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Spectrophotometric Determination of Papaverine Hydrochloride by Using a Membrane Filter Preconcentration Technique with 2,4,5,7-Tetrachlorofluorescein and Palladium(II)[1]

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A simple, rapid and highly sensitive spectrophotometric determination of papaverine hydrochloride (Papav. HCl) by using a preconcentration technique based on membrane filtration of the 2,4,5,7-tetrachlorofluorescein (T.Cl.fl.)–palladium(II)–Papav. HCl ternary complex was developed. A linear calibration graph was obtained in the concentration range of 0—20 μg of Papav. HCl in 5 ml of dimethyl sulfoxide (DMSO). The apparent molar absorptivity for Papav. HCl was 8.0×10^4 dm^3 mol^{-1} cm^{-1} at 540 nm, and was more than twice that measured in an aqueous medium.

Keywords——spectrophotometry; 2,4,5,7-tetrachlorofluorescein; palladium(II); papaverine; ternary complex; preconcentration technique; membrane filter

Recently, application of an organic solvent-soluble membrane filter preconcentration technique to analytical chemistry and spectrophotometric determination of trace phosphorus in water has been reported by Taguchi *et al.*[2a,b] However, the application of this procedure for the determination of organic bases has not been investigated in detail.

Though many spectrophotometric determinations of organic bases have been reported,[3a-d] most of the methods require extraction into an organic solvent, and have disadvantages such as complexity of procedure and lack of reproducibility.

On the other hand, we have already reported[4a-h] simple spectrophotometric determinations of organic bases in the presence of nonionic surfactants by using xanthene dye-metal ion-organic base ternary complexes without solvent extraction. Moreover, we have previously reported[5] that Papav.HCl could also be determined by using the ternary complex of 2,4,5,7-tetrachlorofluorescein (T.Cl.fl.), palladium (II) and Papav.HCl.

In this paper, we present a simple, new and sensitive spectrophotometric method for the determination of micro quantities of Papav.HCl by using a preconcentration technique based on the use of a membrane filter to collect the T.Cl.fl.–palladium(II)–Papav.HCl ternary complex.

Experimental

Reagents and Materials——Solutions of 1.0×10^{-3} M Papav.HCl, T.Cl.fl., palladium(II) and buffer were prepared as reported previously,[5] and a 0.05% polyvinyl alcohol (PVA, $n=2000$, Kishida Chemical Co., Ltd.) solution was prepared by dissolving PVA in water. All other materials and reagents were of analytical grade and were used without further purification.

Apparatus——A Shimadzu model UV-260 recording spectrophotometer with 1.0-cm silica cells was used to record absorption spectra and for absorbance measurements. A Hitachi-Horiba F-7AD glass electrode pH meter was used for pH measurements. A Toyo TM 3 membrane filter (nitrocellulose membrane, 25 mm in diameter, 0.3 μm pore size) and Toyo KGS-25 filter holder were used.

Standard Procedure for the Determination of Papav.HCl——Papav.HCl (0—20 μg) was placed in a 10 ml volumetric flask, then 1.0 ml of a 1.0×10^{-3} M palladium (II) solution, 0.4 ml of a 0.05% PVA solution and 0.5 ml of a 1.0×10^{-3} M T.Cl.fl. solution were added. The pH of the final solution was adjusted to about pH 4.0 with 2.5 ml of a 2.0×10^{-1} M sodium acetate–acetic acid buffer solution. The mixture was diluted to 10 ml with water (A-aqueous solution), kept at 40 °C for 10 min together with reference solution (T.Cl.fl.–palladium (II), B-aqueous solution), and cooled to room temperature. A-aqueous solution and B-aqueous solution were each filtered through a membrane filter, and the filter was washed with about 20 ml of water. These membrane filters were dissolved in 5 ml of dimethyl sulfoxide (DMSO), and then the absorbance of A-DMSO solution was measured at 540 nm against B-DMSO solution as a reference. The concentration of Papav.HCl was determined by using a calibration graph.

Results and Discussion

Figure 1 shows the visible-region absorption spectra in A-DMSO solution and B-DMSO solution.

The absorption maximum of A-DMSO solution was at 540 nm, and this wavelength was chosen for the determination of Papav.HCl. Constant and maximum absorbance of A-DMSO solution was obtained in the pH range of 3.8—4.2 in the aqueous region before the preconcentration technique.

