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Development and validation of sensitive kinetic spectrophotometric method for the determination of moxifloxacin antibiotic in pure and commercial tablets

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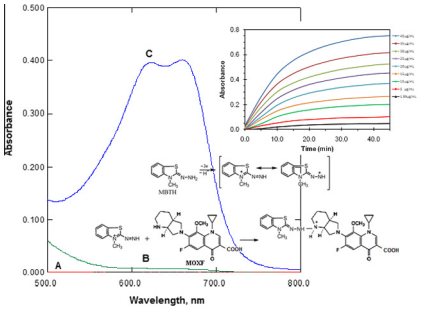
HIGHLIGHTS

- A novel kinetic method for analysis of moxifloxacin based on the reaction with MBTH was developed.
- We found that acidic medium is necessary to success the spectrophotometric method.
- The method validation demonstrated good recoveries and low detection limit.
- The method was successfully applied for analysis of real pharmaceutical samples.

GRAPHICAL ABSTRACT



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ABSTRACT

New, accurate, sensitive and reliable kinetic spectrophotometric method for the assay of moxifloxacin hydrochloride (MOXF) in pure form and pharmaceutical formulations has been developed. The method involves the oxidative coupling reaction of MOXF with 3-methyl-2-benzothiazolinone hydrazone hydrochloride monohydrate (MBTH) in the presence of Ce(IV) in an acidic medium to form colored product with lambda max at 623 and 660 nm. The reaction is followed spectrophotometrically by measuring the increase in absorbance at 623 nm as a function of time. The initial rate and fixed time methods were adopted for constructing the calibration curves. The linearity range was found to be 1.89–40.0 μg mL^{-1} for initial rate and fixed time methods. The limit of detection for initial rate and fixed time methods is 0.644 and 0.043 μg mL^{-1}, respectively. Molar absorptivity for the method was found to be 0.89×10^4 L mol^{-1} cm^{-1}. Statistical treatment of the experimental results indicates that the methods are precise and accurate. The proposed method has been applied successfully for the estimation of moxifloxacin hydrochloride in tablet dosage form with no interference from the excipients. The results are compared with the official method.

Introduction

Moxifloxacin, 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4*aS*,7*aS*)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-3-quinoline carboxylic acid, is a new fourth generation 8-methoxy fluoroquinolone antibacterial agent with a broad spectrum and improved activity against Gram-positive bacteria (including staphylococci, streptococci, enterococci), anaerobes and atypical

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bacteria [1,2]. Several methods have been described for the quantitative determination of moxifloxacin hydrochloride in pharmaceutical dosage forms by flow injection with chemiluminescence detection [3], atomic absorption spectrometry [4], atomic absorption spectroscopy, conductometry and colorimetry [5], spectrophotometry [4,6–10], kinetics spectrophotometry [4,11], voltammetry [12,13], differential pulse polarography [14], spectrofluorimetry [15–17] and capillary electrophoresis [18,19]. Chromatographic methods such as reversed-phase HPLC/fluorescence [20–22], HPLC with ultra violet detection [23–25] and high-performance thin-layer chromatography [26] have been reported for the estimation of moxifloxacin hydrochloride in pharmaceutical products. Voltammetry [12,13], spectrofluorimetry [15], high-performance liquid chromatography with fluorescence [27–29] or UV detection [30–34], liquid chromatography tandem mass spectrometry (LC/MS/MS) [35,36] and capillary electrophoresis [37,38] are also reported for determination of moxifloxacin hydrochloride from human body fluids. Literature survey reveals that moxifloxacin hydrochloride is official in British Pharmacopeia (BP) [39]. The official procedure in pharmaceutical preparations utilize liquid chromatographic method.

3-Methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) is one of the widely used chromogenic reagents for spectrophotometric analysis of phenols [40]. It undergoes an interesting reaction with phenolic, amino, ketonic and aldehydic compounds in the presence of oxidizing agent such as H_2O_2, cerium(IV), iron(III), chromium(VI) yielding a highly colored reaction products [40]. MBTH had been used for spectrophotometric determination of caffeine and theophylline [41], acetaminophen and phenobarbital [42], ritodrine hydrochloride [43], metronidazole and tinidazole [44] and ketoprofen [45].

