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Non-equilibrium determination of metoclopramide and tetracaine hydrochloride by sequential injection spectrophotometry

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Abstract

A new sequential injection spectrophotometric method was proposed for the determination of metoclopramide and tetracaine hydrochloride. The method was based on the detection of an unstable red intermediate compound resulting from the reaction of metoclopramide or tetracaine hydrochloride with potassium dichromate, in the presence of sodium oxalate, in sulfuric acid solution. The related reaction mechanisms of this new method have been studied. The experimental conditions were optimized for the stopped-flow and continuous-flow sequential injection models. For continuous flow, the linear range for determination of metoclopramide, the detection limit and the sampling frequency were 13–130 $\mu g\,ml^{-1}$, 9.4 $\mu g\,ml^{-1}$ and 40 samples per hour, respectively. For stopped flow, they were 3–42 $\mu g\,ml^{-1}$, 1.0 $\mu g\,ml^{-1}$ and 18 h^{-1}, respectively. Adopting the continuous-flow model for tetracaine hydrochloride, the linear range was 25–300 $\mu g\,ml^{-1}$, and the detection limit was 18.0 $\mu g\,ml^{-1}$ with sampling frequency of 40 h^{-1}. This method has been used to determine metoclopramide and tetracaine hydrochloride in pharmaceutical preparations, and the results are compared with those determined by the pharmacopoeia method. Statistical analysis reveals that there was no evidence of significant difference between the methods.

Keywords: Sequential injection; Spectrophotometry; Metoclopramide; Tetracaine hydrochloride

1. Introduction

Sequential injection analysis (SIA) was proposed in 1990 by Ruzicka and Marshall [1] as a rugged flow analysis technique to meet the requirements for industrial process control with minimal needs for maintenance and recalibration. Compared with flow injection analysis (FIA), SIA can save more samples and reagents, greatly decreasing the accumulation of toxic residues. More importantly, SIA is liable to integrate, miniaturize, automatically control and make the determination convenient and precise. Meanwhile, this technology can accomplish the analysis of different targets with the same apparatus without alteration of the device of the flow line, and is especially suitable for the process analysis and simultaneous determination of multi-components [2–3]. The principles of reproducible time and mixing in SIA are similar to those in FIA, so that the chemical reaction does not need going to completeness for analytical use [4]. An important trend is the growing interest in the exploitation of unstable chemical reactions for quantitative assays [5]. Based on the fact that most of the unstable intermediate compounds could not be determined by using the common apparatus, SIA can be regarded as an ideal method to reproducibly monitor the transient signal. At present, SIA has been used in the field of pharmaceutical analysis [6–9]. However, to our best knowledge, a few papers were published in the analysis of pharmaceuticals using transient intermediate [9–10].

Metoclopramide (MCP) is used as an anti-emetic in the treatment of some forms of nausea and vomiting and to increase gastrointestinal motility [11]. Many analytical methods have been developed for the determination of metoclopramide, and most of them are based on fluorimetric [12], spectrophotometric [13–14] and chromatographic

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[15–16] techniques. The fluorimetric method has a higher sensitivity, but solvent extraction is needed and the procedure is laborious. The spectrophotometric method is chiefly based on the diazotisation reaction, so that it is time-consuming. The chromatographic method needs long time of extraction and expensive instrument, so that it is difficult to popularize. Recently, Al-Arfaj [17] developed a flow-injection (FI) methodology for the rapid and sensitive determination of metoclopramide hydrochloride by using (2,2′-dipyridyl) ruthenium(II) [$Ru(dipy)_3^{2+}$] chemiluminescence (CL).

