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SPECTROPHOTOMETRIC DETERMINATION OF SULPYRINE USING *o*-HYDROXYHYDROQUINONEPHTHALEIN AND CERIUM(IV) *

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A simple and sensitive spectrophotometric method for the determination of sulpyrine utilizing the decrease in the absorbance of *o*-hydroxyhydroquinonephthalein - cerium(IV) complex was established. The method could be used in the concentration range of 2 - 20 μg/10 ml of sulpyrine; where the effective molar "desorptivity" at 570 nm was 1.2×10^5 dm^3 mol^{-1} cm^{-1}. The other pyrazolone derivatives(antipyrine, aminopyrine and phenylbutazone) could be also determined in the same way. The proposed method was successfully applied to the determination of sulpyrine in commercial injections.

Various methods have been described for the determination of sulpyrine [sodium methyl(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)aminomethanesulfonate hydrate, dipyrone], which is widely used as an antipyretic-analgesic drug. The used methods include gravimetric[1], titrimetric[2)-6)], polarographic[7], and spectrophotometric[8)-17)] methods. There are several spectrophotometric procedures using *p*-dimethylaminobenzaldehyde[8)9)], *p*-dimethylaminocinnamaldehyde[10)11)], 1,2-naphthoquinone-4-sulfonate[12)13)], phosphomolybdic acid[13)14)], and nitrous acid[15]. Lately, Buhl *et al.*[16] reported the sensitive spectrophotometric method for pyrazolone derivatives based on the reduction of cerium(IV) by pyrazolone derivatives and formation of a complex between cerium(III) and arsenazo III. However, detailed investigation and application of the method have not yet been performed.

On the other hand, we found that the absorbance of *o*-hydroxyhydroquinonephthalein(Qn.Ph.)-cerium(IV) complex solution remarkably decreased in the coexistence of a pyrazolone derivative such as sulpyrine, and that the magnitude of the decrease of its absorbance was proportional to the concentration of the pyrazolone derivative.

In this paper, fundamental conditions for the spectrophotometric determination of pyrazolone derivatives(as sulpyrine) using Qn.Ph. and cerium(IV) were discussed. The proposed method was applied to the determination of sulpyrine in commercial injections.

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* APPLICATION OF XANTHENE DERIVATIVES FOR ANALYTICAL CHEMISTRY. Part 43. The previous paper is : Y. Fujita, I. Mori, S. Kitano, Y. Koshiyama, Chem. Pharm. Bull., in press (1984).

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EXPERIMENTAL

Reagents and apparatus

A standard solution(1.0×10^{-3} M, M = mol dm^{-3}) of sulpyrine was prepared by dissolving sulpyrine(Sumitomo Ind., Co. Ltd., Osaka) in water. The working solution was prepared by suitable dilution of this stock solution as required; these solutions were stored in a dark and cool place with an amber glass bottle.
A standard solution(1.0×10^{-1} M) of cerium(IV) was prepared by dissolving 6.8 g of ammonium cerium(IV) sulfate in sufficient volume of 1 N sulfuric acid to make 100 ml, and then standardized by titrimetry[17]. The working solution(5.0×10^{-4} M) of cerium(IV) was made by suitable dilution of this standard solution. A Qn.Ph. solution was prepared as 1.0×10^{-3} M methanol solution. A 2.0×10^{-2} M solution of cetyltrimethylammonium chloride(CTAC) was prepared by dissolving a proper quantity of CTAC in water. A 0.1 M sodium carbonate - 0.1 M sodium hydrogencarbonate buffer solution was used for the pH adjustment. All other reagents and materials were of analytical grade. Double-distilled water was used throughout this work.

The spectrophotometric measurements were carried out on a Shimadzu Model UV-240 recording spectrophotometer with 1.0 cm silica cells. A Hitachi-Horiba Model F-7 AD glass electrode pH meter was used for pH measurements.

