Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 192 (2018) 108–116

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Spectrophotometric and spectrofluorimetric methods for determination of certain biologically active phenolic drugs in their bulk powders and different pharmaceutical formulations

Mahmoud A. Omar [a,*], Kalid M. Badr El-Din [a], Hesham Salem [b], Osama H. Abdelmageed [c]

[a] Analytical Chemistry Department, Faculty of Pharmacy, Minia University, Minia, Egypt
[b] Pharmaceutical Chemistry Department, Faculty of Pharmacy, Deraya University, Minia, Egypt
[c] Pharmaceutical Chemistry Department, Faculty of Pharmacy, King Abdulaziz University, Jeddah, Saudi Arabia

ARTICLE INFO

Article history:
Received 27 August 2017
Received in revised form 20 October 2017
Accepted 25 October 2017
Available online xxxx

Keywords:
Spectrophotometry
Spectrofluorimetry
Phenolic drugs
Cerium (IV)
Pharmaceutical analysis

ABSTRACT

Two simple and sensitive spectrophotometric and spectrofluorimetric methods for the determination of terbutaline sulfate, fenoterol hydrobromide, etilefrine hydrochloride, isoxsuprine hydrochloride, ethamsylate, doxycycline hyclate have been developed. Both methods were based on the oxidation of the cited drugs with cerium (IV) in acid medium. The spectrophotometric method was based on measurement of the absorbance difference (ΔA), which represents the excess cerium (IV), at 317 nm for each drug. On the other hand, the spectrofluorimetric method was based on measurement of the fluorescent of the produced cerium (III) at emission wavelength 354 nm ($\lambda_{excitation} = 255$ nm) for the concentrations studied for each drug. For both methods, the variables affecting the reactions were carefully investigated and the conditions were optimized. Linear relationships were found between either ΔA or the fluorescent of the produced cerium (III) values and the concentration of the studied drugs in a general concentration range of 2.0–24.0 μg mL^{-1}, 20.0–24.0 ng mL^{-1} with good correlation coefficients in the following range 0.9990–0.9999, 0.9990–0.9993 for spectrophotometric and spectrofluorimetric methods respectively. The limits of detection and quantitation of spectrophotometric method were found in general concentration range 0.190–0.787 and 0.634–2.624 μg mL^{-1}respectively. For spectrofluorimetric method, the limits of detection and quantitation were found in general concentration range 4.77–9.52 and 15.91–31.74 ng mL^{-1} respectively. The stoichiometry of the reaction was determined, and the reactions pathways were postulated. The analytical performance of the methods, in terms of accuracy and precision, were statistically validated and the results obtained were satisfactory. The methods have been successfully applied to the determination of the cited drugs in their commercial pharmaceutical formulations. Statistical comparison of the results with the reference methods showed excellent agreement and proved that no significant difference in the accuracy and precision.

1. Introduction

Terbutaline sulfate; 5-[2-[(1,1-Dimethylethyl) amino]-1–hydroxyethyl]-1,3–benzenediol (**TER**), fenoterol hydrobromide; 5-[1-Hydroxy–2-[[2-(4–hydroxyphenyl)-1–methylethyl]amino]ethyl]-1,3–benzenediol (**FEN**) and isoxsuprine hydrochloride; 4-hydroxy-α-[1-[(1-methyl-2-phenoxyethyl) amino]ethyl] benzenemethanol (**ISO**) are β_2-selectiveadrenoreceptor [1,2]. Terbutaline sulfate and fenoterol hydrobromide both are used in the treatment of bronchial asthma, while isoxsuprine hydrochloride is used to inhibit uterine contraction in cases of premature labor or fetal distress [1,2]. Etilefrine hydrochloride; α-[(Ethylamino)methyl]-3–hydroxybenzenemethanol (**ETI**) is a selective α_1 receptor agonist; it activates α receptors only at much higher concentrations. The drug causes marked arterial vasoconstriction. The major clinical effects of a number of sympathomimetic drugs are due to activation of α adrenergic receptors in vascular smooth muscle. As a result, peripheral vascular resistance is increased and blood pressure is maintained or elevated [2]. Doxycycline hyclate (**DOX**); is a semisynthetic derivative of tetracyclines. It is bacteriostatic antibiotic with activity against a wide range of aerobic and anaerobic gram-positive and gram-negative bacteria [1,2]. Ethamsylate; *N*-ethylethanamine-2,5-dihydroxybenzenesulfate (**ETH**) is a synthetic compound which has a haemostatic action. It basically normalizes the balance between coagulants and anti-coagulants. This drug raises the formation of platelet plug by increasing the aggregation and adhesiveness of platelet. Also it augments fibrin formation, by increasing the generation of thromboplastin, which is the III coagulation factor and is able to accelerate the clotting of blood [1,2].

