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Determination of captopril with potassium permanganate chemiluminescence system*

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ABSTRACT

Chemiluminescence (CL) emission can be generated by mixing potassium permanganate with captopril under acidic conditions. Formaldehyde can significantly enhance the CL signal. This phenomenon has been utilized to design a new flow-injection chemiluminescence method for the determination of captopril with the permanganate-formaldehyde-captopril CL system. Under the optimum experimental conditions, the proposed method has a quantitation linear range of captopril between 0.02 and 2.0μg mL^{-1}, with a detection limit of 0.01μg mL^{-1} and a correlation coefficient of 0.9998. The method was applied to the determination of captopril in pharmaceutical preparations and the results were satisfactory.

Keywords：flow injection, chemiluminescence, potassium permanganate, formaldehyde

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INTRODUCTION

Captopril, or 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline, is an angiotensin-converting enzyme inhibitor widely used for the treatment of hypertension, congestive heart failure, and coronary artery disease. An accurate, convenient and economic method of the determination of captopril is thus of great practical significance. Currently available methods include titration [1], chromatography [2, 3], spectrophotometry [4-6], atomic absorption spectroscopy [7, 8], polarography [9], and chemiluminescence methods [10-13]. Among the methods mentioned above, titration is subject to experimental error due to indeterminate color at the endpoint; chromatography requires costly equipment; spectrophotometry is significantly influenced by the color of coordination complex and thus has limited sensitivity. Recently, methods based on chemiluminescence have been widely applied because it has high sensitivity and fast speed, requires only simple equipment, and is able to be easily automated. Previously developed methods based on chemiluminescence are limited, because the preparation of Ce (IV) was complex, ClO^- used in the methods was generated by electrolysis of potassium chloride and the conditions for the determination were difficult to control. Potassium permanganate can oxidize captopril under acidic conditions and generate vague CL signal. And the CL signal can be further enhanced by formaldehyde. Therefore the concentration of captopril can be determined directly by the intensity of the CL signal. This phenomenon allowed us to develop a new method for determination of captopril with the potassium permanganate-formaldehyde-captopril chemiluminescence system, utilizing the flow injection technique. Up to now, this method for determination of captopril concentration has not been reported. The method requires only common reagents (potassium permanganate and formaldehyde) and no complicated solution preparation, thus can be easily adopted. It is also fast and produces stable CL signal, thus can achieve high sensitivity. The method was applied successfully to the determination of captopril in pharmaceutical preparations and the results were satisfactory.

MATERIALS AND METHODS

1.1 Apparatus and Reagents

1.1.1 Apparatus

IFIS-D intelligent flow injection injector, MPI-A capillary electrophoresis electrochemiluminescence detector – multi-function chemiluminescence detector (Xi'an Remex Analysis Instrument Co.Ltd), and MPI-A capillary electrophoresis electrochemiluminescence detector – electrochemical detector (Xi'an Remex Analysis Instrument Co. Ltd).

1.1.2 Reagents

All the reagents were of analytical-reagent grade unless specified otherwise; doubly distilled water was used for the preparation of solutions. Captopril standard was supplied by Cangzhou Food and Drug Inspection Institute. Captopril tablets were purchased locally.

1.1.2.1 Preparation of standard solutions

An accurate weight portion of the homogenized powder containing 20mg of captopril standard was transferred to a 100mL volumetric brown flask and diluted to volume with doubly distilled water to obtain the 200μg mL^{-1} standard solution. The powder was completely disintegrated by a mechanical shaker and the solution was filtered. Working solutions were prepared by appropriate dilution of the concentrated standard solutions with water and the final concentration was in the working range.

1.1.2.2 Preparation of sample solutions

The average tablet weight was calculated from the weight of 10 tablets. An accurate weight portion of the homogenized powder containing 25mg of captopril was transferred to a 100ml volumetric brown flask and diluted to volume with doubly distilled water. The powder was completely disintegrated by a mechanical shaker and the solution was filtered. Working solutions were prepared by appropriate dilution of the concentrated sample solutions with water and the final sample concentration was in the working range.

