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Short communication

Spectrophotometric determination of cetylpyridinium chloride in pharmaceutical products☆

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Abstract

The aim of this work is to study the formation of chelate compound of strontium (Sr(II)) with bromopyrogallol red (BPR) and cetylpyridinium chloride (CPC) and to develop a simple, rapid and sensitive method for spectrophotometric determination of CPC in pharmaceutical products, based on the influence of micellar media on the absorption spectra of the complex of Sr(II) with BPR. The formation of the ternary complex (Sr(II)-BPR-CPC) is accompanied by a marked increase in the absorbance and a bathochromic shift in the maximal absorption of the complex from 555 to 627.5 nm, hence, there is a difference ($\Delta\lambda = \lambda_{Sr\ BPR\ CPC} - \lambda_{Sr\ BPR} = 72.5$ nm) and large hyperchromic shift in λ_{max} ($\Delta A = A_{Sr\ BPR\ CPC} - A_{Sr\ BPR} = 0.258$), and the ternary complex is stable for at least 2 days. The optimum pH range for the reaction is 4.0–5.0 and Beer's law is obeyed over the concentration range 0.01–0.07 mg/ml. The method has been successfully applied to the direct determination of cetylpyridinium chloride in pharmaceutical product where excellent agreement between reported and obtained results were achieved. The relative standard deviation was better than 1% in all cases.

Keywords: Spectrophotometry; Cetylpyridinium chloride; Pharmaceutical products

1. Introduction

Cetylpyridinium is classified as a cationic surfactant and is one of the very important surfactants that is widely used in industrial and pharmaceutical substances, especially in manufacturing of dermal ointments, drugs and cosmetics. In water at low concentration, the surfactant molecules exist mostly as monomers. When the concentration reaches an appropriate value, called critical micelle concentration (cmc), aggregation

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occurs spontaneously to form micelles. A growing application of micelles in analytical chemistry involves the beneficial alteration of metal ion–ligand complex spectral properties via surfactant association [1–4]. The addition of micelles to these chelates can affect both the wavelength of choice and increase the absorbance of the resulting species over that normal binary complex. Surfactants and micellar systems are currently used in spectrophotometric determination of metals to solubilize reactants and products and to improve the sensitivity and selectivity of these methods [5–10]. These effects show the advantage of such surfactant systems in the development of many new spectrophotometric methods for determining micro amounts of metals ions, anions, biological compounds, drugs and pesticides.

Surfactant cetylpyridinium is generally determined in pharmaceutical and cosmetic products by HPLC [11], reversed-phase ion-pair HPLC [12], ion-pair extraction-TLC [13], ion-pair extraction-spectrophotometry [14], simple extraction-spectrophotometry [15]. The accuracy of these analytical methods is determined by the distribution constant of ion pairs between the organic and aqueous phases. For insufficiently high distribution constants, extraction must be repeated several times.

In this work, we present an improved spectrophotometric method which can be used to quantitate cetylpyridinium chloride (CPC) directly, based on the influence of micellar media on the absorption spectra of the complex of strontium ion (Sr(II)) with bromopyrogallol red (BPR). The study is intended to improve the analytical features of surfactant determinative methods in pharmaceutical and cosmetic products as regards rapidity, operational simplicity and selectivity. The method saves time and effort as well as much chemicals. Different variables that affect the reaction of strontium ion with bromopyrogallol red in micellar solutions as well as detailed description of procedures are presented below. The method proposed has been successfully applied to the determination of cetylpyridinium chloride containing a pharmaceutical product Alodont, used in baths of mouth.

2. Experimental

2.1. Apparatus

A Shimadzu UV-2101PC double beam UV–VIS spectrophotometer (Japanese model) with a fixed slid width 0.5 nm and its recorder were used. The curves of the visible spectra of reference and test solutions were recorded in a 1-cm pathlength cells over the wavelength range 360–800 nm. A 3420 electrochemistry analyser (Jenway) with a combined glass-saturated calomel electrode was used for pH measurements.

