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ORIGINAL ARTICLE

Kinetic spectrophotometric method for the determination of some fourth generation fluoroquinolones in bulk and in pharmaceutical formulations

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Abstract A kinetic spectrophotometric method for accurate and sensitive determination of gemifloxacin (GMFX) and gatifloxacin (GTFX) has been described. The method is based on the reaction of the studied drugs with potassium permanganate in the presence of sodium hydroxide to form a water-soluble green product which shows maximum absorbance at 604 nm. The determination of GMFX and GTFX drugs by rate constant, fixed-concentration, and fixed time methods was feasible with the calibration equations obtained but the fixed time method had been found to be more applicable. The concentration of the selected drugs is calculated using the calibration equation for the fixed time method. The absorbance–concentration plot is linear over the range of 4–36 μg mL^{-1} and 4–40 μg mL^{-1} with correlation coefficient of 0.9998 and 0.9991, for GMFX and GTFX, respectively. The molar absorptivity, Sandell sensitivity, detection and quantification limits were also calculated. The different experimental parameters affecting the development and stability of the color were carefully studied and optimized. The intra- and inter-day RSD values indicated the ruggedness of the method. The proposed method has been successfully applied to pharmaceutical formulations of each drug. Statistical comparison of the results with a well established reported method showed excellent agreement and proved that there is no significant difference in the accuracy and precision.

1. Introduction

Fluoroquinolones, as a group, have shown excellent activity against the most frequently occurring gram-positive and -negative ocular pathogens [1,2,3,4,5]. Earlier generation fluoroquinolones, such as ciprofloxacin and ofloxacin, have been used widely to treat various pathogenic conditions.

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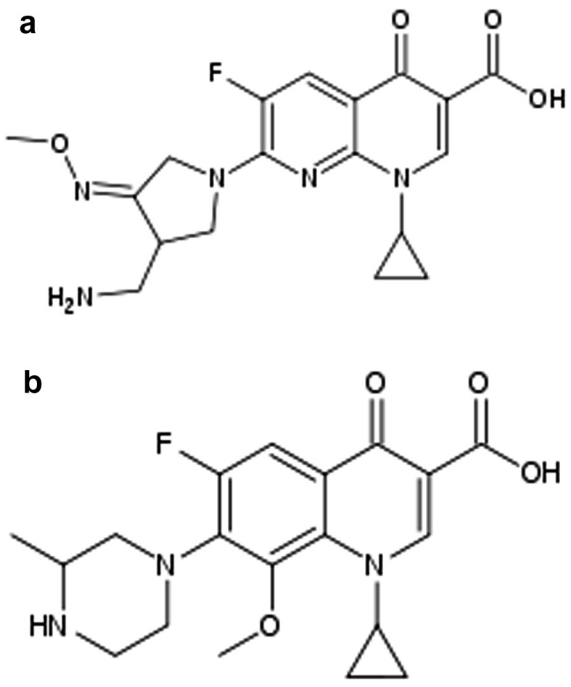

Figure 1 Chemical structure of (a) gemifloxacin and (b) gatifloxacin.

However, the development of a resistant strain against these fluoroquinolones has been reported [6,7]. Gemifloxacin and gatifloxacin are fourth-generation fluoroquinolones, possess an improved antibacterial spectrum, particularly against resistant staphylococcus and streptococcus pathogens, compared with older fluoroquinolones [8,9].

Gemifloxacin (GMFX) (R,S)-7(3-aminomethyl-4-syn-methoxyimino-1-pyrrolidinyl)-1-cyclopropyl-6-fluro-1, 4 dihydro-4-oxo-1, 2 naphthyridine-3-carboxylic acid (Fig. 1a) [10]. Gemifloxacin is an antibacterial compound with enhanced affinity for bacterial topoisomerase IV and is being used for the treatment of respiratory and urinary tract infections. The compound has a broad spectrum of activity against gram-positive and gram-negative bacteria. Gemifloxacin mesylate is not official in any pharmacopoeia.

Literature survey revealed that few analytical methods have been reported for the estimation of GMFX in pharmaceutical preparations or human plasma by visible spectrophotometry [11,12], capillary electrophoresis [13], high performance liquid chromatography–tandem mass spectrometry [14,15], and microchip electrophoresis [16]. These methods were related with some major drawbacks such as having inadequate sensitivity, being time-consuming, tedious, and dedicated to sophisticated and requiring expensive instruments.

Gatifloxacin (GTFX) (1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxyl-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid), (Fig. 1b) [17]. It is widely used in the treatment of urinary tract infection, acute bacterial sinusitis, community acquired pneumonia, and acute bacterial exacerbation of chronic bronchitis [18]. Gatifloxacin is an antibacterial drug having selective antimicrobial activity against streptococcus pneumoniae and penicillin-resistant pneumococci. It is also active against anaerobic pathogen, bacteroides fragilis, and mouth anaerobes [19]. It is available in the tablet form and not official in any pharmacopoeia.

Several techniques have been proposed for the quantification of GTFX in pure, pharmaceutical dosage forms and in biological fluids by titrimetry (Marona et al., 2003), voltammetry [20,21], chromatography [22,23,24,25,26,27], capillary electrophoresis [28], atomic absorption spectrometry [29], chemiluminescence [30], fluorimetry, [31]; and [32] and spectrophotometry [29,33,34,35,36]. The titrimetry is insensitive and time consuming. The voltammetric, chromatographic, electrophoretic, atomic absorption spectrometric and chemiluminometric methods utilized dedicated and/or expensive instruments that are not available in most quality control laboratories' analytical technique. Spectrophotometry is considered the most convenient analytical technique, because of its inherent simplicity, low cost, and wide availability in most quality control laboratories [37]. However, few spectrophotometric methods were reported for the determination of GTFX in its pharmaceutical dosage forms [29,33,34,35,36]. These methods were associated with some major drawbacks such as decreased selectivity due to measurement in ultraviolet region, [33] and/or decreased simplicity of the assay procedure e.g. tedious precipitation, [29] or liquid–liquid extraction steps are based on the formation of ion-pair complex [36].

The kinetic spectrophotometric method offers an easy, less time consuming, sensitive analysis, by using simple and available reagents, which are able to be used for routine determinations of drug substances. Therefore kinetic spectrophotometric analysis is one of the major interests of analytical pharmacy. This work represents the first attempt at assaying gemifloxacin (GMFX) and gatifloxacin (GTFX) in pharmaceutical preparations by the use of the kinetic spectrophotometric method. The method is based on oxidizing the drugs with alkaline potassium permanganate. The reaction is followed up spectrophotometrically and the rate of change of absorbance at 604 nm is measured. The fixed time method is adopted after full investigation and understanding of the kinetics of the reaction. The proposed method is simple, accurate and sensitive.

2. Experimental

2.1. Apparatus

All the absorbance spectral measurements were made using spectroscan 80 D double-beam UV/Vis spectrophotometer (Biotech Engineering Ltd., UK), with a wavelength range of 190–1100 nm, spectral bandwidth 2.0 nm, with 10 mm matched quartz cells. A water bath shaker was used to control the heating temperature for color development.

2.2. Reagents and solutions

All chemicals and reagents used were of analytical grade. High purity double distilled water was used throughout.

i. Standard stock solutions of GMFX and GTFX containing 200 μg mL^{-1} were prepared separately in distilled water. GMFX and GTFX were kindly supplied from the Egyptian International Pharmaceutical Industries Company (EIPICO), Egypt. Samples of adrenergic blocker drugs were generously supplied by their respective manufacturers and were used without further purification. The stock and working standard solutions must be freshly prepared.