Standard procedure

A 2 - 20 μg amount of sulpyrine was placed in a 10 ml calibrated flask; to this were added 0.75 ml of 5.0×10^{-4} M cerium(IV) solution, 1.0 ml of 2.0×10^{-2} M CTAC solution and 0.75 ml of 1.0×10^{-3} M Qn.Ph. solution. The pH of the final solution was adjusted to about pH 7.5 with 3.0 ml of the carbonate buffer solution. The mixture was diluted to 10 ml with water and kept at 20 - 25°C for 30 min. The difference of absorbance(Δ A) between the Qn.Ph.-cerium(IV)-sulpyrine solution (Solution A) and the Qn.Ph.-cerium(IV) solution(Solution B) at 570 nm against water was measured. The concentration of sulpyrine was determined by using a calibration graph.

RESULTS AND DISCUSSION

Absorption spectra

The absorption spectra of Qn.Ph.-cerium(IV) solutions containing various concentrations of sulpyrine at pH 7.5 are shown in Fig. 1. The absorbance at around 570 nm of the solutions decreased in proportion to the concentration of sulpyrine.

Effect of pH

The effect of pH on the reaction was examined using various buffer solutions, such as 0.1 M sodium carbonate - 0.1 M sodium hydrogencarbonate, 0.1 M tris(hydroxymethyl)aminomethane - 0.1 M hydrochloric acid, 0.1 M triethanolamine hydrochloride - 0.1 M sodium hydroxide, 0.1 M potassium dihydrogenphosphate - 0.1 M sodium hydroxide, 0.1 M ammonia - 0.1 M ammonium chloride, and 0.05 M borax - 0.1 M hydrochloric acid solutions. The maximum and constant Δ A was obtained with 3.0 ml of 0.1 M sodium carbonate - 0.1 M sodium hydrogencarbonate solution.

Effects of cerium(IV) and Qn.Ph. concentrations

The effect of metal ions was examined and the results are given in Table 1.

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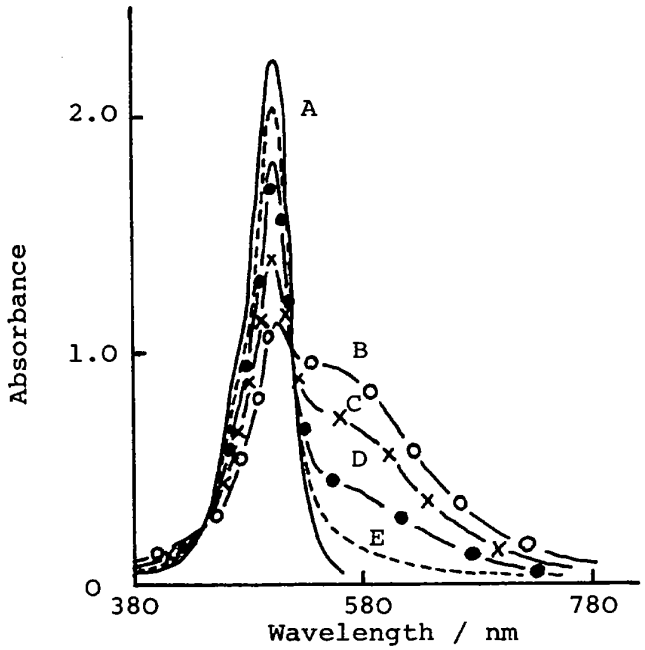

Fig. 1 Absorption spetra of Qn.Ph.-Ce(IV) solutions containing various concentrations of sulpyrine
Ce(IV), Qn.Ph. : 3.75 X 10^{-5} M;
CTAC : 2.0 X 10^{-3} M; pH : 7.5;
Reference : water;
Curve A : Qn.Ph. solution;
curve B ~ E : Qn.Ph.-Ce(IV) solutions(sulpyrine concentration : curve B, 0; curve C, 3.0 X 10^{-6} M; curve D, 6.0 X 10^{-6} M; curve E, 9.0 X 10^{-6} M).

Table 1 Effect of metal ions

Metal ion	λ max	Δ A at λ max
Ce(IV)	570	0.465
Ce(III)	570	0.390
Cr(VI)	555	0.040
Cr(III)	-	0
U(VI)	575	0.025
Cu(II)	555	0.030
Os(VIII)	-	0
V(V)	-	0
Co(II)	-	0
Zn(II)	-	0

Sulpyrine : 2.5 X 10^{-6} M;
metal ions : 3.75 X 10^{-5} M;
Qn.Ph. : 7.5 X 10^{-5} M;
CTAC : 2.0 X 10^{-3} M;
pH : 7.5;
Reference : water.