1.2 Experimental methods

The schematic diagram of the flow-injection analyzer for the determination of captopril with potassium permanganate-formaldehyde-captopril chemiluminescence system is shown in Figure 1. Tubes were inserted into corresponding reagents in the flow path. Power supply and peristaltic pump were turned on. Then measurement based on the peak value was taken after the baseline was stable. In the diagram, formaldehyde is mixed with captopril, while potassium permanganate is mixed with sulfuric acid. When the two mixtures meet in the reaction cell, strong CL signal is generated, which is subsequently converted into electric signal and amplified by the photomultiplier (held at a negative high voltage of 600V), and finally recorded by the computer. Under specific experimental conditions, the concentration of captopril scaled linearly with the intensity of CL signal.

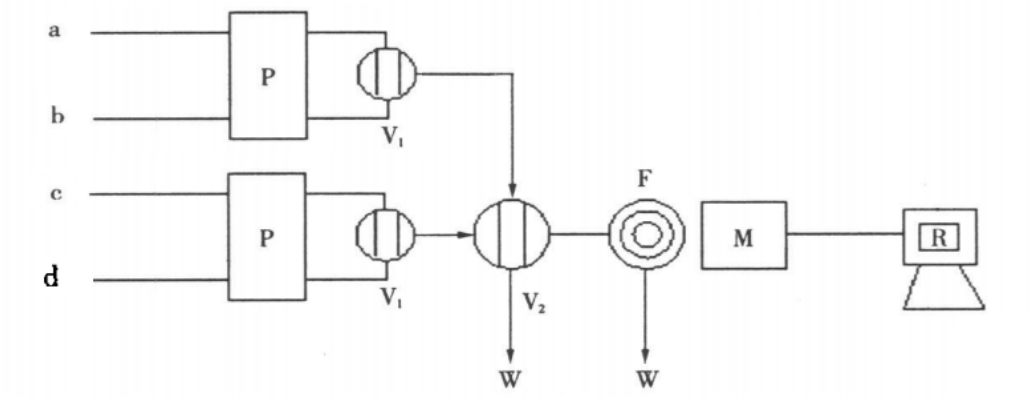

Figure 1 Schematic diagram of the flow-injection analyzer

a. Captopril standard solution or sample solution; b. Formaldehyde solution; c. Potassium permanganate solution; d. Sulfuric acid solution; P. Peristaltic pump; V_1 Six-way valve; V_2 Eight-way valve; F. Flow cell; M. Photomultiplier; R. Computer; W. Waste.

RESULTS AND DISCUSSION

2.1 Selection of experimental conditions

2.1.1 Selection of acid medium and its concentration

The potassium permanganate-formaldehyde-captopril chemiluminescence system generates considerable CL signal only under acidic conditions. The optimum acid medium needs to be selected. The intensity of the CL signal generated by potassium permanganate-formaldehyde-captopril chemiluminescence system was measured, using hydrochloric acid, sulfuric acid, and nitric acid of the same concentration as the acid medium, respectively, where potassium permanganate of 0.1mmol L^{-1}, 2% formaldehyde by volume, and captopril of 0.5μg mL^{-1} were used in all of the three cases. The results showed that the intensity of CL signal was the highest in sulfuric acid, lower in hydrochloric acid, and lowest in nitric acid, as shown in Table 1. Thus sulfuric acid was chosen as the acid medium.

Table 1 Effect of different acid mediums on the intensity of the CL signal
(Concentration of the acid was 0.1mol L^{-1} in each case)

Acid medium	Sulfuric acid	Nitric acid	Hydrochloric acid
Relative intensity	100	70	80

The concentration of sulfuric acid has a direct effect on the intensity of the CL signal. This effect was studied in the concentration range of 0~0.16mol L^{-1}, as shown in Figure 2. The results showed that, the relative intensity of CL signal increased as the concentration of sulfuric acid increased. When the concentration of sulfuric acid was above 0.1mol L^{-1}, the relative intensity of CL signal plateaued. Thus the optimum concentration of sulfuric acid was determined to be 0.1mol L^{-1}.

