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Spectrophotometric determination of some vic-diol containing drugs using ion-exchange resins

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Abstract

Periodic acid and its salts have been widely used for the quantitative oxidation of vic-diol containing compounds including carbohydrates and catecholamine drugs. The advantage of using a polymeric resin (periodate form) over free periodate ions is that the resin quantitatively retains both unconsumed periodate ions and the iodate ions produced in the oxidation and, hence, enables one to undertake further studies on the structural, synthetic or preparative work. The resin (periodate form) was found to be a clean and sensitive chromogenic reagent for the spectrophotometric determination of some catecholamine drugs. The calibration graphs of absorption versus concentration in the range studied (5–50 ppm) were linear. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

Catecholamine drugs are widely used in the treatment of bronchial asthma, hypertension, heart failure associated with organic heart disease, myocardial infarction and cardiac surgery [1]. The determination of catecholamines in biological specimens normally requires the use of trace analysis techniques, mainly chromatographic methods [2]. In contrast, catecholamines that form the active constituents in pharmaceutical preparations are present therein in relatively large amounts and increasing efforts are being directed towards the development of simple, rapid and reliable analytical methods. Recently, spectrophotometric, fluorimetric, coulometric, titrimetric and kinetic methods [3–8] have been used for the determination of catecholamines in pharmaceuticals.

Periodate salts have been used as sensitive chromogenic reagents for the spectrophotometric determination of some catecholamines either in drug substances or in pharmaceutical formulations [1]. The purpose of the present investigation was to develop a simple, rapid and reliable assay for epinephrine (EP) and norepinephrine (NE) bitartarate which is the main kind of catecholamines in most pharmaceutical preparations. The method utilizes the use of periodate salts in conventional system and in the form of ion-exchange resin as oxidizing reagent. The feasibility of the resin (pe-

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riodate form) was investigated in batch and column system.

2. Experimental

2.1. Apparatus

All absorbance measurements were made with a Shimadzu UV–Visible spectrometer, UV.265 FW with 1 cm matched quartz cells. A thermostatically controlled water bath and a Metrohm 654 pH meter were used.

2.2. Reagents

All reagents were of analytical-reagent grade and distilled water was used throughout. Standard Solutions of EP and NE (Aldridge Chemical Company) were prepared by dissolving 10–50 mg of catecholamine in 100 ml of 0.1% aqueous metabisulphite solution, Sodium metabisulphite solution, freshly prepared 0.1% in water. Sodium metaperiodate solution, aqueous 0.2%.

Anion exchange resin, Dowex 1 × 8 or Amerlite IRA-400 BDH Chemicals in the chloride form, was soaked overnight in distilled water and slurried into a large column. It was then converted to the acetate form by passing sodium acetate solution (2 M) over the resin at flow rates up to 5 ml min^{-1} until the effluent gave negative test for chloride ions. The resin was then washed with distilled water to remove any excess sodium acetate. The acetate form of the resin was then treated with an adequate volume of sodium periodate solution (10^{-2} M) in a column at flow rates up to 10 ml min^{-2}. followed by washing with distilled water. The resin was then removed from the column and stored in a dark colored bottle.

2.3. Calibration

A 1 ml portion of each standard solution, EP or NE, was pipetted into 10 ml volumetric flasks.

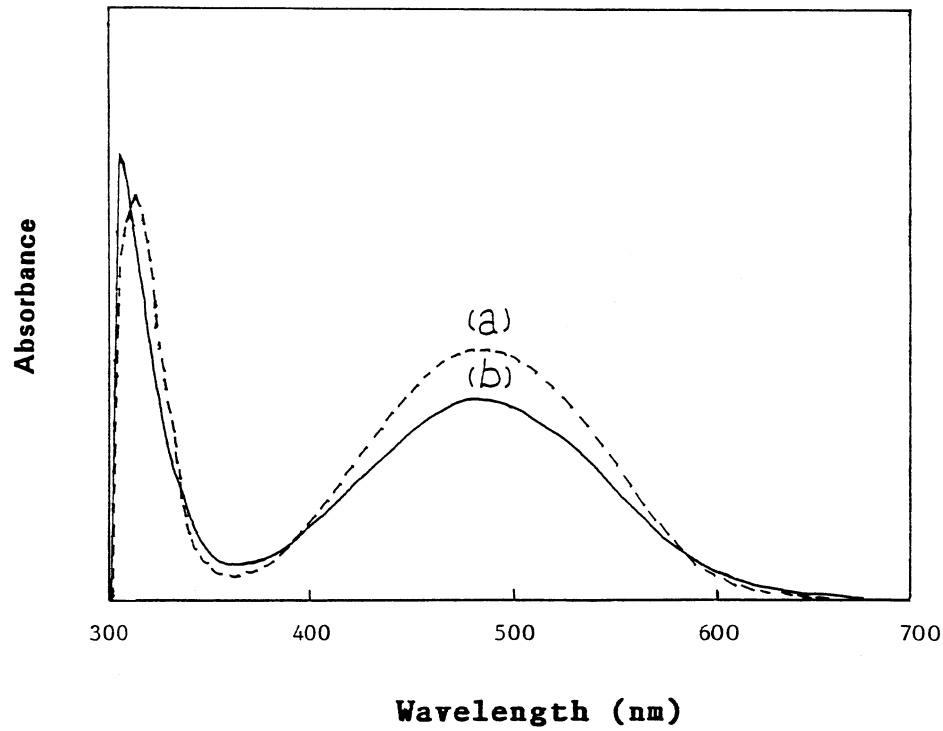

Fig. 1. Absorption spectra of the reaction products of metaperiodate with: (a) EP; and (b) NE (20 ppm).

