quantitation limit was 0.167 µg/ml. The strategy was shown to be robust after changing the parameters, such as detection. wavelength (± 2 nm) and flow rate (± 0.1 ml). The percentage RSD for each variation was calculated and reported.

Various organic modifiers (acetonitrile, methanol) and volatile buffers (ammonium acetate, ammonium formate, and formic acid) were tested in mobile phase conditions with varying potential composition and flow rates. The analyte and IS retention that was best were was attained using a UPLC^{BEH} C18 column (2.1 x 100; 1.7 µm) and a mobile phase consisting of 10 mM ammonium acetate and acetonitrile in a 60:40 ratio at a flow rate of 300 µl/min. The mobile phase also contained 0.1% formic acid.

2.2 Ultraviolet (uv) spectrophotometry

Principle

The term "UV principle" relates to the principle of UV-Visible Spectroscopy, a method for determining how well a material reflects or absorbs light in the ultraviolet and visible spectrum. The idea is based on the Beer-Lambert Law, which asserts that a solution's absorbance is directly related to both its concentration and route length. The principle also explains how an electron gets excited from a lower to a higher energy level when energy is absorbed by the sample, and the energy difference is equal to the energy of the received radiation**.**

Methodology

Determination of wavelength of maximum absorption

A standard stock arrangement (LS) of levofloxacin (20 µg/ml) was arranged utilizing diluents and 3 mL of LS was then weakened to 10 mL with a similar diluent to get 6 µg/ml levofloxacin reference arrangement (LR). An UV spectroscopic checking (190-400 nm) was completed with the LR to decide the λmax for the recognition of levofloxacin involving diluent as clear **[10]**.

Linearity and Range

For linearity study, seven arrangements at various fixations (1, 2, 4, 6, 8, 10 and 12 µg/ml) were arranged utilizing seven distinct aliquots of LS, and the acquired information were utilized for the linearity adjustment plot. Cutoff of discovery (LOD) and breaking point of measurement (LOQ) for the examine were additionally determined.

Intra-day precision (repeatability) and inter-day precision study (intermediate precision)

Levofloxacin tablets were finely powdered and the example stock arrangement (LP) of 20 µg/ml was arranged following a similar

weakening example of LS. Three unique aliquots of LP were then weakened to 10 ml to acquire the convergences of 4, 6 and 8 µg/ml. This strategy was rehashed before very long.

2.3 UV Spectrophotometric for ciprofloxacin:

Table 1

Drug	Method	Result
ciprofloxacin	UV spectroscopy	Absorption maximum 270nm and 277nm

As compared to preparation of stock solution for nalidixic acid is the concentrations of the internal standard and nalidixic acid stock solutions were 1000 mg l^{-1} and 50 mg l^{-1}, respectively, in double-distilled water. Appropriate dilution of the stock solution produced workable solutions. A calibration curve was made using the concentration range of 1 to 800 µg l^{-1} (1, 5, 10, 25, 50, 100, 200, 300, 400, 500, 600, 700, and 800 µg L^{-1}). Using least squares linear regression, the peak area ratio of the internal standard vs the analyte concentration was examined in order to produce an equation. Every solution was stored in a refrigerator that was dark and cold **[11]**.

By adding 2.5, 20, and 60 µl of standard stock solution of analyte to 100 µl of urine, standard working solutions of nalidixic acid were generated. The solution had concentration levels of 25, 200, and 600 µg l^{-1}. To optimize the DLLME procedure, a resolution of 200 µg l^{-1} of nalidixic acid and 50 mg l^{-1} of internal standard were used. Urine samples were taken from healthy donors and stored in a refrigerator away from the sun. Following the samples' centrifugation and filtration, Before analysis, filter paper (Whatman No. 42). The urine sample was divided into 100 µl aliquots and put into a 5 ml volumetric flask for examination. After that, pure water, analyte, and an internal standard were used to stabilize it and dilute it to volume using double-distilled water. The sample solution was treated with phosphoric acid (0.05 mol l^{-1}) to lower its pH to 5.

Analytical Method Development

A variety of media were investigated in order to develop an appropriate UV spectrophotometric method for the detection of moxifloxacin in formulations. The pricing of the solvents, the method's adaptability, its durability for various uses, the sensitivity of the technique, the ease of sample preparation, and the medication's solubility were all taken into account while selecting the media. Upon the determination of moxifloxacin's absorbance in the stipulated medium at the appropriate wavelength, the usual formulas were utilized to compute Sandell's sensitivity coefficients and apparent molar absorptivity **[12]**.