Cerium(IV) was the most effective in terms of sensitivity among various metal ions. The color reaction between Qn.Ph. and cerium(III) was slower than that between Qn.Ph. and cerium(IV) under the standard conditions. Cerium(IV) did not oxidize or decompose Qn.Ph.

The effect of amount of Qn.Ph. was examined by varying the molar ratio of Qn.Ph. to cerium(IV). The molar ratio of cerium(IV) to Qn.Ph. in the complex was found to be 1 : 2 by the molar-ratio method, and the molar ratio of cerium(IV) 1 : Qn.Ph. 2 was the most effective for the determination of sulpyrine.

Accordingly, all further works were carried out with 3.75 X 10^{-5} M cerium(IV) and 7.5 X 10^{-5} M Qn.Ph. solutions.

Effect of surfactant

The effect of surfactants on Δ A was examined. Among various cationic, anionic and nonionic surfactants tested, CTAC, a cationic surfactant, was the most effective. Since absorbance and stability of the complex were remarkably

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influenced by the CTAC concentration, relationship between standing time and ΔA in the various concentrations of CTAC was studied. As is shown in Fig. 2, the use of 2.0×10^{-3} M CTAC in the final concentration was the most suitable in terms of sensitivity and stability at 20 - 25°C.

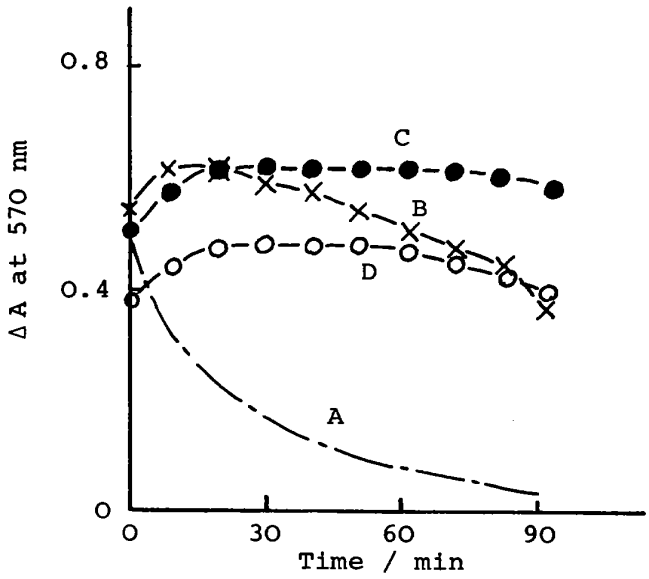

Fig. 2 Relationship between standing time and ΔA in various concentrations of CTAC at 20 - 25°C
Sulpyrine : 5.0×10^{-6} M; Ce(IV) : 3.75×10^{-5} M; Qn.Ph. : 7.5×10^{-5} M; pH : 7.5; Reference : water; (CTAC concentration : curve A, 5.0×10^{-4} M; curve B, 1.0×10^{-3} M; curve C, 2.0×10^{-3} M; curve D, 3.0×10^{-3} M).

Calibration curve

Under the optimum conditions described above, a calibration curve was constructed for sulpyrine at 570 nm. A good linear relationship was obtained over the range of 2 - 20 μg of sulpyrine in the final volume of 10 ml. The effective molar "desorptivity" for sulpyrine was estimated to be 1.2×10^5 dm^3 mol^{-1} cm^{-1}. When the determination of solution containing 8.8 μg of sulpyrine was repeated 5 times by the standard procedure, the coefficient of variation was 1.0%.

The other pyrazolone derivatives (antipyrine, aminopyrine and phenylbutazone) were also determined in the same conditions. The results obtained are given in Table 2.

