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Reagents regeneration flow injection analysis (RRFIA) for spectrophotometric determination of methamphetamine coupled with solvent extraction

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Abstract

Methamphetamine (MPA), being a stimulant drug, reacts with tetrabromophenolphthalein ethyl ester (TBPEH) to form a red-violet ion associate, TBPEHMPA, in 1,2-dichloroethane (DCE) at pH 9. The maximum absorption wavelength was at 570 nm. After measuring, yellow TBPEH with DCE could be regenerated by mixing with the buffer solution at pH 3. The regenerated TBPEH/DCE could be reused as an ion association reagent and extracting solvent. In addition, the reagent regeneration could be performed by the on-line flow injection system and the cyclic flow injection analysis system was demonstrated for the determination of MPA without consumption of ion association reagent and organic solvent. The calibration curve was linear in the range of $0.5–3.5 \times 10^{-5}$ M with good repeatability. The sample throughput was 20 h^{-1}.

Keywords: Tetrabromophenolphthalein ethyl ester; Methamphetamine; Reagents reuse; On-line regeneration system; Cyclic flow injection method

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1. Introduction

Most of methods for the spectrophotometric determination of quaternary ammonium salts and amines hydrochloride in pharmaceuticals are based on reactions with chromogenic reagents [1,2] and ion association reaction with acidic dyestuffs [3,4]. On the other hand, one (T. Sakai) of the authors has proposed the sensitive and selective spectrophotometric determination of stimulant drugs using tetrabromophenolphthalein ethyl ester (TBPE) and/or thermochromism of ion associates [5–7]. However, these batchwise methods were tedious, time- and reagents-consuming. To develop the procedures using TBPE and other diprotic acid dyes, flow injection (FI) systems coupled with solvent extraction were assembled for the rapid and sensitive determination of quaternary ammonium salts and aromatic amines [8–10]. In the previous flow systems, TBPEH dissolved in 1,2-dichloroethane was delivered as the ion association reagent with extracting solvent. Flow injection analysis has some advantages on rapidity, simplicity, reproducibility and repeatability, however, all reagents are consumed continuously even without measurements.

Mottola et al. [11–14], Ishii et al. [15] and Zenki et al. [16,17] have reported cyclic flow injection systems for metals and thiamine determinations in the aqueous media and these are unique as the environmentally benign and no-reagent consumption technology. Sequential injection analysis (SIA) proposed as a new technology is effective for less reagent consumption [18]. Nakano et al. have reported a thin organic film extraction with SIA [19]. However, there is no report with cyclic flow injection analysis coupled with solvent extraction.

In this paper, we demonstrate on-line reagents regeneration cyclic FIA with ion association reaction and solvent extraction for the determination of methamphetamine (MPA).

2. Experimental

2.1. Apparatus

A JASCO V-560 spectrophotometer (Tokyo, Japan) with 10 mm path length cell was used for the absorbance measurements and recording spectra. A Horiba F-22 pH meter

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with a combined glass electrode was used to measure pH. In FIA, a Soma Optics S-3250 double beam spectrophotometer with a 10 mm flow cell (8 μl), a CHINO EB22005 recorder and a double-plunger micro-pump (Sanuki Kogyo, DMX-2000) were used. The hydrophobic PTFE membrane (Advantec, 0.8 μm pore size) was used for phase separation. Flow lines were of PTFE tubing (0.5 mm i.d.) except for the back-pressure tubing (35 cm × 0.25 mm i.d.). Two needle valves were used to control the recovery of organic phase.

2.2. Reagents

2.2.1. Buffer solutions

Buffer solutions (pH 7.0–10.5) were made from equal volumes of 0.1 M potassium dihydrogenphosphate and 0.1 M tetraborate decahydrate, and were adjusted to the desired pH with 1 M sodium hydroxide solution.

2.2.2. TBPEH/DCE solution

TBPEH/DCE solution was prepared according to the previous paper [7]. The TBPEH/DCE solution stocked in a brown bottle was stable for at least 2 months.

2.2.3. Methamphetamine (MPA) standard solution

Stock solution of 1.0×10^{-4} M was prepared by dissolving 0.0147 g methamphetamine hydrochloride (Dainippon Pharmaceutical, Osaka, Japan) in 100 ml of distilled water.