Procedure for Calibration Curve

Phosphate buffer (PBS) (pH 7.4) and media (1.2) each contained 50 ml of 5 mg of moxifloxacin dissolved in them. A series of 10 ml standard volumetric flasks were filled with aliquots of stock solutions to create different concentrations, and the corresponding media volumes were prepared. A range of 1 to 12 g ml^{-1} moxifloxacin concentrations in HCl were prepared. In the same way, the phosphate buffer was used to create five different moxifloxacin concentrations for the standard curve, ranging from 1 to 14 g ml^{-1}. Moxifloxacin was measured to be 289 and 296 nm in phosphate buffer medium and HCl, respectively.

Sample preparation

Two distinct media were used to grind and separate the loxifloxacin-containing pills: 0.1N HCl and PBS (pH 7.4). 5 g ml^{-1} was the final concentration after the solutions were filtered and suitably diluted. The ultimate dose of 4 g ml^{-1} was achieved by suitably diluting the IV infusions and eyedrops. The moxifloxacin nanoparticles were extracted using acetone and then appropriately diluted to a final concentration of 5.50 g ml^{-1}.

UV of Balofloxacin

In methanol, balofloxacin displayed a wavelength maximum of 293 nm. the regression equation y = 0.078*X + 0.022; (r2 = 0.997), demonstrating the linearity of the suggested strategy in the 2–14 µg/ml range. % Balofloxacin recoveries were found to be satisfied, with a range of 99.04 to 101.47%. This clearly demonstrates the accuracy of the method being offered. The percentage RSD is 1.06 and 0.461 for the intra-day and inter-day precision results, respectively.

2.4 Mass spectrometry (MS)

Principle

The fundamental guideline of mass spectrometry is to create particles from either inorganic or natural mixtures, separate these particles by their mass-to-charge proportion (m/z), and distinguish them subjectively and quantitatively by their individual m/z and abundance. Mass spectrometry depends on the movement of a charged molecule, called a particle, in an electric or attractive field.

Methodology

Stock arrangements of different focuses were ready in methanol. Two groups of levofloxacin and dimethyl levofloxacin stock arrangements of 200 mg/l in methanol were made. One group was utilized to set up the adjustment tests in clear human serum by spiking with an appropriate volume of sequentially weakened stock answers for make eight distinct focuses for the adjustment bend. The sum of stock arrangement added to the serum didn't surpass 5% of the absolute volume. The interior standard arrangement was made by

weakening a stock arrangement of 200 mg/l levofloxacin $^{13}C2$ H3 also, dimethyl-levofloxacin $^{2}H8$ to a last concentration of 0.2 mg/l for both interior standards **[13]**.

Sample preparation

Tests were ready by adding 750 µl hastening reagent containing inward principles to 100 µl of serum in a polypropylene tube. The combination was then vortexed for 1 min and centrifuged for 5 min at 10.000 rpm after which 2 µl of supernatant was infused into the LC-MS/ MS framework. The portable stage had a progression of 300 µl/min and comprised of super unadulterated water, acetonitrile and an aqueous cradle (containing ammonium acetic acid derivation 5.0 g/L, 100 percent acidic corrosive 35 ml/l and trifluoroacetic corrosive 2 ml/l in water. The method had a run time of 2.5 min. The entire LC column effluent was transferred into the ion source for APCI using a heated nebulizer probe that used nitrogen as the probe and bath gas (200 l/h) at a source temperature of 120 "C.

2.5 Fluorimetry

Basic And Application in Levofloxacin Analysis

Individual doses of the tested medications were dissolved in methanol for ETO and ethanol for both MOX and NAL in order to generate the stock solutions of 100.00 µg ml^{-1}. Standard working solutions were prepared by dilution of the stock solutions of ETO, MOX, and NAL with ethanol at different concentrations (10.00 µg ml^{-1} for ETO, 4.00 µg ml^{-1} for MOX, and 50.00 µg ml^{-1} for NAL). After that, these solutions were stored at 2°C in the refrigerator until they were required, and it was found that they held their stability for 10 d **[14, 15]**.

