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Sensitive determination of phenothiazines in pharmaceutical preparation and biological fluid by flow injection chemiluminescence method using luminol–$KMnO_4$ system

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Abstract

A flow injection chemiluminescence method was described for the determination of four phenothiazine drugs, namely, chlorpromazine hydrochloride, perphenazine hydrochloride, fluphenazine hydrochloride and thioridazine hydrochloride. Strong Chemiluminescence (CL) signal was produced when above-mentioned drug was injected into the mixed stream of luminol with $KMnO_4$. The linear ranges of the method were 0.0020–1.0 μg/mL chlorpromazine hydrochloride, 0.0040–3.0 μg/mL perphenazine hydrochloride, 0.0020–5.0 μg/mL fluphenazine hydrochloride and 0.0050–1.0 μg/mL thioridazine hydrochloride. The detection limits were 0.4 ng/mL chlorpromazine hydrochloride, 0.7 ng/mL perphenazine hydrochloride, 2 ng/mL fluphenazine hydrochloride and 0.7 ng/mL thioridazine hydrochloride. The proposed method was applied to the determination of chlorpromazine hydrochloride in injections and in mental patient's urine samples and the satisfactory results were achieved. The possible CL reaction mechanism was also discussed briefly.

Keywords: Chemiluminescence; Flow injection; Phenothiazines

1. Introduction

Phenothiazine derivatives are a large group of tricyclic antidepressants which are commonly used for the treatment of psychiatric patients suffering depressions [1]. The monitoring of these compounds is important for quality assurance in pharmaceutical industry and for obtaining optimum therapeutic concentrations in body fluids to minimize the risk of toxicity. Therefore, it is important to develop simple and sensitive methods for the determination of these drugs. A wide variety of analytical techniques are available for the determination of phenothiazine drugs in pharmaceutical preparations and biological samples, such as spectrophotometry [2–4], electrochemical methods [5–7], chromatography [8] and capillary electrophoresis [9].

Chemiluminescence (CL) method has been frequently used for the analysis of pharmaceutical compounds in recent years [10–14] because of its promising advantages of low detection limit, wide linear dynamic range and relatively simple and inexpensive instrumentation. Several CL systems have been reported for the determination of phenothiazine drugs [15–23]. They were based on the acidic $KMnO_4$ reaction [15–17], Ce(IV) reaction sensitized by rhodamine B [18], luminol–H_2O_2–Cr^{3+} reaction [19], luminol–Fe^{2+} reaction [20], luminol reaction in micelles [21] and electrogenerated $Ru(bpy)_3^{2+}$ reaction [22,23]. The analytical parameters of the previous reported CL methods for the determination of phenothiazine drugs were summarized in Table 1.

We here proposed a simple and sensitive flow injection CL method for the determination of four phenothiazine drugs, including chlorpromazine hydrochloride, perphenazine hydrochloride, fluphenazine hydrochloride and thioridazine hydrochloride. It was based on the fact that strong CL signal could be produced when above-mentioned drug was injected into the reaction mixture of luminol with $KMnO_4$. The method

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Table 1
Analytical parameters of the previous CL methods for the determination of phenothiazine drugs (unit: μg/mL)

Species	CL reactions	Linear ranges	Detection limits	References
Chlorpromazine	Acidic $KMnO_4$ reaction		7.1	[15]
Thioridazine	Acidic $KMnO_4$ reaction	1.0–30.0	0.5	[17]
Fluphenazine	Ce(IV) reaction sensitized by rhodamine B	0.5–90	0.01	[18]
Chlorpromazine	Luminol–H_2O_2–Cr^{3+} reaction	3.6–355	13	[19]
Chlorpromazine	Luminol–Fe^{2+} reaction	0.7–7.1		[20]
Chlorpromazine	Luminol reaction in reverse micelles	0.05–10	0.006	[21]
Chlorpromazine	Electrogenerated $Ru(bpy)_3^{2+}$ reaction	0.3–6.4	0.24	[22]
Chlorpromazine	Electrogenerated $Ru(bpy)_3^{2+}$ reaction	0.004–1.1	0.001	[23]

was successfully applied to the determination of chlorpromazine hydrochloride in injections and in mental patient's urine samples.