Tetracaine hydrochloride (TCH), also known as amethocaine, is an estertype local anesthetic. This drug is very potent, long-acting agent with a low therapeutic dose, being commonly used to induce spinal anesthesia [18]. It is known that the use of local anesthetic in spinal anesthesia occasionally results in sudden death of the patient [19]. Some useful methods have been proposed for the analysis of tetracaine hydrochloride, such as electrochemistry [20], phosphorescence [21], liquid chromatography [22–24] and chemical luminescence [25]. Some of these methods have high sensitivity, but the apparatus used are always complex and the manipulations are time-consuming; others have effective separation, but their costs are higher. Literature survey indicated that the determination of metoclopramide and tetracaine hydrochloride by SIA spectrophotometry has not been reported. In this paper, we found that in the presence of sodium oxalate, potassium dichromate reacted with metoclopramide or tetracaine hydrochloride in the medium of diluted sulfuric acid, producing a red unstable intermediate compound was observed. The related reaction mechanism has been investigated. This phenomenon has been used to determine the quantity of MCP and TCH in pharmaceutical preparations under the non-equilibrium condition by SIA. The results were compared well with those obtained by the pharmacopoeia method [26].

2. Experimental

2.1. Apparatus and reagents

A FIAlab 3500 sequential injection instrument (FIAlab Instruments Inc., USA) was used in all experiments in the mode shown in Fig. 1. Sample and reagent solutions were driven to the holding coil by the syringe pump (2500 μl) and eight-port rotary selection valve, which were controlled by a computer (FIAlab for Windows 5.0 Revision E). Then, the solutions were propelled reversely to a detector through the reaction coil. The holding coil was made of 2.0 m × 0.7 mm i.d. Teflon (PTFE) tubing. The reaction coils were PTFE tubing of 0.8 m × 0.5 mm i.d. for determination of metoclopramide and 0.6 m × 0.5 mm i.d. for determination of tetracaine hydrochloride, respectively. All other tubing connections were made of 0.5 mm i.d. PTFE tubing, PTFE nuts and ferrules. An USB2000-UV–vis spectrophotometer (Ocean Optics Inc., USA) was used as a detector with a Z-type flow cell with a 10 mm light path-length and connected with optical fibers.

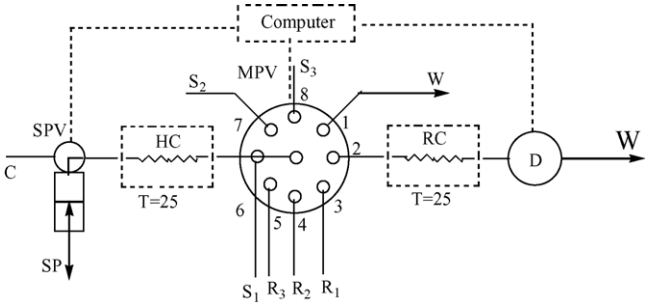


Fig. 1. Sequence injection analysis system: C: carrier (H_2O); SP: syringe pump; SPV: syringe pump valve; MPV: multi-position valve; HC: holding coil (200 cm × 0.7 mm i.d.); RC: reaction coil (for MCP: 80 cm × 0.5 mm i.d.) for TCH: 60 cm × 0.5 mm i.d.); R_1: reagent 1: $K_2Cr_2O_7$ and H_2SO_4; R_2: reagent 2: $Na_2C_2O_4$; R_3: reagent blank (H_2O); S_1–S_3: samples 1–3; D: detector; W: waste.

Stock solutions (1.0 mg ml^{-1}) of metoclopramide and tetracaine hydrochloride (China Pharmaceutical and Biological Inspection Institute) were prepared by dissolving metoclopramide or tetracaine hydrochloride in 0.1 mol l^{-1} sulfuric acid and water, respectively. Working solutions were prepared by suitable dilution. Regent solutions of 2.0 mol l^{-1} H_2SO_4, 1.82×10^{-2} mol l^{-1} $K_2Cr_2O_7$ and 0.78 mol l^{-1} sodium oxalate were prepared with distilled-deionized water. All reagents were of analytical or guaranteed grade, supplied by Beijing Chemical Reagent Ltd.