Procedure

Construction of calibration graphs

The measurement of ETO, MOX, and NAL was made possible by transferring the previously prepared standard solutions of these three chemicals into a series of 10 ml volumetric flasks. Consequently, the final concentrations of MOX, ETO, and NAL were 0.04–0.40, 0.10–1.00, and 0.50–5.00 µg ml^{-1}, respectively, after filling the mark with ethanol and well mixing. The first derivative of the synchronous fluorometric method (1D) was used for the quantification of NAL and ETO, and the conventional synchronous fluorometric approach was used for MOX estimate. In ethanol, conventional synchronous fluorometric monitoring of MOX was carried out at 371 nm, while 1D synchronous fluorometric observations of NAL and ETO were recorded at 257 and 273 nm, respectively. The synchronous fluorescence was scanned at $\Delta\lambda$ of 60 nm for both methods. Consequently, the design of the calibration curve was determined by graphing the relative synchronous fluorescence intensity (RSFI) for MOX or the peak amplitude of the (1D) technique for ETO and NAL

against the final drug concentration in µg ml^{-1} **[14] [16]**.

Analysis of MOX, ETO and NAL in their pharmaceutical formulation

The synchronous fluorescence was scanned at Δλ of 60 nm for both methods. Consequently, the design of the calibration curve was determined by graphing the relative synchronous fluorescence intensity (RSFI) for MOX or the peak amplitude of the (1D) technique for ETO and NAL against the final drug concentration in µg ml^{-1}. The synchronous fluorescence was scanned at Δλ of 60 nm for both methods. Consequently, the design of the calibration curve was determined by graphing the relative synchronous fluorescence intensity (RSFI) for MOX or the peak amplitude of the (1D) technique for ETO and NAL against the final drug concentration in µg ml^{-1}. The synchronous fluorescence was scanned at Δλ of 60 nm for both methods. Consequently, the design of the calibration curve was determined by graphing the relative synchronous fluorescence intensity (RSFI) for MOX or the peak amplitude of the (1D) technique for ETO and NAL against the final drug concentration in µg ml^{-1}.

2.6 Capillary electrophoresis (CE)

An analytical method called capillary electrophoresis (CE) divides ions according to their electrophoretic mobility. The charge, size, and shape of the molecule, as well as the viscosity of the medium, all affect electrophoretic mobility. An electric field generated by CE's small capillary and applied voltage directs the ions toward electrodes. CE is a quick and high-resolution technique for analysing proteins, DNA, and tiny molecules**.**

2.7 High performance thin layer chromatography

Preparation of sample stock and working solution

To produce the sample, exactly weigh 10 mg of powdered ciprofloxacin base into a 10ml container. Methanol and water (9:1%v/v) were used to dissolve volumetric flasks, providing a stock concentration of 1 mg ml^{-1}. Methanol was then further diluted to provide a working concentration of 0.1 mg ml^{-1}. Before adding the organic solvent, ciprofloxacin hydrochloride was immediately dispersed in deionized water.

Chromatography

There was no need to pre-wash the activated TLC plates as they were taken out of their packaging right before usage. The plates were labeled and the solvent front was marked at 70 mm from the bottom before spotting. Before developing, five microliters were applied using a Linomar 5 room, 8 mm from the bottom as an 8 mm band. Before the plate was developed, the development tank's long side was covered with filter paper to help with saturation. The mobile

phase was then poured into the tank by soaking it, and the lid was closed for 30 min.

Table 2

Drug	Method	Plate	Detection Wavelength	Rp Value
ciprofloxacin	HPTLC	20cm×10cm	280	0.27