3. Results and discussion

3.1. Ion association reaction with TBPEH and reagents regeneration reaction

The ion association reaction with TBPEH and MPA is shown as follows:

$$\underset{\text{yellow}}{\mathrm{TBPEH_0}} \overset{\text{pH 9}}{\rightleftharpoons} \underset{\text{blue}}{\mathrm{TBPE^-_{aq}}} + \mathrm{H^+_{aq}} \quad (1)$$

$$\mathrm{TBPE^-_{aq}} + \mathrm{HMPA^+_{aq}} \rightleftharpoons \underset{\text{red-violet (570 nm)}}{\mathrm{TBPEHMPA_0}} \quad (2)$$

When $\mathrm{TBPEH_0}$ is shaken in the alkaline media (pH 9), blue TBPE anion transfers into the aqueous phase. TBPE anion reacts with a protonated MPA ($\mathrm{HMPA^+}$) to form the ion associate bonded by hydrogen bridge [20]. The associate showed λ_{max} at 570 nm as shown in Fig. 1. The absorbance was measured for the determination of MPA. In many solvent extraction systems, the ion association reagent and an analyte in the aqueous phase are extracted into the organic solvent and each ion forming the associate can be passed over into the aqueous phase under other conditions. Accordingly, it is difficult to assemble the reagent regeneration cyclic FIA because both of the extracting reagent and the analyte exist in the aqueous phase. Fortunately, $\mathrm{TBPEH_0}$ could be regenerated in the organic phase again when $\mathrm{TBPEHMPA_0}$ was shaken with aqueous solution below pH 3, and $\mathrm{HMPA^+}$ passed over into the aqueous phase. The reaction is as follows:

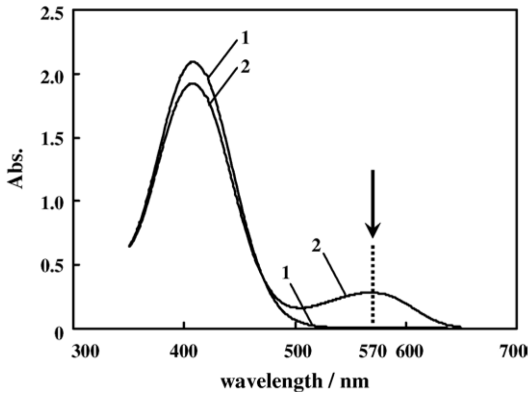

Fig. 1. Absorption spectra of (1) TBPEH and (2) TBPEHMPA associate. pH 9.0, TBPEH/DCE, 8.0×10^{-5} M; MPA: 3.0×10^{-5} M.

$$\mathrm{TBPEHMPA_0} + \mathrm{H^+_{aq}} \overset{\text{pH<3}}{\rightleftharpoons} \mathrm{TBPEH_0} + \mathrm{HMPA^+_{aq}} \quad (3)$$

The regenerated TBPEH/DCE can be reused as the ion association reagent and extracting solvent for the determination of MPA. Thus the reagent regeneration cyclic FIA system is considerably novel in the solvent extraction system.

3.2. Conditions for FIA system for MPA determination

The effect of pH on the formation of the charge transfer complex was investigated in the range of 7.0–10.5. At pH 9.0, the peak height was highest and was not significantly changed over this pH. The TBPEH concentration was varied from (4.0 to 10.0) $\times 10^{-5}$ M. Over 8.0×10^{-5} M, the highest peak was obtained. However, in the higher concentration, the baseline was slightly noisy. In this study, 8.0×10^{-5} M was used. The extraction tubing was suitable over 3 m. In this system, a 5 m-tubing was used. The buffer solution and TBPEH/DCE solution were delivered at 0.8 ml $\mathrm{min^{-1}}$, respectively. The calibration graph was linear for $0.5 - 3.5 \times 10^{-5}$ M MPA at 570 nm: $y = (1.85 \times 10^5)\,x$ where y and x were the absorbance and the concentration of MPA in M (mol $\mathrm{l^{-1}}$), respectively. The sample volume was 100 μl. The relative standard deviation (R.S.D., $n = 5$) for 1.5×10^{-5} M MPA was 1.66%.