The effect of surfactant on the preconcentration through a membrane filter was investigated in the absence or presence of various surfactants. Although the reproducibility and sensitivity in the absence of surfactant were unsatisfactory, the coexistence of a small amount of PVA, a nonionic surfactant, was found to be effective for dispersion. Maximum and constant absorbance of A-DMSO solution was observed upon the addition of 0.2—0.5 ml of 0.05% PVA solution in a final volume of 10 ml. The effects of various filters in this reaction system were examined. Nitrocellulose with 0.3 μm pore size was effective among the various types and pore sizes tested: nitrocellulose and acetylcellulose; pore sizes 0.20, 0.30, 0.45, 0.65 and 0.80 μm. The effect of water miscible organic solvents was also tested: DMSO, *N*,*N*-dimethylformamide, acetone, acetonitrile, methyl isobutylketone, methyl ethyl ketone, cyclohexanone, diethylacetamide, ethyl acetate, methyl cellosolve and tetrahydrofuran. It was found that a combination of DMSO and a nitrocellulose membrane filter with 0.3 μm pore size was the best in terms of sensitivity and reproducibility.

Beer's law held in the concentration range of up to 20 μg of Papav.HCl per 5 ml. The apparent molar absorptivity and the coefficient of variation were 8.0×10^4 dm^3 mol^{-1} cm^{-1} and 1.4% ($n=5$) for 11.3 μg of Papav.HCl, respectively.

The interference of various metal ions and substances with the determination of

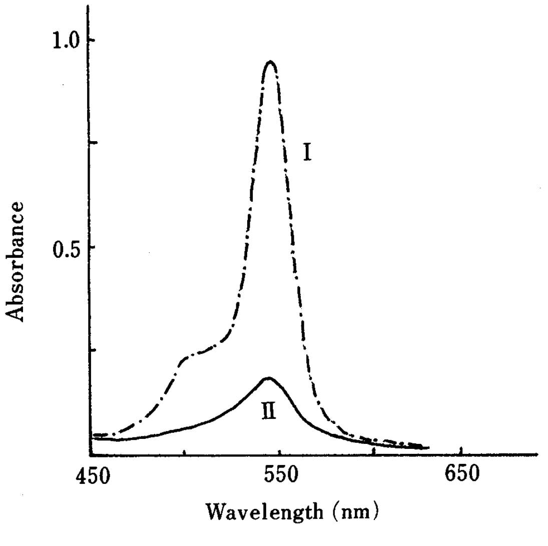

Fig. 1. Absorption Spectra of T.Cl.fl.–Palladium(II) and T.Cl.fl.–Palladium(II)–Papav.HCl Solutions

Curve I: A-DMSO solution (T.Cl.fl.–palladium (II)–Papav.HCl soln.).

Curve II: B-DMSO solution (T.Cl.fl.–palladium (II) soln.).

T.Cl.fl., 5.0×10^{-5} M; palladium(II), 1.0×10^{-4} M; Papav.HCl, 5.0×10^{-6} M; PVA, 0.4 ml of 0.05% PVA soln.; membrane filter, Toyo TM 3; reference, DMSO blank.

TABLE I. Effects of Foreign Ions on the Determination of Papav.HCl

Foreign ions	Added as	Added, mol ratio foreign/Papav.HCl	Absorbance at 540 nm
—	—	—	0.460
Cu(II)	Nitrate	50	0.466
Fe(III)	Sulfate	6	0.466
Al(III)	Nitrate	100	0.444
Th(IV)	Nitrate	3	0.465
Tartrate	Sodium salt	50	0.460
Glucose		5000	0.460
Taurine		500	0.460
Salicylic acid		500	0.460
Urea		500	0.458
Ethyl aminobenzoate		50	0.460

Papav.HCl taken, 11.3 μg; T.Cl.fl., 5.0×10^{-5} M; palladium(II), 1.0×10^{-4} M; PVA, 0.4 ml of 0.05% PVA soln./10 ml, reference, B-DMSO soln.

TABLE II. Analytical Results for Papav.HCl Added to Pharmaceutical Preparations

Sample[a]	Papav.HCl				Papav.HCl added μg/10 ml	Recovery[b] %
	Calcd	Found				
	%	Proposed %	Previous[4a] %	J.P.IX[6] %		
10% Papav.HCl powder	10.0	9.9	9.8	9.7	11.3	100.0
Papav.HCl, Scopolia and ethyl aminobenzoate powder	1.5	1.6	1.6	1.6	11.3	94.1

Palladium(II), 1.0×10^{-4} M; T.Cl.fl., 5.0×10^{-5} M; PVA, 0.4 ml of 0.05% PVA solution; reference, B-DMSO solution. *a*) Papav.HCl pharmaceutical preparations; A portion of powder was exactly weighed and dissolved in water by shaking. The solution was filtered or centrifuged, and then the Papav.HCl content was determined according to the standard procedure. *b*) Mean of 5 determinations.

