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Enhanced spectrophotometric determination of Losartan potassium based on its physicochemical interaction with cationic surfactant

Laila Abdel-Fattah [a], Lobna Abdel-Aziz [b,*], Mariam Gaied [b]

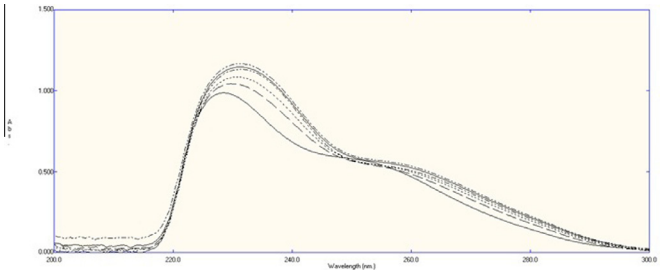
[a] Analytical Chemistry Department, Faculty of Pharmacy, Misr University for Science & Technology, Al-Motamayez District, P.O. Box 77, 6th of October City, Egypt
[b] Pharmaceutical Analytical Chemistry Department, Faculty of Pharmacy, Ain Shams University, Egypt

HIGHLIGHTS

- Calculation of the degree of drug/micelle interaction is reported.
- Understand the interactions with biomembranes and structure–activity relationship of drugs.
- Describing the effect of cationic micelles on the spectroscopic and acid–base properties of LST K.

GRAPHICAL ABSTRACT

The absorbance spectrum of 43.38 μm LST (20 μg ml^{-1}) in absence and in presence of increasing concentrations of CTAB (0.01–0.6 mM).



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ABSTRACT

In this study, a simple and sensitive spectrophotometric method was developed for determination of Losartan potassium (LST K), an angiotensin-II receptor (type AT_1) antagonist, in presence of cationic surfactant cetyltrimethylammonium bromide (CTAB). The physicochemical interaction of LST K with CTAB was investigated. The effect of cationic micelles on the spectroscopic and acid–base properties of LST K was studied at pH 7.4. The binding constant (K_b) and the partition coefficient (K_x) of LST K-CTAB were 1.62×10^5 M^{-1} and 1.38×10^5; respectively. The binding of LST K to CTAB micelles implied a shift in drug acidity constant ($\Delta pK_a = 0.422$).

The developed method is linear over the range 0.5–28 μg mL^{-1}. The accuracy was evaluated and was found to be 99.79 ± 0.509% and the relative standard deviation for intraday and interday precision was 0.821 and 0.963; respectively. The method was successfully applied to determine LST K in pharmaceutical formulations.

Introduction

LST K, 2-Butyl-4-chloro-1 [[2-(1H-tetrazol-5-yl)[1, 1_-biphenyl]-4-yl]methyl]-1Himidazole-5-methanol, is a non-peptide angiotensin-II receptor (type AT1) antagonist [1]. It is an excellent antihypertensive drug, which is used in congestive heart failure [2]. It is the prototype of a new class of antihypertensive agents, the angiotensin receptor antagonists was approved in 1995 by the U.S. Food and Drug Administration. Losartan has the potential to offer the advantage of increased selectivity, specificity and consistent blockade of circulating and tissue renin-angiotensin at AT1 receptor level without some of the shortcomings associated with the use of ACE inhibitors [3,4]. Several methods have been described for the determination of LST K drug substance in tablets including high performance thin layer chromatography [5], radio receptor assay [6], normal and reverse phase HPLC [7–14], capillary electrophoresis (CE) [15] and spectrophotometric methods [16,17].

* Corresponding author.
E-mail address: Lobna.analytical@yahoo.com (L. Abdel-Aziz).

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Micelles are aggregates formed by amphiphilic compounds (hydrophobic chain/hydrophilic head group) above their critical micelle concentration (CMC). The specific structure (hydrophilic surface/hydrophobic core) makes the micelles able to establish chemical interactions with either hydrophilic or lipophilic molecules [18]. Micelles, dynamic aggregates of microscopic order, are known for their significance in biological, synthetic and energy-transfer systems wherein the solubilized species can under appropriate conditions serve either as an electron acceptor or as an electron donor. There are varieties of interactions, which may be operative between solubilized substrates and host micelles [19].

Drug interactions with heterogeneous media (micelles, lipid bilayer vesicles, biomembranes) induce changes in some physicochemical properties of drugs (solubility, spectroscopic and acid–base properties) [20,21]. By monitoring these changes it is possible to quantify the degree of drug/micelle interaction which is normally expressed as drug/micelle binding constant, K_b and micelle/water partition coefficient, K_x. The elucidation of these constants is important for the understanding of interactions with biomembranes, quantitative structure–activity relationship of drugs [22], micellar HPLC or micellar electrokinetic capillary chromatography (MEKC) [23–25].