2.2. Sequential injection analysis procedure

The sequential injection manifold was illustrated in Fig. 1. Sensitivity of the determination was strongly influenced by the order of sequential aspiration of samples and reagents. The different sequential aspirations induce the different reactant zones thorough mixing. It is shown that the reaction zone was maximum and the sensitivity for determination was the highest, when the mixture solutions of sulfuric acid and potassium dichromate, sodium oxalate solution and sample solution (the standard solution or the blank solution) were aspirated in sequence. Therefore, these solutions were aspirated in the sequence, and then reversely propelled to the detector through the reaction coil. The absorbance A_s of the solution was determined at 495 nm for metoclopramide and at 572 nm for tetracaine hydrochloride. After determination of the absorbance A_0 of the blank, the values of $\Delta A = A_s - A_0$ were calculated. Table 1 shows the sequence of operation of the sequence injection system.

3. Results and discussion

We found from the experiment that metoclopramide, procaine, procainamide and tetracaine hydrochloride (their

Table 1
Sequence of operation of the sequence injection system

Sequence no.	MPV position	SPV position	Flow rate ($\mu l\,s^{-1}$)		Volume[a] (μl)		Function
			MCP	TCH	MCP	TCH	
1	1	Left	50	50	920	1070	Aspiration carrier
2	2	Right	25	30	−400	−400	Clean the detector
3	3	Right	35	30	80	60	Aspiration $K_2Cr_2O_7 + H_2SO_4$
4	4	Right	35	30	20	10	Aspiration $Na_2C_2O_4$
5	5(6, 7, 8)	Right	35	30	180	60	Aspiration sample or blank
6	2[b]	Right	35	30	−800	−800	Push into the flow cell and detect, waste

[a] "+" for aspirating in holding coil; "−" for pushing out holding coil.
[b] By the stopped-flow method, firstly push into 380 μl, stopped-flow 100 s and determine the absorbance; then push out 500 μl again for wasting and cleaning the detector.

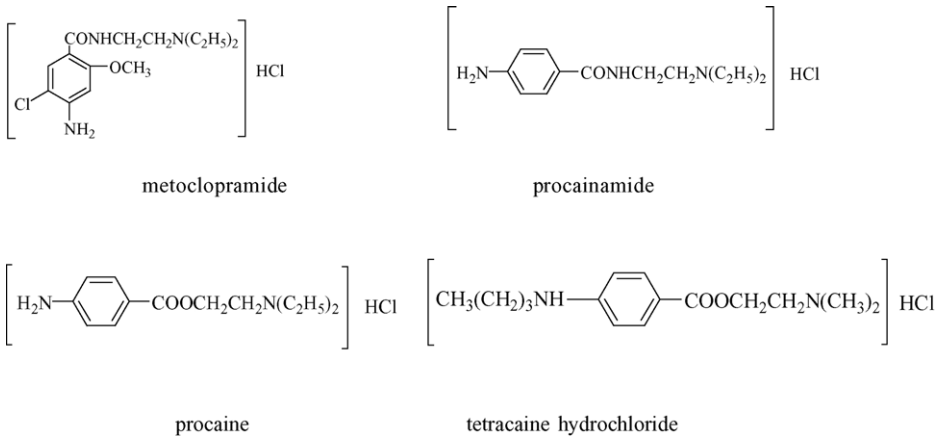
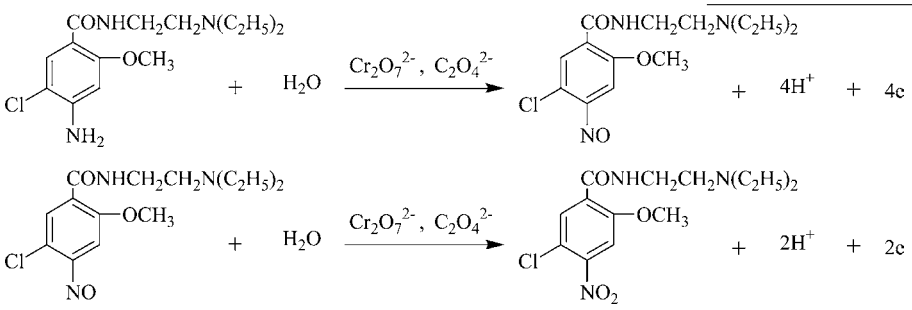