2.2. Reagents and solutions

Unless otherwise stated, all commercial reagents used were of analytical grade, without further purification, and their solutions were prepared by weighing with distilled water as solvent.

Strontium(II) stock standard solution 1×10^{-2} mol l^{-1} was prepared by dissolving 0.6666 g of $SrCl_2 \cdot 6H_2O$ (Merck) in freshly distilled water and diluting to 250 ml in calibrated flask.

Bromopyrogallol red (BPR) (Labosi) solution 1×10^{-3} mol l^{-1} was prepared by dissolving 0.1116 g in 200 ml of distilled water.

Cetylpyridinium chloride (CPC) (Labosi) solution 1×10^{-2} mol l^{-1} was prepared by dissolving 0.8950 g in 250 ml of distilled water.

Acetate buffers (0.5 mol l^{-1}) of pH range 3.0–7.0 were prepared by mixing appropriate volumes of 0.5 mol l^{-1} acetic acid (Riedel-de Haen) and 0.5 mol l^{-1} sodium hydroxide (Labosi) solutions.

2.3. Pharmaceutical preparation

A commercial pharmaceutical (Alodont, used for baths of mouth and gargarism, 200 ml bottle, Parke-Davis Ind., France) whose declared contents were as follows:

- Cetylpyridinium chloride, 5 mg;
- Veratrol, 5 mg;
- Chlorobutanol, 50 mg;
- Eurogenol, 4 mg;
- Excipient: ethanol 95°, ricinoleic glyceride polyoxyethylene, sodium saccharinate, essence

of peppery menthe, purified water, blue licensed.

2.4. Procedures

2.4.1. Standard procedure

Transferred the sample solution containing not more than 0.75 mg of CPC into a 25 ml volumetric flask, containing 2 ml of 1×10^{-3} mol l^{-1} Sr(II), 2 ml of acetate buffer pH 4, 1 ml of 1×10^{-4} mol l^{-1} BPR, diluted to the mark with distilled water, mixed well and let stand for about 30 min. Measure the absorbance of the coloured solution in a 1 cm cell at 580 nm against a reagent blank. All the experiments were carried out at room temperature. Determined the CPC concentration using calibration graph prepared with standard solutions of CPC.

2.4.2. Procedure for the determination of cetylpyridinium chloride in pharmaceutical products

The proposed procedure has been applied to the determination of CPC in pharmaceutical sample, Alodont solution. To determine CPC directly, a portion of the pharmaceutical solution of Alodont equivalent to 0.625 mg of CPC was transferred into a 25 ml volumetric flask and the procedure was continued as described under the standard procedure.

3. Results and discussion

3.1. Characteristics of the reagent and the complex

The absorption spectra of BPR and its Sr(II) complex in the presence and the absence of surfactant CPC are shown in Fig. 1. In the absence of surfactant, the binary Sr(II)–BPR complex formed at pH 4.0 show maximum absorbance 0.158 at 555 nm (curve B), and the blank (reactif) 0.154 at 550.5 nm (curve A). Addition of CPC to the binary complex at the same pH is accompanied by a marked increase in the absorbance of the complex from 0.158 to 0.416 and its absorption maximum is shifted from 555 to 627.5 nm with a bathochromic shift of 77 nm (curve C).

3.2. Conditions for complex formation

The influence of pH on the absorbance of binary and ternary Sr(II) complexes were studied over the pH range 3.0–7.0 at 555 and 627.5 nm, respectively. The pH was adjusted to the desired value using acetate buffer. The relationship between pH and the absorbance of binary and ternary complexes were linear over the pH ranges 4–5. Therefore, the value, pH 4.0 was selected in the recommended procedure for CPC determination as the ternary complex.

The effect of the acetate buffer on the complex formation was studied and the results demonstrated that it does not affect the absorbance signal of the system when the buffer is in the concentration ranges of 0.2–1.0 mol l^{-1} acetate.