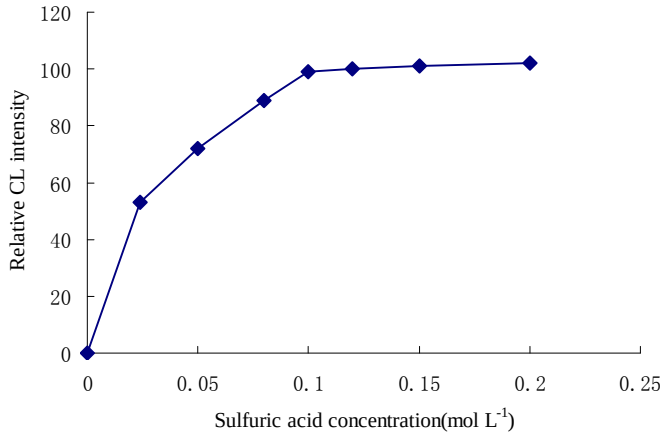

Figure 2 Effect of sulfuric acid concentration on the intensity of CL signal
(Potassium permanganate 0.1mmol L^{-1}; formaldehyde 2%; captopril 0.5μg mL^{-1})

2.1.2 Selection of potassium permanganate concentration

Potassium permanganate is the oxidizing agent in the chemiluminescence reaction. Thus its concentration has an immediate effect on the intensity of the CL signal. This effect was studied in the concentration range 0~0.8mmol L^{-1}, as shown in Figure 3. The results showed that, the relative intensity of CL signal increased as the potassium permanganate concentration increased within the range 0~0.1mmol L^{-1}. The relative intensity reached its maximum at potassium permanganate concentration of 0.1mmol L^{-1}. Within the range of 0.1~0.8mmol L^{-1}, the relative intensity of CL signal decreased as the potassium permanganate concentration increased. Thus the optimum potassium permanganate concentration was determined to be 0.1mmol L^{-1}.

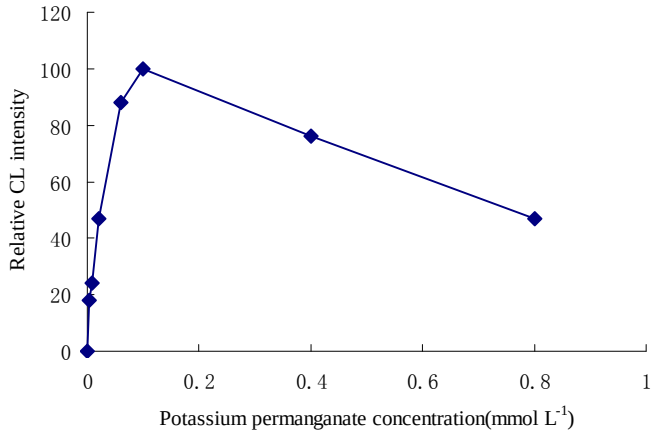

Figure 3 Effect of potassium permanganate concentration on the intensity of CL signal (Sulfuric acid 0.1mol L^{-1}; formaldehyde 2%; captopril 0.5μg mL^{-1})

2.1.3 Selection of the volume fraction of formaldehyde

Under acidic conditions, potassium permanganate reacts with captopril and generates vague CL signal. Adding formaldehyde can enhance the CL signal in this reaction. Thus formaldehyde acts as a sensitizing agent in the potassium permanganate-formaldehyde-captopril chemiluminescence system. The effect of the volume fraction of formaldehyde on the intensity of CL signal was studied within the range of 0~5%, as shown in Figure 4. The results showed that, within the range of 0~3%, the relative intensity of CL signal increased as the volume fraction of formaldehyde increased. The relative intensity of CL signal reached its maximum at 3% volume fraction of formaldehyde. Within the range of 3~5%, the relative intensity of CL signal decreased as the volume fraction of formaldehyde increased. Thus the optimum volume fraction of formaldehyde was determined to be 3%.