* Corresponding author.
E-mail address: momar71g@mu.edu.eg (M.A. Omar).

https://doi.org/10.1016/j.saa.2017.10.065
1386-1425/

Several methods have been reported for the determination of the studied drugs in their pure forms, pharmaceutical preparations or biological fluids. These methods include spectrophotometric [3–19], spectrofluorimetric [19–20], chromatographic [21–30], electrophoresis [31], immunoassay [32–33], flow injection [34–36] and electrochemical methods [37–40].

According to the literatures, it has been reported that **ISO** has been determined fluorimetrically after oxidation with cerium (IV) [18]. Therefore the objective of the current work is to expand the use of cerium (IV) as oxidizing agent in order to develop not only spectrofluorimetric method for the rest of the cited compounds but also another spectrophotometric method for all the cited drugs. Both methods were utilized for the construction of calibration graphs to determine the concentration of the studied drugs either in their pure forms or in their pharmaceutical formulations. This study also involves the investigation of the structure variations of the selected compounds on sensitivities of both methods. In addition, the stoichiometry as well as the reaction mechanism of the reaction of cerium with the cited drugs was also studied.

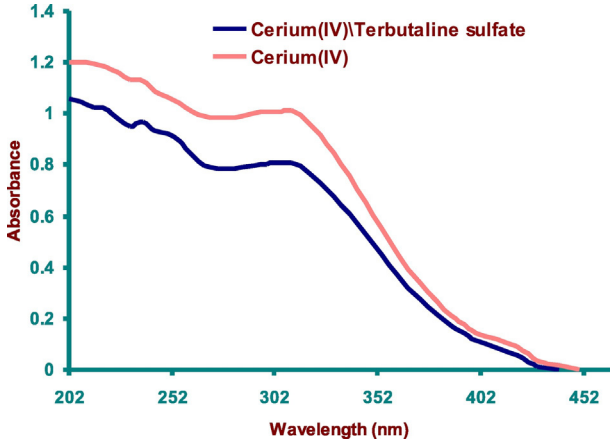

Fig. 1. Absorption spectra of cerium ammonium sulfate in presence and absence of terbutaline sulfate as a representative example (4.0 μg mL^{-1}).

2. Experimental

2.1. Instrumentation and Apparatus

Spectronic™ Genesys™ UV/Visible spectrophotometer (Milton Roy Co, Westhaven, USA) connected with IBM computer loaded with Winspec™ application software and Jenway® 6505, UV/Visible spectrophotometer (Jenway Co, London, UK) with matched 1 cm quartz cell were used for all measurements.

Perkin-Elmer UK model LS 45 Luminescence spectrometer, equipped with a 150 W Xenon arc lamp, grating excitation and emission monochromators were set at 10 mm. A 1 cm quartz cell was used, connected to an IBM computer loaded with the FL Winlab™ application software.

Thermostatically controlled water bath (Salvis AG Emmenbruck, Luzern, Germany), digital analytical balance (AG 245, MetlerTaledo, Switherland) and sonicator (Bender + Hobein, B-220, Germany) were also used.