3.3. On-line RRFIA system

The on-line regeneration system was investigated (Fig. 2). Twenty-five millilitres of fresh TBPEH/DCE was added in the glass reservoir as an initial reagent and 10 ml of aqueous phase was kept at lower pH with sulfuric acid. The blue aqueous phase and red-violet organic phase produced after measurements were collected in the reservoir and the solutions were mixed by the magnetic stirrer slowly and continuously and the resulting TBPEH/DCE was delivered again by the pump. Table 1 shows the recovery tests by on-line

Table 1
Recovery tests by on-line RRFIA using MPA standard solution

Reagent solution	MPA concentration								Recovery (%)			
	Added ($\times 10^{-5}$ M)				Found ($\times 10^{-5}$ M)							
1	0.50	1.00	2.00	3.00	–	–	–	–	100	100	100	100
2	0.50	1.00	2.00	3.00	0.53	0.99	1.95	2.87	106	99.7	97.6	95.6

1, Fresh TBPEH; 2, on-line regenerated TBPEH.

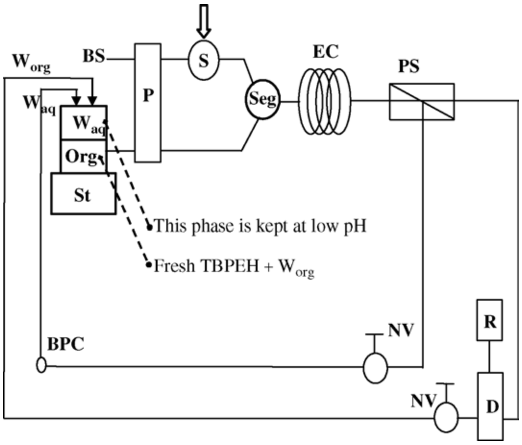

Fig. 2. On-line RRFIA system for methamphetamine analysis. BS, 0.1 M phosphate buffer (pH 9.0); Org, 8.0×10^{-5} M TBPEH/DCE; St, stirrer; P, pump (0.8 ml min^{-1} for each line); S, sample injection valve (100 μl); Seg, segmentor; EC, extracting coil (5 m × 0.5 mm i.d.); PS: phase separator; BPC, back-pressure coil (0.35 m × 0.25 mm i.d.); D, detector (570 nm); R, recorder; NV, needle valves; W_{aq}, waste of aqueous phase; W_{org}, waste of organic phase.

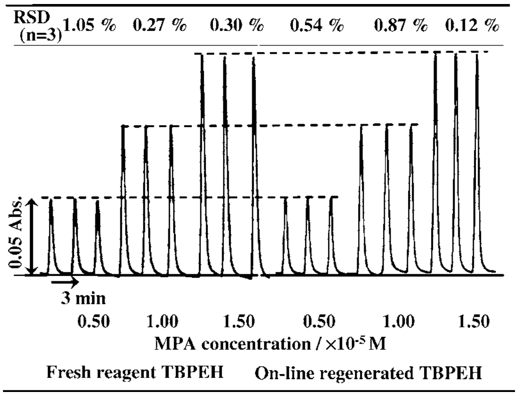

Fig. 3. Flow signals obtained by on-line RRFIA system.

RRFIA. Three standard solutions were injected into the carrier stream. TBPEH was regenerated using waste solutions collected after 30 measurements. The recoveries obtained using the regenerated TBPEH were 95.6–106%. In addition, the reproducibility was investigated for on-line regenerated reagent. The results are shown in Fig. 3. The reproducibility was excellent. The proposed on-line RRFIA system was feasible for 6 h continuous runs.

The synthesized urine sample was prepared for the applicability of the on-line RRFIA. A solution of MPA (1×10^{-3} M) was prepared in human urine. After 50- and 100-fold dilutions, the samples were injected. The recoveries were 100 ± 1 and 101 ± 2%. Consequently, the on-line RRFIA is suitable for the MPA screening test in urine samples.

In conclusion, the cyclic FIA using the on-line reagents regeneration system was demonstrated. The novel technique without any reagents consumption is effective for the continuous measurements of quaternary ammonium salts and amines hydrochloride in pharmaceuticals and urine samples.

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