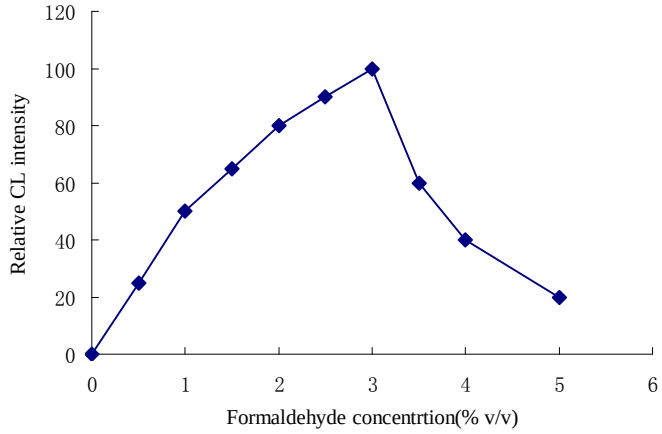

Figure 4 Effect of the volume fraction of formaldehyde on the intensity of CL signal (Potassium permanganate 0.1mmol L^{-1}; sulfuric acid 0.1mol L^{-1}; captopril 0.5μg mL^{-1})

2.2 Standard curve, detection limit and precision

Under the optimum experimental conditions described above, the calibration of CL intensity versus captopril concentration was linear at the range of 0.02~2.0μg mL^{-1}. The regression equation was I=47.098C+4.0808, with correlation coefficient r=0.9998, where I is the emission intensity (mV) and C is the concentration of captopril (μg mL^{-1}). The detection limit of captopril was 0.01μg mL^{-1}. The concentration of 0.5μg mL^{-1} captopril was measured in 5 consecutive experiments. The relative standard deviation was 2.8%.

2.3 Interference of coexisting elements

Under the optimum experimental conditions described above, the interference of coexisting elements was studied using 0.5μg mL^{-1} captopril. The results showed that, within relative standard deviation of ±5 %, there was no detectable interference of 150 fold dextrin, glucose, or starch, 100 fold Na^+, K^+, Ni^{2+}, Zn^{2+}, Mg^{2+}, or Ca^{2+}, or 5 fold CO_3^{2-}.

2.4 Sample analysis

In order to evaluate the validity of the proposed method for the determination of captopril, the method was applied to captopril tablets. The sample captopril solution was first diluted to the linear range. The relative intensity of CL signal was then measured according to the procedure shown in Figure 1 under optimum conditions. The concentration of captopril was determined according to the relative intensity of the CL signal. Recovery test was carried out, which yielded satisfactory results as shown in Table 2.

Table 2 Determination of captopril concentration in tablets

Sample	Marked /mg	Measured /mg	RSD [a]	Added / mg	Recovered / mg	Recovery /%
Tablet 1	25.0	24.8	3.6	25.0	50.2	101.6
Tablet 2	25.0	24.4	2.9	25.0	48.9	98.0

[a] RSD: (n=5)

Tablet 1: Beijing Jingfeng Pharmaceutical Co. Ltd

Tablet 2: Changzhou Pharmaceutical factory Co. Ltd

CONCLUSION

A new method was developed for determination of captopril with the potassium permanganate-formaldehyde-captopril chemiluminescence system, utilizing the flow injection technique. The reaction mechanism is not yet clear. The luminous body in the system may be caused by the excited state of the intermediate product in the reaction process, and formaldehyde can significantly enhance the CL signal. Up to now, this method for determination of captopril concentration has not been reported in previous literature. The method requires only common reagents (potassium permanganate and formaldehyde) and no complicated solution preparation, thus can be easily adopted. It is also fast and produces stable CL signal, thus can achieve high sensitivity. Therefore the present study provided a convenient as well as accurate method for determination of captopril, which is of potential practical significance.

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