11.3 μg/5 ml of Papav.HCl was checked. Copper (II), zinc (II), calcium (II) and magnesium (II) did not interfere in 100-fold excess, and iron (III), thorium (IV), *etc.* did not interfere in 2—5 fold excess over Papav.HCl. However, the coexistence of large amounts of aluminum (III) and iron (III) caused negative errors, though these interferences could be overcome by the addition of masking agents such as sodium fluoride, potassium cyanide and nitrilotriacetic acid (NTA). On the other hand, high concentrations of sodium chloride, sodium fluoride, potassium sulfate, glucose, urea, salicylic acid and ethyl aminobenzoate did not interfere.

The proposed method was applied to the determination of Papav.HCl in pharmaceutical preparations, and the experimental results were in good agreement with the values measured in aqueous medium obtained by another method.[6] Recovery of Papav.HCl added to the pharmaceutical preparations by the proposed method was satisfactory, being about 97.1% ((100+94.1)/2%). The results are given in Table II.

In conclusion, this proposed method based on a membrane filter preconcentration technique and spectrophotometric determination of Papav.HCl is more than twice as sensitive as the method employing aqueous medium.[5] The method is simple, rapid and sensitive compared with the solvent extraction methods.[3a-d]

Though further investigation is necessary, this preconcentration technique based on collection of an insoluble ternary complex such as xanthene dye-organic base or xanthene dye-metal ion-organic base on a membrane filter may be applicable as a new analytical procedure for a simple and sensitive assay of various organic bases.

References and Notes

1) The paper is Part IL of series entitled "Application of Xanthene Derivatives for Analytical Chemistry," Part XLVIII: I. Mori, Y. Fujita, H. Kawabe and K. Fujita, *Bunseki Kagaku*, **34**, 648 (1985).
2) *a*) S. Taguchi, E. Itooka and K. Goto, *Bunseki Kagaku*, **33**, 453 (1984); *b*) S. Taguchi, E. Itooka, K. Matsuyama, I. Kasahara and K. Goto, *Talanta*, **32**, 391 (1985).
3) *a*) M. Tachizawa, S. Nakayama and A. Ookawara, *Bunseki Kagaku*, **19**, 761 (1970); *b*) Sh. T. Talipov, R. Kh. Dzhiyanbaeva and I. P. Shesterova, *Nauch. Tr. Tashk. Gos. Univ.*, **1973**, 44; *idem, Anal. Abstr.*, **29**, 1E6 (1975); *c*) V. Ariesan, F. Daniu, Asuciu, G. Luputiu and C. Ban, *Arch. Pharm.*, **299**, 220 (1966); *d*) C. Hsi-Kung, *Acta Pharm. Scin.*, **13**, 280 (1966); *idem, Anal. Abstr.*, **14**, 4967 (1967).
4) *a*) I. Mori, Y. Fujita and K. Sakaguchi, *Bunseki Kagaku*, **30**, 261 (1981); *b*) *Idem, ibid.*, **31**, 477 (1982); *c*) I. Mori, Y. Fujita and S. Kitano, *ibid.*, **31**, 475 (1982); *d*) Y. Fujita, I. Mori and S. Kitano, *ibid.*, **33**, E195 (1984); *e*) Y. Fujita, I. Mori, S. Kitano and Y. Kamada, *ibid.*, **32**, E375 (1983); *f*) I. Mori, Y. Fujita, K. Sakaguchi and S. Kitano, *ibid.*, **31**, E305 (1982); *g*) I. Mori, Y. Fujita and S. Kitano, *ibid.*, **32**, E1 (1983); *h*) *Idem, Chem. Pharm. Bull.*, **31**, 1389 (1983).
5) I. Mori, Y. Fujita, H. Kawabe and K. Fujita, *Bunseki Kagaku*, **34**, 648 (1985).
6) Society of Japanese Pharmacopoeia, "The Pharmacopoeia of Japan," 9th ed., Yakuji Nippo, Ltd., Tokyo, 1978, p. 482.