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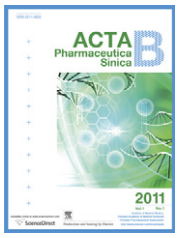

ORIGINAL ARTICLE

Spectrophotometric methods for the determination of gemifloxacin in pharmaceutical formulations

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Abstract This paper describes two simple spectrophotometric methods for the determination of the antibiotic gemifloxacin mesylate (GFX) in pharmaceutical formulations. The first (A) is an indirect method in which oxidation of the drug with a known excess of cerium (IV) sulphate is followed by determination of the residual oxidant by adding excess methyl orange and measuring residual dye at 507 nm. The second (B) is a derivatisation method involving reaction of GFX with 1,2-naphthoquinone-4-sulphonate (NQS) in alkaline medium (pH 11) to form an orange-coloured product exhibiting maximum absorption (λ_{max}) at 411 nm. The methods were linear in the concentration ranges 2–9 and 5–30 μg/mL for methods A and B, respectively, with intra-day precision (as RSD) $<1.5\%$ for both. When applied to the determination of GFX in pharmaceutical tablets, the results were in good agreement with those obtained by capillary electrophoresis. The two methods are useful for routine analysis of GFX in quality control laboratories.

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1. Introduction

Over the last twenty years, fluoroquinolones have emerged as one of the most important classes of antibiotics[1]. Gemifloxacin mesylate (GFX) [(*R*,*S*)-7-[(4*Z*)-3-(aminomethyl)-4-(methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid mesylate] is a fourth generation fluoroquinolone used for the treatment of pneumonia and bronchitis[2]. It is also currently under review by the U.S. Food and Drug Administration for the treatment of upper respiratory tract infections[3].

A number of analytical methods have been reported for the determination of GFX in pharmaceutical dosage forms including capillary electrophoresis[4], reversed phase high performance liquid chromatography (RP-HPLC) with UV and fluorescence detection, liquid chromatography–tandem mass spectrometry (LC–MS/MS), spectrofluorimetry and spectrophotometry[5–10]. The electrophoretic and chromatographic methods require sophisticated and/or expensive instruments and, although spectrofluorimetry is a simple technique, the only reported spectrofluorimetric method[8] involves an extraction step and heating to 80 °C.

Spectrophotometry is probably the most convenient analytical technique for routine analysis because of its inherent simplicity, low cost and wide availability in quality control laboratories. Two spectrophotometric methods have been previously reported for the determination of GFX[9,10]. One was based on the charge transfer complexation reaction of GFX with iodine and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone-7,7,8,8-tetracyanoquinodimethane (TCNQ) and tetracyanoethylene (TCNE)[9], and the other on ion-pair complex formation with safranin O and methylene blue in basic medium or napthol blue 12BR and azocaramine G in acidic medium[10]. The two methods are associated with major drawbacks such as the need for multiple extraction steps in the latter and for GFX free base in the former. In this paper, we report two new spectrophotometric methods for the determination of GFX in pharmaceutical tablets that overcome these drawbacks.

2. Materials and methods

2.1. Instrumentation

Absorbance was measured in 1 cm quartz cuvettes using a double beam UV-1800 ultraviolet–visible spectrophotometer (Shimadzu, Japan) with temperature maintained at 25 °C. pH was determined using a model pH211 pH meter (Hanna, Italy).

2.2. Materials

All chemicals used were of analytical reagent grade. Chemicals (suppliers) were as follows: Cerium (IV) sulphate (Loba-Chemie Indoaustranal Co., India); methyl orange (MO, Fluka Chemika Sigma-Aldrich); sulphuric acid (S. d. Fine Chem, Mumbai, India); sodium 1,2-naphthoquinone-4-sulphonate (NQS) (Aldrich Chemical Co., St. Louis, USA). Doubly distilled water was used to prepare all solutions.

2.3. Reagents

2.3.1. Cerium (IV) sulphate (250 μg/mL)

A 0.01 g/mL cerium (IV) sulphate solution was prepared by dissolving 0.5 g in 50 mL of 1.0 mol/L sulphuric acid. This stock solution was diluted with 1 mol/L sulphuric acid to produce a 250 μg/mL solution.

2.3.2. Methyl orange (50 μg/mL)

A 500 μg/mL solution was prepared by dissolving 50 mg in 100 mL water. After filtration, the solution was diluted 10-fold to obtain 50 μg/mL working solution.

2.3.3. Sulphuric acid (5 mol/L)

This was prepared by adding 274 mL concentrated sulphuric acid to 726 mL water with cooling.

2.3.4. NQS (0.3%, w/v)

This was prepared by adding 150 mg NQS in 50 mL water. The solution was freshly prepared and protected from light during use.

2.3.5. Buffer solution pH 11.0

This was prepared by adding 55 mL 0.2 mol/L NaOH and 35 mL 0.2 mol/L NaH_2PO_4 to 100 mL water and adjusting to pH 11.0. Other buffer solutions were also prepared according to literature methods.

2.4. Preparation of GFX stock and sample solutions

2.4.1. GFX stock solution

A stock solution (1 mg/mL) of GFX was prepared by dissolving 10 mg of pure drug in 10 mL water.

2.4.2. Sample solution

A sample of finely powdered tablet nominally equivalent to 100 mg GFX was dissolved in about 40 mL distilled water in a 100 mL volumetric flask. After shaking for 15 min, the contents were made up to volume with water, filtered (rejecting the first portion of the filtrate) and the filtrate diluted to obtain a suitable concentration for the analysis.

2.5. Assay procedures

2.5.1. Method A

Aliquots of the GFX stock solution were added to 10 mL volumetric flasks to give final concentrations of 2–9 μg/mL. Each flask was added 1 mL of 5 mol/L sulphuric acid and 1 mL of 250 μg/mL cerium (IV) sulphate solution. After mixing, flasks were allowed to stand at room temperature for 10 min with occasional swirling. Finally 1 mL of 50 μg/mL methyl orange solution was added and the solution diluted to the mark with water and mixed. After 5 min, the absorbance of each solution was measured at 507 nm against a reagent blank prepared in the same manner using 1 mL water instead of 1 mL methyl orange solution.

2.5.2. Method B

Aliquots of GFX solution were added to 10 mL volumetric flasks to give final concentrations of 5–30 μg/mL. Buffer solution (pH 11.0, 1 mL) was added followed by 1 mL NQS solution (0.3%, *w*/*v*). The reaction was allowed to proceed at room temperature for 15 min after which the reaction mixture was made up to the mark with water and the absorbance measured at 411 nm against a water blank similarly prepared.