2.2. Pharmaceuticals and Reagents

Samples of the investigated drugs were generously supplied by their respective manufacturers with overall general estimated purities 99.44–99.82% and were used without further purification. Those are Terbutaline sulfate, fenoterol hydrobromide and etilefrine hydrochloride (**TER**, **FEN**, **ETI**; CID Co., Cairo, Egypt). Isoxsuprine hydrochloride (**ISO**; Pharco Co., Alexandria, Egypt). Ethamsylate (**ETH**; Memphis Co., Cairo, Egypt). Doxycycline hyclate (**DOX**; El-Nile Co., Cairo, Egypt). Ceric ammonium sulfate (Riedel De-Haen, AG, Seelze - Hamnover, Germany). Perchloric acid 70% aqueous solution, sulfuric acid (Sigma Co., St. Louis, USA). Nitric acid, hydrochloric acid and acetic acid (El-Nasr Co, Cairo, Egypt). Two molar solutions of ceric ammonium sulfate were prepared, 2.0×10^{-3} M and 5.0×10^{-4} M, in different solvents. 2.0×10^{-3} molar solution was prepared by dissolving 126.5 g in 100 mL of 2 molar perchloric acid solution. 5.0×10^{-4} molar solution was prepared by dissolving 31.6 g in 100 mL of 2 molar sulfuric acid solution. Both standards were freshly prepared daily and kept in brown glass bottles to avoid photochemical reaction. All solvent used throughout this study such as absolute methanol, absolute ethanol, n-propanol, acetone and acetonitrile (El-Nasr Co, Cairo, Egypt) were of analytical grade. In addition, double distilled water was also used. The following available commercial dosage forms were analyzed; Bricanyl® tablets and syrups (CID Co., Cairo, Egypt) are labeled to contain 2.5 mg of **TER** per tablet or 1.5 mg per 5 mL of syrup. Berotec® tablets and syrups (CID Co., Cairo, Egypt) are labeled to contain 2.5 mg of **FEN** per tablet or per 5 mL syrup. Effortil® tablets and oral drops (CID Co., Cairo, Egypt) are labeled to contain 5 mg of **ETI** per tablet or 5 mg per 10 drops. Duvadilan® tablets (Pharco Co., Alexandria, Egypt) are labeled to contain 20 mg of **ISO** per tablet. Dicynon® tablets and ampoules (Memphis Co., Cairo, Egypt) are labeled to contain 250 mg of **ETH** per tablet or ampoule. Doxymycin® capsules (El-Nile Co., Cairo, Egypt) are labeled to contain 100 mg of **DOX** per capsule.

2.3. Preparation of Standard Solutions

Stock solutions containing 1.0 mg mL^{-1} of the investigated drugs were prepared in double distilled water. The working standard solutions containing 40.0 μg mL^{-1} for spectrophotometric determination or 0.4 μg mL^{-1} for spectrofluorimetric determination, were prepared daily by suitable dilution of stock solutions with double distilled water.

2.4. Preparation of Sample Solution for Pharmaceutical Formulation

2.4.1. Tablets

An accurately weighed amount equivalent to 10.0 mg of each drug from composite of 20 powdered tablets was transferred into a 100 mL volumetric calibrated flask, dissolved in about 20 mL of double distilled water and then diluted to the volume with same solvent. The resultant mixture was sonicated for 10 min, filtered off and the first portion was rejected. Further dilutions with double distilled water were made to yield working solutions of 40.0 μg mL^{-1} and 0.4 μg mL^{-1} for spectrophotometric and spectrofluorimetric methods respectively. Then the general procedure was continued, as described under Section 2.5.

2.4.2. Capsules

The contents of 20 capsules were evacuated, mixed well, and then an accurately weighed amount equivalent to 10.0 mg of each drug was

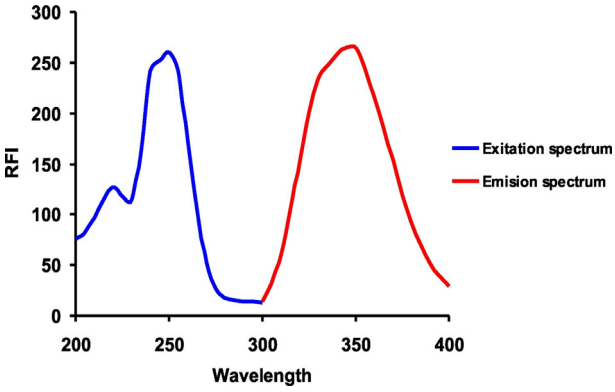

Fig. 2. Excitation and emission spectra of cerium ammonium sulfate (5.0×10^{-4} M) in presence of fenoterol hydrobromide as a representative example (100 ng mL^{-1}).