In this work, the effect of cationic micelles of cetyltrimethylammonium bromide (CTAB) on the spectroscopic and acid–base properties of LST K is described, Fig. 1. The absorption spectrophotometry was used to quantify the LST K/CTAB binding constant and CTAB/water partition coefficient. That was done by applying mathematical models that consider partitioning of the drug between the micellar and aqueous pseudo-phases. Therefore, the aim of the present study is to establish a validated spectrophotometric procedure to determine LST K drug substance. The developed method combines the advantages of being simple, rapid and sensitive. The method was applied successfully for the determination of LST K in pharmaceutical preparations.

Experimental

Instruments

Absorption spectra were recorded on Double beam Schimadzu (Japan) 1601 PC UV–VIS spectrophotometer connected to a computer fitted with UVPC personal spectroscopy software version 3.7, using matched quartz cuvettes in a thermostated cell holder. Measurements took place at 25 °C (±0.2). The pH adjustments were carried out using Jenway pH-meter 3310 pH/mV/°C.

Materials

Reference samples

Losartan potassium was kindly provided by Alkan Pharma, Egypt. Purity was reported to be 100.0 ± 0.2%.

Reagents

All chemicals used were of analytical grade. Cetyltrimethylammonium bromide (CTAB) was purchased from Sigma, Germany. Disodium hydrogen phosphate and citric acid (anhydrous) were obtained from BDH Prolabo UK. Double-distilled water was used. All reagents were handled under fume hood.

Standard solutions

Stock solution of 4.34×10^{-4} M LST K (0.2 mg ml^{-1}) was prepared by dissolving the drug in citrate–phosphate buffer pH 7.4. Stock solution of 0.002 M CTAB (0.73 mg ml^{-1}) was prepared by dissolving an appropriate amount of the surfactant in the same buffer. The final concentrations were prepared by diluting appropriate aliquots from stock solutions using citrate–phosphate buffer pH 7.4.

Pharmaceutical formulation

Cozaar® tablets, 50 mg and 100 mg MSD, were purchased from the market, batch no. G015502.

Effect of CTAB on UV spectrum of Losartan K

UV spectrum of LST K in was scanned at fixed concentration (4.34×10^{-5} M LST K) in phosphate-citrate buffer at pH range 2–11. To determine the effect of CTAB, the UV spectrum of LST K (4.34×10^{-5} M LST K) was scanned at pH 7.4 in presence of increasing concentrations of CTAB (2×10^{-5}–6×10^{-4} M) against same concentration of CTAB at pH 7.4 as blank.

Losartan–CTAB interactions

Drug/micelle binding constant and micelle/water partition coefficient were determined by measuring absorption of fixed concentration of the drug (4.34×10^{-5} M) LST K and increasing concentrations of CTAB (2×10^{-5}–6×10^{-4} M) against same concentration of CTAB as blank at 237 nm.

The effect of CTAB on pK_a of LST K was studied using 4.34×10^{-5} M (20 μg L^{-1}) LST K in 0.01 M CTAB. The spectrum of the acid solution was first obtained at a pH at which the compound to be measured was present wholly as a molecular species. This spectrum was then compared with that of the purely ionized species similarly isolated at another suitable pH. The wavelength, where the greatest change in absorbance was observed, was chosen. At this wavelength and at various intermediate pH values, the absorbance values of the acid solutions were recorded. All absorbance measurements were corrected with the help of blank solutions containing the same concentration of surfactant in the buffer of required pH and were done at 25 ± 0.1 °C.

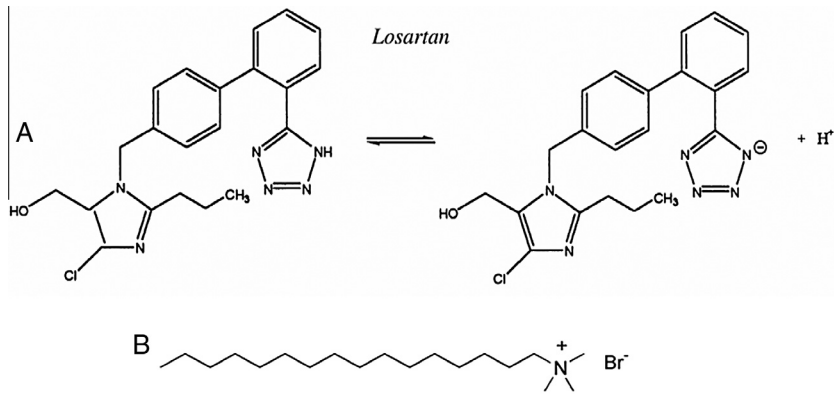

Fig. 1. A: Losartan potassium and B: Cetyltrimethylammonium bromide (CTAB).