Fig. 2. Structural formula of the drugs.

structural formulas were shown in Fig. 2) could react quickly with potassium dichromate in sulfuric acid medium containing sodium oxalate, producing a red unstable intermediate compound (see Figs. 3 and 4). Oxalate usually served as a promoting activator or catalyst in the oxidation system of chromium(VI) [4,27]. Fig. 3 indicated that sodium oxalate greatly promoted the signal. In the study of the oxidation of procainamide by electroanalysis, similar phenomenon was observed and the reaction mechanism investigated by Bishop and Hussein [28]. According to the structural formulas of these drugs, the oxidation process of metoclopramide and procaine might be similar to procainamide. Therefore, the possible oxidation mechanism of metoclopramide was suggested as follows:

For metoclopramide, procaine and procainamide, the red unstable intermediate compounds resulted from the oxidation of the aniline groups into nitroso groups, which were further oxidized into nitryl, with the color fading quickly (see Fig. 4). It is noted that the maximum wavelength of the oxidized production of tetracaine hydrochloride was shifted farther and its reaction rate was faster than those of metoclopramide, procaine and procainamide. These experimental facts suggested that the oxidation process of tetracaine hydrochloride might be different from those of the other drugs investigated in this work. Concentrations of potassium dichromate and sodium oxalate have greatly effect on lifetime of the intermediate compound. For metoclopramide, when potassium dichromate is greatly excessive, the absorbance of the red intermediate can quickly reach the maximum and then the