The effect of varying the concentration of BPR ranging between 2×10^{-4} and 10^{-5} mol l^{-1} on the colour development at a constant concentration 1×10^{-3} mol l^{-1} of Sr(II) and 1×10^{-4} mol l^{-1} of CPC was examined by measuring the absorbance at the optimum pH and at 627.5 nm. Full colour development was obtained in the presence of 1×10^{-4} mol l^{-1} of reagent. Thus, 1-ml solution of BPR was selected as optimal for general procedure.

The effect of the surfactant CPC concentration on the formation of Sr(II) ternary complex was studied over the CPC concentration range 10^{-2}–10^{-5} mol l^{-1} in the final solution. The study

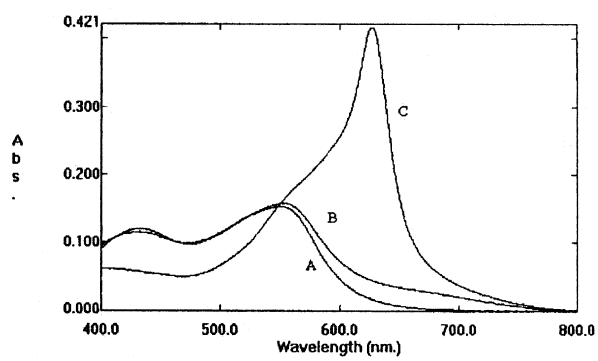

Fig. 1. Absorption spectra of CPC ternary complex and their reagent blank. Curves: (A) BPR; (B) Sr(II)–BPR; (C) Sr(II)–BPR–CPC. Conditions: $[Sr(II)] = 10^{-3}$ mol l^{-1}; $[BPR] = 10^{-4}$ mol l^{-1}; $[CPC] = 10^{-4}$ mol l^{-1}; pH = 4.

revealed that sensitization of the colour reaction occur at surfactant concentrations well below its cmc 8.5×10^{-4} mol l^{-1}. This value has been achieved by conductivity [16] and spectrophotometry [17] measurements.

The order of addition of the reagents was studied and the results demonstrated that the complex formation was affected by it. Consequently, the order Sr(II) + buffer + BPR + CPC was utilised in the proposed procedure.

At room temperature, the maximal colour development of ternary Sr(II)–BPR–CPC complex formation is completed immediately after all reagents were added and the absorbance is stable for least 2 days. All the measurements were made 20 min after the preparation of the solution in all the experiments.

3.3. Analytical characteristics of the method

A calibration graph for the determination of CPC was constructed under optimum experimental conditions described above. Beer's law was obeyed over the concentration ranges 0.01–0.07 mg ml^{-1} of CPC and the molar absorptivity is 4.2×10^3 l mol^{-1} cm^{-1}. The obtained correlation coefficient is, $r = 0.9998$.

3.4. Analytical application

In order to confirm the usefulness of the proposed spectrophotometric method, it has been applied to determination of cetylpyridinium in pharmaceutical product Alodont, used in baths of mouth (manufactured in Parke-Davis Ind., France). The result obtained is 4.95 ± 0.07 mg ($n = 5$) whereas the certified value is 5 mg. The recovery of CPC was 99% and the relative standard deviation was better than 1%.

4. Conclusion

First, the proposed method is simple, rapid and accurate and can, therefore, be applied to the determination of surfactant cetylpyridinium in pharmaceutical and cosmetic preparations without fear of interferences caused by excipients expected to be present. The maximal colour development of ternary Sr(II)–BPR–CPC complex formation is completed immediately after all reagents were added and the absorbance is stable for atleast 2 days. No heating or standing was needed. Second, the proposed method can be used to quantitate cetylpyridinium chloride directly in some pharmaceutical products and does not involve extraction with organic solvents, which significantly simplifies the procedure. The method saves time and effort, as well as much chemicals.

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