Table 2 Results of the application of the present method to some pyrazolone derivatives

Pyrazolone derivative	Applicable range (μg / 10 ml)	$\lvert\varepsilon\rvert$* (dm^3 mol^{-1} cm^{-1})
Sulpyrine	2 - 20	1.2×10^5
Antipyrine	2 - 10	1.0×10^5
Aminopyrine	2 - 15	1.4×10^5
Phenylbutazone **	0.6 - 6	5.0×10^5

Ce(IV) : 3.75×10^{-5} M; Qn.Ph. : 7.5×10^{-5} M; CTAC : 2.0×10^{-3} M; pH : 7.5; Reference : water;
* $\lvert\varepsilon\rvert$: effective molar "desorptivity".
** pyrazolidinedione derivative.

Interference

Under the standard conditions, the influences of various ions and substances

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on the determination of 8.8 μg of sulpyrine were studied. The presence of various heavy metal ions interfered with the determination. Anions and substances having reducing ability such as iodide, nitrite, sulfite, thiosulfate, oxalate, and L-ascorbic acid interfered in small amounts with respect to sulpyrine. When small amounts of these interfering anions and substances might be present in the sample solution, a standard addition method could be used. Acetaminophen, caffeine, thiamine and salicylic acid did not interfere in 1- to 5-fold excess, and chlorpheniramine, D-glucose and tartrate in 10- to 200-fold molar excess of sulpyrine. Some of the results are summarized in Table 3.

Table 3 Effect of foreign substances

Substance	Added (μg/10 ml)	Mole ratio (Substance/ Sulpyrine)	Sulpyrine, found (μg/10 ml)	Recovery, %
-	-	-	8.8	100.0
Copper(II) nitrate	2.3	1/2	6.6	75.0
Bismuth nitrate	4.9	1/2	6.3	71.6
Magnesium chloride	47.6	20	8.8	100.0
Potassium iodide	0.8	1/5	9.3	105.7
Sodium nitrite	0.4	1/5	9.4	106.8
Sodium sulfite	3.2	1	9.7	110.2
Sodium thiosulfate	0.8	1/5	10.9	123.9
Sodium oxalate	3.4	1	10.6	120.5
Tartaric acid	75.0	20	8.8	100.0
L-Ascorbic acid	2.2	1/2	10.6	120.5
Acetaminophen	7.6	2	10.4	118.2
Caffeine	10.6	2	8.8	100.0
Thiamine hydrochloride	42.2	5	8.8	100.0
Salicylic acid	17.3	5	8.8	100.0
Chlorpheniramine Maleate	97.7	10	8.8	100.0
D-Glucose	900.8	200	8.8	100.0

Sulpyrine taken : 8.8 μg/10 ml; Ce(IV) : 3.75×10^{-5} M; Qn.Ph. : 7.5×10^{-5} M; CTAC : 2.0×10^{-3} M; pH : 7.5; Reference : water.

Application to the determination of sulpyrine in commercial injection

The present method was applied to the determination of sulpyrine in commercial injection. The results are shown in Table 4.

Table 4 Determination of sulpyrine in commercial injections

	Amount manifested, %	Amount found**, %		Sulpyrine added (μg/10 ml)	Recovery by the present method, ** %
		present method	JP X method		
Injection*	25.0	25.2	25.1		
				4.4	102.8

* An aliquot volume of injection was diluted with water and the sulpyrine content in diluted solution was determined. ** Mean of 5 determinations.

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The recovery of sulpyrine added to the injections was satisfactory(about 103 %). Furthermore, the sulpyrine content of the injection determined was in good agreement with that obtained by the JP X method[11].

The method was about 3 times more sensitive than the method using *p*-dimethylaminocinnamaldehyde[10)11)], and was as sensitive as the cerium(III)-arsenazo III method[16]. In addition, this method was superior to those methods[10)16)] in terms of reproducibility. This proposed method may be applicable to the determination of various pyrazolone derivatives in pharmaceutical preparations, as well as for assay of sulpyrine in injeotion.

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Keyword phrases

spectrophotometric determination of pyrazolones with *o*-hydroxyhydroquinonephthalein - cerium(IV); in the presence of cetyltrimethylammonium chloride; sulpyrine in injection.

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