A simple solution of ethanol, water, and ammonia was used as the mobile phase in the green RP-HPTLC approach. In contrast, the NP-HPTLC method used a mixture of ethyl acetate, methanol, and ammonia solution as the mobile phase. The program the RP-HPTLC method has several advantages over NP-HPTLC, including the avoidance of the non-polar fractions of the sample on the TLC plates, the creation of a compact spot, the prevention of contamination-related interference, and the clarity of the detection **[16, 17]**. The green RP-HPTLC approach for determining DLFX will also lessen the possibility of environmental harm as opposed to the NP-HPTLC method **[17, 18]**. Several formulae for ethanol utilized in this study: Water: ammonia solutions were investigated as possible mobile phases for RP-HPTLC-densitometric analysis of DLFX. The solutions had different volume to volume ratios (v/v/v), such as 6:4:1 (v/v/v), 5:5:1 (v/v/v), 4:5:2 (v/v/v), 4:4:3 (v/v/v), and 5:4:2 (v/v/v). The evolution of the era of green mobility. 6:4:1 (v/v/v) and 5:5:1 (v/v/v) ethanol, water, and ammonia solutions resulted in a low densitometric peak and poor DLFX symmetry. However, good densitometric data were obtained with the ethanol : water: ammonia solution combinations 4:5:2 (v/v/v) and 4:4:3 (v/v/v). peaks, despite the unsatisfactory peak symmetry of DLFX. A compact and well-resolved DLFX peak at Rf = 0.84 ± 0.01 was obtained by the ternary mixture of ethanol:water:ammonia solution 5:4:2 (v/v/v) among the various compositions of ethanol, water, and ammonia solutions that were investigated circumstances of chamber saturation.

2.8 HPTLC of Sparflocxacin:

Table 3: Precision data of HPTLC assay for Sparflocxacin

Concentration added(ng)	Peak area(mean+-S.D)	RSD(%)
Inter-day		
200	5509.93+-70.40)	1.28
400	11130.00+-134.35)	1.21
800	21907.75+-269.29)	1.23
Intra-day		
100	2731.50+-35.44	1.30
400	10951.48+-138.11	1.26
500	14048.30+-169.99	1.21

2.9 HPTLC method of Balofloxacin

The method was linear in the 150–550 ng/spot range, according to five replicates (r= 0.999). The LOD and LQ of Balofloxacin were found to be 30 and 100 ng/spot, respectively. The intraday precision was established by analysis. The percentage RSD of Balofloax's intraday and interday precision ranges from 0.5 to 0.9. The technique appears to have value based on its value. Six times, 3.5 µl of the drug solution were applied to a TLC plate, let to develop, and the peak area of the spots was quantified to assess the repeatability of sample application. Balofloxacin's percentile RSD peak area values were determined to be 0.32. On a TLC plate, a 3.5µl spot of Balofloxacin solution was created in order to assess peak area repeatability. After six scans of the partitioned region without rotating the plate, the percentile RSD measurement of the Balofloxacin peak area value was found to be 0.19.

2.10 HPTLC method of Delafloxacin

The green RP-HPTLC and NP-HPTLC methods for assessing DLFX were both verified in terms of "linearity, precision, accuracy, robustness, sensitivity, and specificity", in accordance with ICH Q2 (R1) standards. The linearity of DLFX was determined by plotting the concentration. in relation to the measured HPTLC area of DLFX. Linearity was found in the concentration range of 25–1000 ng/band for the RP-HPTLC and 50–600 ng/band for the NP-HPTLC, respectively. The method accuracy was determined to be the recovery percentage (%) at each of the four different DLFX concentrations. Because of variations in their linearity ranges, the concentrations analyzed for accuracy measurement were different for the NP-HPTLC and RP-HPTLC approaches.

3.9 Fourier transform infrared spectroscopy for ciprofloxacin

Table 4

Drug	Absorbance range	Dil. sample of drug in dry potassium bromide	AUC	%RSD
Ciprofloxacin	3532, 3373, 3088, 2932 and 2620	2.0 absorbance unit	1710-1703cm^{-1}	0.837-1.707[48]

3. Future Prospects

As per a few sources, the deals of Levofloxacin in China have shown a vertical pattern from 2016 to 2019 and are supposed to have a supportive development from 2021 to 20251. Levofloxacin enjoys benefits like an expansive antibacterial range, solid antibacterial movement, high bioavailability, and great tissue cell permeability. In any case, it might likewise have a few secondary effects like

queasiness, looseness of the bowels, cerebral pain, dazedness, or insomnia.

4.CONCLUSION

This survey depicts norfloxacin properties, its antimicrobial actives, pharmacokinetic/pharmacodynamic attributes, and remedial use, it additionally presents an outline of the logical techniques for evaluation of this medication pharmaceutical formulations must abide by the law and guarantee their effectiveness without increasing the risk to the patient's life or the cost of their care. As a result, a comprehensive quality control of the medicine under investigation must be carried out carefully. Norfloxacin is utilized in animals as well as people, and it is given to their food. It is Controlling the use of norfloxacin for treating animal illnesses is crucial because can take of bacterial treatment resistance in people.

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