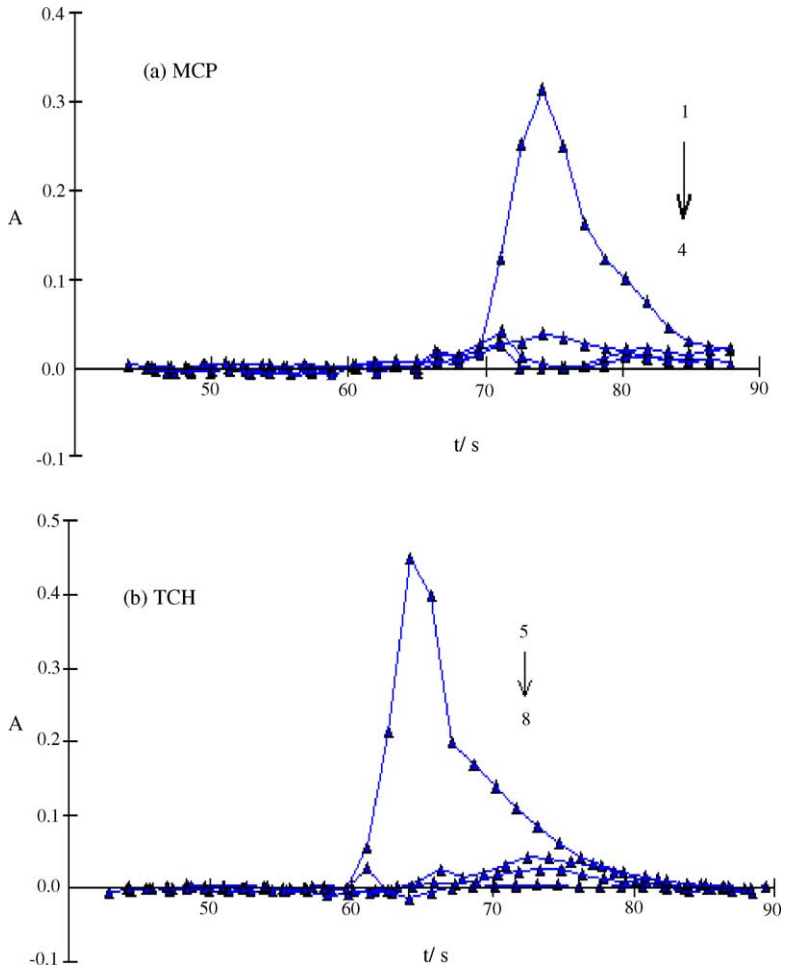


Fig. 3. Intermediate compounds absorbance for determination of MCP and TCH as a function of time: (a) MCP (at 495 nm): 1: $K_2Cr_2O_7 + H_2SO_4 + Na_2C_2O_4 + MCP$; 2: $K_2Cr_2O_7 + H_2SO_4 + Na_2C_2O_4 + H_2O$; 3: $K_2Cr_2O_7 + H_2SO_4 + H_2O + MCP$; 4: $H_2O + H_2SO_4 + Na_2C_2O_4 + MCP$. H_2SO_4: 0.7 mol l^{-1}; $K_2Cr_2O_7$: 5.46×10^{-3} mol l^{-1}; $Na_2C_2O_4$: 0.624 mol l^{-1}; MCP: 64.80 μg ml^{-1}. (b) TCH (at 572 nm): 5: $K_2Cr_2O_7 + H_2SO_4 + Na_2C_2O_4 + TCH$; 6: $K_2Cr_2O_7 + H_2SO_4 + Na_2C_2O_4 + H_2O$; 7: $K_2Cr_2O_7 + H_2SO_4 + H_2O + TCH$; 8: $H_2O + H_2SO_4 + Na_2C_2O_4 + TCH$. H_2SO_4: 0.65 mol l^{-1}; $K_2Cr_2O_7$: 4.55×10^{-3} mol l^{-1}; $Na_2C_2O_4$: 0.373 mol l^{-1}; TCH: 200.0 μg ml^{-1}.

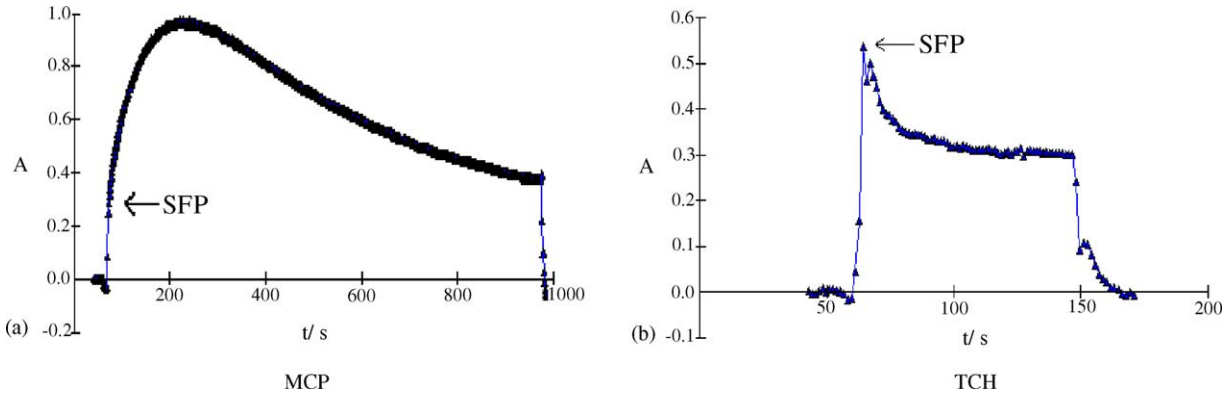


Fig. 4. Plots of the kinetics of the stopped-flow (a) MCP: stopped-flow position (SFP): 380 μl; $K_2Cr_2O_7$: 5.46×10^{-3} mol l^{-1}; H_2SO_4: 0.7 mol l^{-1}; $Na_2C_2O_4$: 0.624 mol l^{-1}; MCP: 41.63 μg ml^{-1}. (b) TCH: stopped-flow position (SFP): 210 μl; $K_2Cr_2O_7$: 4.55×10^{-3} mol l^{-1}; H_2SO_4: 0.65 mol l^{-1}; $Na_2C_2O_4$: 0.373 mol l^{-1}: TCH: 275.0 μg ml^{-1}.