Kinetic methods have certain advantages in pharmaceutical analysis regarding selectivity and elimination of additive interferences, which affect direct spectrophotometric methods. The literature is still poor in analytical assay methods based on kinetics for the determination of moxifloxacin in dosage forms. Some specific advantages that the kinetic methods possess are as follows: simple and fast methods because some experimental steps such as filtration, extraction, etc., are avoided prior to absorbance measurements, high selectivity since they involve the measurement of the absorbance as a function of reaction time instead of measuring the concrete absorbance value, other active compounds present in the commercial dosage forms may not interfere if they are resisting the chemical reaction conditions established for the proposed kinetic method and colored and/or turbid sample background may possibly not interfere with the determination process [46,47].

In this work, the reaction between MBTH and moxifloxacin was kinetically studied in an attempt to develop a reliable and specific spectrophotometric method for the determination of moxifloxacin in pure form and pharmaceutical preparations. The method is based on oxidation of MBTH with Ce(IV) then coupling with moxifloxacin in presence of H_2SO_4, the colored condensation product is measured at 623 nm kinetically using the Initial rate and fixed time methods.

Experimental

Instrumentation

Double beam UV/Visible spectrophotometer (Shimadzu, model 1800, Japan) with matched 10 mm quartz cells was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software ver.2.43 under the following operating conditions: scan speed medium, scan range 500–800 nm and slit width 0.1 nm. Electronic balance (Kern, Germany) was used for weighing the samples.

Materials

Working reference standard of moxifloxacin hydrochloride (MOXF) was obtained from Matrix Laboratories Limited (India). Its purity was found to be 99.8%. 3-Methyl-2-benzothiazolinone hydrazone hydrochloride monohydrate (MBTH) 97% was from Aldrich Chemical Co., St. Louis (USA). All other chemicals and reagents used were of analytical grade and were of Merck (Germany). All solutions were prepared with double distilled water. The commercial formulations containing moxifloxacin hydrochloride 400 mg per tablet were subjected to the analytical procedures.

Solutions

Standard solution of MOXF was prepared by direct weighing of standard substance with subsequent dissolution in double distilled water. The concentration of the stock standard solution was 0.5 mg mL^{-1}. A series working standard solutions of MOXF (1.89–40.0 μg mL^{-1}) were prepared by diluting the stock standard solution with the double distilled water. Standard solutions were found to be stable for one month at least when stored in the dark at 2–8 °C. 1×10^{-2} M MBTH solution was prepared with double distilled water and 1% $Ce(SO_4)_2$ solution was prepared with sulfuric acid (0.360 M) medium. Freshly prepared solutions were always used.

General procedures

Initial rate method

Aliquots of standard MOXF solution (0.038–0.8 mL, 0.5 mg mL^{-1}) were transferred into a series of 10 mL calibrated volumetric flasks. Then 0.75 mL of MBTH solution was added. After that, 1.0 mL of $Ce(SO_4)_2$ solution was added. The volume was made up to the mark with distilled water. After mixing, the contents of each flask were immediately transferred to the spectrophotometric cell and the increase in absorbance was recorded at 623 nm as a function of time between 0 and 45 min against reagent blank treated similarly. The initial rate of the reaction (v) at different concentrations was obtained from the slope of the tangent to the absorbance–time curve. The calibration curve was constructed by plotting the logarithm of the initial rate ($\log v$) versus the logarithm of the molar concentration of the MOXF ($\log C$). The amount of the drug was obtained either from the calibration graphs or the regression equation.

Fixed time method

Aliquots of standard MOXF solution (0.038–0.8 mL, 0.5 mg mL^{-1}) were transferred into a series of 10 mL calibrated volumetric flasks. Then 0.75 mL of MBTH solution was added. After that, 1.0 mL of $Ce(SO_4)_2$ solution was added. The volume was made up to the mark with distilled water. After mixing, the absorbance was measured after 40 min at 623 nm against reagent blank treated similarly. The calibration curve was constructed by plotting the absorbance against the final concentration of the drug. The amount of the drug in each sample was computed either from calibration curve or regression equation.

Procedure for formulations

Twenty tablets containing MOXF were weighed and finely powdered. An amount of the powder equivalent to 25 mg of the cited drug was dissolved in a 25 mL of methanol and mixed for about 5 min and then filtered through Whatman filter paper number 40. The methanol was evaporated to about the dryness. The