2. Experimental

2.1. Apparatus

The schematic diagram of the CL flow system used was shown in Fig. 1. PTFE tubing (0.8 mm i.d.) was used as the connect material in the flow system. A peristaltic pump was used to deliver all solutions; each at a flow rate of 2.1 mL/min. Sample injection (50 μL) was automated operated by means of a six-way valve. The CL signal produced in the flow cell was measured using an IFFS-A multifunction CL analyzer (Xi'an Remax Electronic Science-Tech Ltd. Co., China). The CL data acquisition and treatment were performed by using an MCDR-A multifunction data processing system (Xi'an Remax). CL spectra and fluorescence spectra were taken on CRT-970 fluorescence spectrophotometer (Shanghai Third Analytical Instrumental Plant).

2.2. Reagents and solutions

All chemicals were of analytical reagent grade except luminol, which was synthesized by the Institute of Analytical Science of Shaanxi Normal University (Xi'an, China). Doubly distilled water was used throughout the experiments. Chlorpromazine hydrochloride, perphenazine hydrochloride, fluphenazine hydrochloride and thioridazine hydrochloride were obtained from the Chinese Pharmaceutical and Biological Test Institute (Beijing, China). Potassium permanganate was purchased from Xi'an Chemical Plant (Xi'an, China). Stock solutions (500.0 μg/mL) of each drug were prepared by dissolving 50.0 mg of the drug in 100 mL of water. They were stored in a refrigerator and protected from light. Working solutions were prepared by appropriately diluting the stock solution when used. Stock solution (0.01 mol/L) of luminol was prepared by dissolving 1.771 g luminol in 50 mL of 1 mol/L sodium hydroxide and diluting to 1 L with water. Stock solution (0.02 mol/L) of potassium permanganate was prepared by dissolving 3.16 g of $KMnO_4$ in 1 L of boiled water, filtering through glass wool and protecting from light.

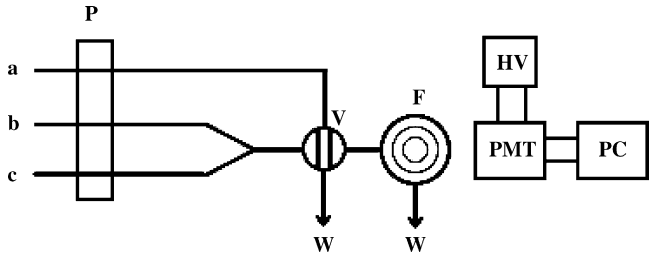

Fig. 1. Schematic diagram of CL flow system. (a) Phenothiazines solution; (b) luminol solution; (c) potassium permanganate solution; P, peristaltic pump; V, injection valve; F, flow cell; PMT, photomultiplier tube; HV, high voltage; PC, personal computer; W, waste.

2.3. Procedure

As shown in Fig. 1, flow lines were connected with phenothiazine solution, luminol solution and $KMnO_4$ solution, respectively. Luminol solution was firstly mixed with $KMnO_4$ solution via a Y-piece to give a stable baseline. Then 50 μL solution of phenothiazine was injected into the merged stream of luminol with $KMnO_4$ by means of a six-way valve to produce CL. The concentration of phenothiazine was quantified by the CL intensity.

3. Results and discussion

3.1. Kinetic characteristic of the CL reaction

The CL kinetic characteristic of the reaction was investigated using the static system of the IFFS-A multifunction CL analyzer. Fig. 2 shows the typical CL intensity-time profile. A strong CL was recorded when 1.0 mL solution of 20 μmol/L $KMnO_4$ was injected into 1.0 mL solution of 10 μmol/L luminol (peak a). After CL signal declined about 45s, subsequently injecting 1.0 mL 0.5 μg/mL chlorpromazine hydrochloride resulted in a new CL reaction (peak b). About 80s later, the CL reaction terminated and the CL signal declined to baseline.

3.2. Optimization of experimental conditions

The experimental conditions were optimized using 0.05 μg/mL chlorpromazine hydrochloride solution as a model. The optimized parameters were of reaction medium, luminol concentration and $KMnO_4$ concentration.

It was observed that higher CL signal and better repeatability could be obtained when sodium hydroxide was added into sample solution than into luminol solution. The effect of sodium