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# Extractive determination of ephedrine hydrochloride and bromhexine hydrochloride in pure solutions, pharmaceutical dosage form and urine samples

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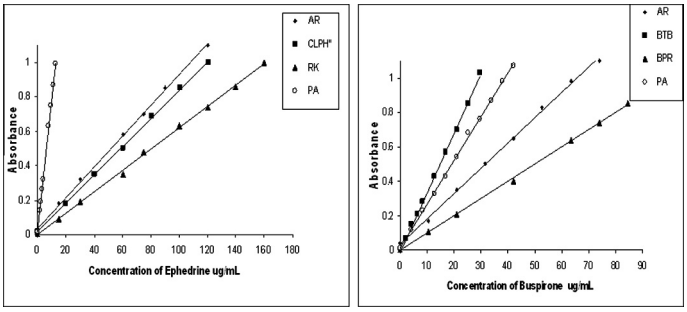
## HIGHLIGHTS

- Ephedrine hydrochloride and bromhexine hydrochloride were determined.
- The methods depend on extraction of the formed ion-associates into solvent.
- Different factors were studied to establish the best conditions for the investigation.
- The methods are applied in pharmaceutical preparations and urine samples.
- Statistical treatments of the proposed methods were applied.

## GRAPHICAL ABSTRACT

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## ABSTRACT

Simple, rapid, sensitive, precise and accurate spectrophotometeric methods for the determination of ephedrine hydrochloride (E-HCl) and bromhexine hydrochloride (Br-HCl) in bulk samples, dosage form and in spiked urine samples were investigated. The methods are based on the formation of a yellow colored ion-associates due to the interaction between the examined drugs with picric acid (PA), chlorophyllin coppered trisodium salt (CLPH), alizarin red (AR) and ammonium reineckate (Rk) reagents. A buffer solution had been used and the extraction was carried out using organic solvent, the ion associates exhibit absorption maxima at 410, 410, 430 and 530 nm of (Br-HCl)with PA, CLPH, AR and Rk respectively; 410, 410, 435 and 530 of (E-HCl) with PA, CLPH, AR and Rk respectively. (E-HCl) and (Br-HCl) could be determined up to 13, 121, 120 and 160; 25, 200, 92 and 206 μg $mL^{-1}$, using PA, CLPH, AR and Rk respectively. The optimum reaction conditions for quantitative analysis were investigated. In addition, the molar absorptivity, Sandell sensitivity were determined for the investigated drug. The correlation coefficient was $\geqslant 0.995$ ($n = 6$) with a relative standard deviation (RSD) $\leqslant 1.15$ for five selected concentrations of the reagents. Therefore the concentration of Br-HCl and E-HCl drugs in their pharmaceutical formulations and spiked urine samples had been determined successfully.



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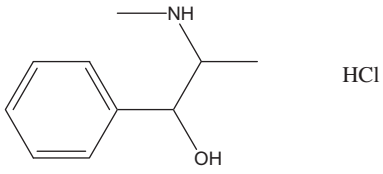
## Introduction

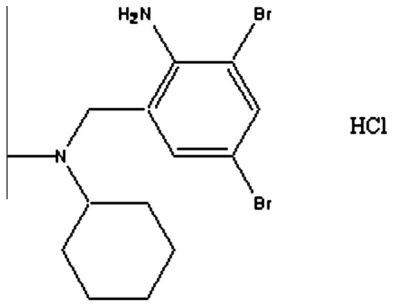
Ephedrine hydrochloride (αR)-α-[(1S)-1-(Methylamino) ethyl] benzene methanol hydrochloride, is a sympathomimetic drug. It is important drug which is used in the treatment of bronchial asthmas, in allergic conditions like utricaria.[1]




Ephedrine hydrochloride

Several analytical methods have been applied to determine Ephedrine hydrochloride (E-HCl) quantitatively in their dosage forms including spectrophotometric method [2–14], liquid chromatography mass spectrometry LC/MS [15,16] High Performance Liquid Chromatogrphy HPLC [17–22], gas chromatography mass spectrometry [15,16], capillary electrophoresis [23–30], infrared spectrometry [31], potentiometry [32] and ion selective electrode [33,29].