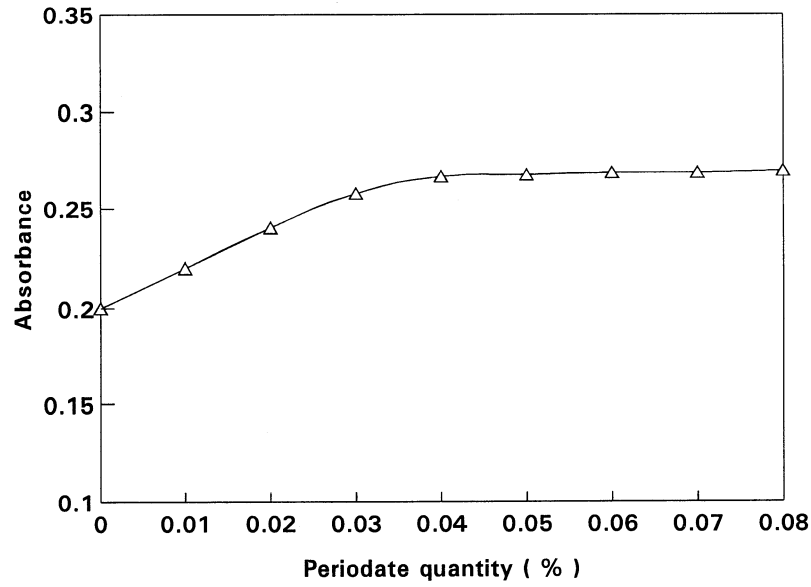

Fig. 2. The influence of periodate quantity on the color intensity of oxidation mixture for EP (10 ppm).

1 ml acetone and 2 ml sodium periodate solution were added to each flask. After 5 min the solutions were made up to volume with ethanol, mixed and the absorbances were measured at 483 nm against a reagent blank. In the case of NE, after adding sodium metaperiodate the solution was heated at 60°C on a water bath.

2.4. Analysis of pharmaceutical preparations

The content of 10 ampules fabled to contain 1 mg of EP or NE were mixed, 2 ml of the mixture was diluted to 10 ml with water and 1 ml of the drug solution was used for the assay as described for standards. The drug content was read from calibration graphs.

2.5. Batch type oxidation of catecholamine drugs with the resin

A 1 ml portion of the wet resin was mixed with 10 ml EP or NE solution (5–50 ppm) in a stoppered conical flask and left for 5 minutes. The resin was separated and the filtrate absorbance was measured at 488.2 or 494 nm for EP or NE, respectively. A calibration graph was then obtained.

2.6. Column type oxidation of catecholamine drugs with the resin.

A 5 ml wet resin packed into a column (1 × 20 cm) was treated with 0.1–1 ml EP or NE stock solution (500 ppm) for 5 min. The column was then eluted with few ml of hot ethanol solution and the oxidation product was collected in a 10 ml volumetric flask and made up to the volume with ethanol solution. The absorbance at 488.2 and 494 nm was measured for EP and NE, respectively and calibration graphs were obtained by plotting absorbance vs. EP or NE concentrations.

3. Results and discussion

3.1. Absorption spectra

The absorption spectra for reaction products of sodium metaperiodate with EP and NE have been shown in Fig. 1. Both catecholamines show two absorption maxima at 309 and 483 nm. Beer's law was obeyed more precisely at 483 nm and this wavelength was chosen for the determination of catecholamines.

3.2. The effect of temperature and time

For EP the red color developed immediately at room temperature. For NE heating was necessary for color development. The maximum color intensity being achieved by heating the solution at 60°C for 2 min. In both cases the color was stable for a few days.

3.3. Effect of metaperiodate quantity

The variation of absorbances versus metaperiodate quantity is shown in Fig. 2. This figure shows that when the concentration of metaperiodate exceeded 0.04% in the final assay solution, the absorbance of the system reached a maximum and remained constant. Therefore a concentration of 0.04% was selected, which corresponds to the addition of 2 ml 0.2% of aqueous metapeiodate solution.

3.4. Effect of pH and solvent type

The pH of the final solution was varied from 2–9 using suitable buffers and the maximum color intensity was attained at pH 7. Among the different solvents which were tested as diluents, ethanol gave the highest absorption intensity. Water severely reduces the absorbance and stability of the chromophore.