color fades fastly within 3 min. However, metoclopramide is excessive, the color fades slowly and disappears after 20 min. It is shown that Tetracaine hydrochloride was rapidly oxidized by potassium dichromate in the presence of sodium oxalate. Lifetime of the intermediate compound was so short that the maximum absorbance could not be detected. Similar phenomena were observed by Pasekova and Polaseka [10] in their determination of tetracaine hydrochloride by chemiluminescence SIA. The chemiluminescence signal decreases rapidly during stopped-flow experiments. They proposed that the formation of partially oxidized secondary amine intermediates such as $Ar–N^+–R$ would be more feasible compared with primary amine due to the stabilizing effect of the alkyl group. It seems reasonable to suggest that similar reaction mechanism exist in the system studied in this work. Based on these experimental phenomena, a new method was proposed for the determination of metoclopramide and tetracaine hydrochloride by using sequential injection technology which could quickly determine the unstable intermediate compound under the non-equilibrium condition.

3.1. Optimization of the operating conditions by univariate approach

3.1.1. Effect of the reaction coil length and the flow rate

The influence of the reaction coil length and the flow rate on ΔA of the system was investigated in detail. It is found that these parameters have great effect on the efficient mixing and sensitively detecting a red unstable intermediate compounds. It is not enough to sensitively detect the intermediate compounds without the reaction coil for promoting mixing of the sample and the reagents. It is shown that ΔA increased with increasing reaction coil length within the range of 10–60 cm. However, when the reaction coil length was beyond 60 cm, ΔA was slowly growing for metoclopramide, and gradually decreased for tetracaine hydrochloride. Considering the sensitivity and the stability, the reaction coil length of 80 cm for metoclopramide and 60 cm for tetracaine hydrochloride were selected for use in all experiments. It is found that ΔA attained the maximum for metoclopramide when the flow rate reached 35 $\mu l\,s^{-1}$. For tetracaine hydrochloride, ΔA was maximum with the flow rate of 25 $\mu l\,s^{-1}$. Therefore, flow rate of 35 and 25 $\mu l\,s^{-1}$ were adopted in this work for the determination of metoclopramide and tetracaine hydrochloride, respectively.

3.1.2. Effect of reaction media and concentration

Hydrochloric acid, phosphoric acid, sulfuric acid, nitric acid and acetic acid have been tried in the present experiment. It is found that the sensitivity is high and reproducibility is good only in sulfuric acid. The influence of concentration of sulfuric acid was studied in the range of 0.1–1.0 $mol\,l^{-1}$. The results showed that ΔA reached maximum at 0.7 $mol\,l^{-1}$ sulfuric acid for the determination of metoclopramide, and at 0.65 $mol\,l^{-1}$ for sulfuric acid for the determination of tetracaine hydrochloride. So these concentrations of sulfuric acid were adopted in this work.

3.1.3. Effect of the concentrations of $K_2Cr_2O_7$ and $Na_2C_2O_4$

The influence of the concentrations of potassium dichromate on the determination of metoclopramide and tetracaine hydrochloride was investigated in the range of 1.82×10^{-3} to $9.10 \times 10^{-3}\,mol\,l^{-1}$. The results showed that ΔA was maximum at $5.46 \times 10^{-3}\,mol\,l^{-1}$ of potassium dichromate for the determination of metoclopramide, and at $4.55 \times 10^{-3}\,mol\,l^{-1}$ for the determination of tetracaine hydrochloride. Therefore, these optimized concentrations of potassium dichromate were used in our experiments.