Bromhexine,2-Amino3,5-dibromo-N-cyclohexyl-N-methylbenzenemeth-anamine, is mucolytic expectorant drug which is used in the treatment of respiratory disorders in the respiratory organs. It is used as expectorant and bronchosecretolytic drug. It stimulates the transportation of the viscous secretion and reduces the standstillness of the secretion in the respiratory organs [1].




Bromhexine hydrochloride

Several analytical methods have been applied to determine Bromhexine hydrochloride (Br-HCl) quantitatively in its dosage forms including spectrophotometric method [34–39], liquid chromatography mass spectrometry LC/MS [40,41] High Performance Liquid Chromatogrphy HPLC [42–48], capillary electrophoresis [49–51] and ion selective electrode [52].

In the present work simple, rapid, sensitive, precise and accurate spectrophotometeric methods for the determination of Ephedrine hydrochloride (E-HCl) and Bromhexine hydrochloride (Br-HCl) in bulk samples, dosage form and in spiked urine samples were suggested.

The proposed methods are useful for routine quality control laboratory and are suitable to be used in forensic Chemical laboratories and drug control laboratories as identification, confirmation and quantitative determination methods.

## Experimental

### *Apparatus*

The electronic absorption spectral measurements of E-HCl and Br-HCl with selected reagents were recorded on Agilent 8543 UV–Vis spectrophotometer equipped with quartz cell of 1 cm optical path length with a resolution of 0.1 nm. The pH measurements of the prepared solutions were adjusted using Jenway 3510 pH meter. All spectrophotometric measurements were carried out at room temperature (25 ± 2 °C). Moreover, doubly distilled water was obtained Millipore distillation apparatus model Direct Q3, France.

### *Materials*

*Ephedrine hydrochloride (E-HCl) and Kaizen ephedrine tablets (8 mg/tablet) (provided from Kaizen Company USA)*

Bromhexine hydrochloride (Br-HCl) and Mucolyte tablets (8 mg/tablet) (provided from EL.Obour Modern Pharmaceutical Industries CO. Egypt). All chemicals used through the work were of analytical reagents grade and solutions were made with doubly distilled water. They included sodium sulfate anhydrous (BDH); highly purified solvents as chloroform (lab-scan), methanol (BDH), methylene chloride (BDH), carbon tetrachloride, benzene (Prolabo), petroleum ether, diethyl ether, toluene, ethyl acetate, acetone (Merck), ammonium reineckate (Merck), chlorophyllin coppered trisodium salt (Aldrich), picric acid (Arablab) and alizarin red S (Fluka).

*Preparation of stock and standard solutions of $2.0 \times 10^{-3}$ M were prepared with doubly distilled water*

Acetate buffer solutions were made of a mixture of 0.1 M acetic acid (1050 g $L^{-1}$) and 0.1 M sodium acetate trihydrate (13.6 g $L^{-1}$). On the other side Phosphate buffer solutions were made of a mixture of 0.1 M disodium hydrogen phosphate (14.2 g $L^{-1}$), 0.1 M HCl and 0.1 M NaOH.

### *General procedure*

Into 125 mL separating funnel, 5.0 mL ($2.0 \times 10^{-3}$ M) of reagents (RK, CLPH, PA and AR) were added to different volumes of solution containing ($2.0 \times 10^{-3}$ M) of (Br-HCl, E-HCl), and 2.0 mL of buffer solution were added and the volume was made up to 10 mL with distilled water. The formed ion-associates were extracted using the separating funnel with 10 mL chloroform in all cases and chloroform:acetone mixture (4:1) in case of RK, the ion-associates were shaked for two minutes and allowed to separate into two phases. The organic layer was collected and dried with anhydrous sodium sulfate then completed to 10 mL chloroform. The absorbance of the extract was measured at the recommended wavelength ($\lambda_{max}$). The blank solutions were prepared using the same method in absence of the examined drug. Linear curves were obtained by plotting absorbance versus concentration at respective $\lambda_{max}$ for each reagent. The calibration graphs were constructed and the concentrations of unknown samples were determined by using these graphs.

### *Application to various dosage forms*

For the analysis of (Br-HCl, E-HCl) in tablets [Mucolyte tablets (8 mg/tablet), Kaizen ephedrine tablets (8 mg/tablet)] respectively, five tablets were weighed into a small dish, powdered and mixed well, then dissolved in 100 mL bidistilled water, a turbid solution was shaken well and filtered through a filter paper to obtain a clear