3.5. Oxidation of EP and NE with the resin

When an EP or NE compound is allowed to react with the resin in an aqueous ethanolic or ethanol solution, a red–violet product is obtained. The absorption spectra is shown in Fig. 3. Investigations were carried out to establish the most favorable conditions for the reaction of catecholamines with the resin and to achieve maxi-

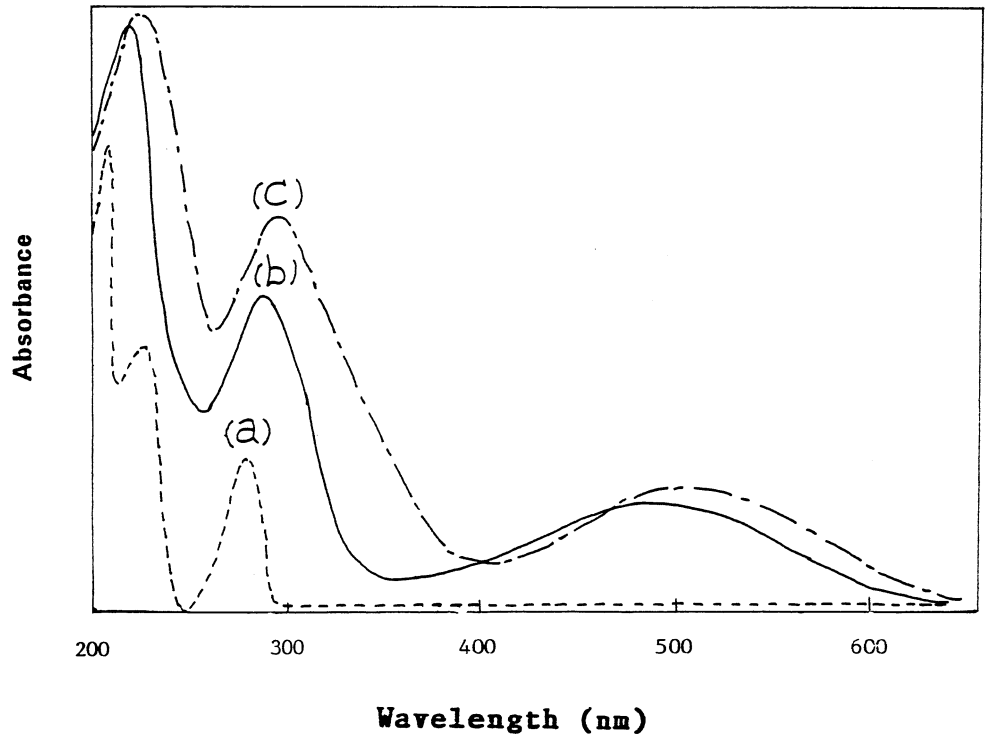

Fig. 3. Absorption spectra of (a) EP or NE before oxidation (b) and (c) NE and EP, respectively, after treatment with the resin.

Table 1
Quantitative parameters of calibration graph, number of standards 6.

Catecholamine	Intercept $\times 10^2$	Slope $\times 10^2$	SD of slope $\times 10^4$	SD of intercept $\times 10^3$	r
EP (batch)	2.60	0.99	0.87	1.13	0.9998
EP (column)	2.43	0.74	1.58	1.19	0.9997
NE (batch)	4.80	0.57	0.59	1.79	0.9993
NE (column)	3.90	1.13	1.17	1.56	0.9998

Table 2
Determination of NE and EP. Each result is the mean of six experiments at $P = 0.05$

Catecholamine	Recovery, % ± SD			
	Proposed method	official method	t-test[a]	F-test[b]
EP	99.15 ± 0.29	99.63 ± 0.17	1.205	1.706
NE	99.45 ± 0.27	99.73 ± 0.12	0.829	2.250

[a] Tabulated value of t for 10° of freedom = 2.23.
[b] Tabulated value of F for 10° of freedom = 5.050.

mum color development in the determination of the drugs. As for free periodate, among solvents tested, ethanol gives the highest absorption intensity. The reaction of the resin with the drugs analyzed was complete at 5 min and longer reaction times did not affect the results.

3.6. Analysis of drugs

A linear correlation was found between absorbance and drug concentration in 5–50 ppm ranges for each catecholamine. The quantitative parameters of calibration graphs are given in Table 1. The resin was successfully applied to the determination of EP and NE ampules in marketed pharmaceutical formulations. As for free periodate, when the resin was applied to catecholamine ampules, acetone had to be added to combine with sodium metabisulfite, the common antioxidant, prior to the reaction with the resin. The optimum quantity of acetone was 1 ml per 10 ml reaction mixture. The results (Table 2) are in good agreement with those obtained by standard official method [9].

3.7. Advantage of the resin over free periodate

In addition to the general advantages of the resin over free periodate, the method seems to be shorter, cleaner and less complex than free periodate system. One packed column with the resin could be repeatedly used for different sample solutions. The oxidation reaction could be carried out in purely non-aqueous media where desirable and the automation of the method seems to be achievable with no great difficulty. The resin quantitatively retains both unconsumed periodate ions and the iodate ions produced in the oxidation reaction. Hence, it enables one to undertake further studies on the structural, synthetic, or preparative work. Furthermore, periodate could be used in great excess with no effect on the absorbance of the final solution.

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