The effect of the concentration of sodium oxalate was studied in the range of 0.078–0.78 and 0.0373–0.746 $mol\,l^{-1}$, respectively. The results showed that ΔA attained the maximum at 0.455 $mol\,l^{-1}$ of sodium oxalate for the determination of metoclopramide, and at 0.373 $mol\,l^{-1}$ for the determination of the tetracaine hydrochloride. Therefore, these concentrations of sodium oxalate were chosen in this work.

3.1.4. Effect of the volumes of reagents and samples

The volumes of reagents and samples play a major role in the sensitivity in SIA. Their effect was investigated in detail. The experiment results suggest that sodium oxalate as a promoting activator was encapsulated by sample solution and oxidant regents, it may be preferable to obtain the maximum of reaction zones. Clearly increasing the sodium oxalate volume leads to a decrease in the analytical signal, since the mixing of sample, sodium oxalate and the oxidant regents is less efficient. The changing trends of ΔA with volumes of reagents and samples were shown in Fig. 5. Considering simultaneously the sensitivity and the stability, the ratio of sample and reagent volumes was 4:1:9 for $H_2SO_4 + K_2Cr_2O_7$:$Na_2C_2O_4$:MCP and 6:1:6 for $H_2SO_4 + K_2Cr_2O_7$:$Na_2C_2O_4$:TCH, respectively. Thus, 80 μl of the mixture of sulfuric acid and potassium dichromate solutions, 20 μl of sodium oxalate solution and 180 μl of sample solution were selected for the determination of metoclopramide; and 60 μl of the mixture of sulfuric acid and potassium dichromate solutions, 10 μl of sodium oxalate solution and 60 μl of sample solution were adopted for the determination of tetracaine hydrochloride.

3.1.5. Effect of stopped-flow parameters

The stopped flow injection technique can offer unique capabilities for quantitative and qualitative analysis. It can eliminate background signals, provide kinetic information and increase the sensitivity. A sensitive method for determination of metoclopramide was reported by Al-Arfaj [17], but the stability of the intermediate oxidation product was not investigated. The intermediate oxidation product of tetracaine hydrochloride was so unstable that tetracaine hydrochloride could not promote the sensitivity using the stopped flow technique [10]. We noted from Fig. 4 that stopped-flow

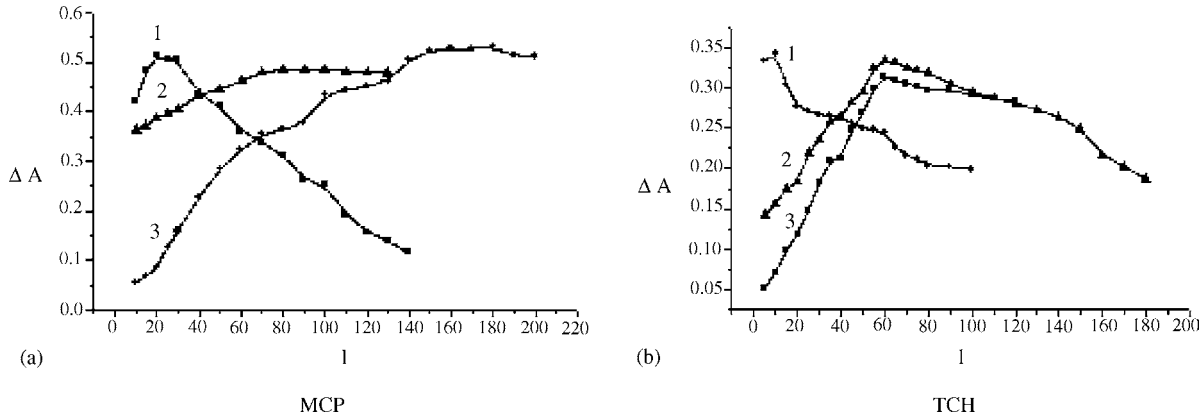


Fig. 5. The effects of the aspiration volume of reagents and samples: (a) MCP: 1: $Na_2C_2O_4$; 2: $H_2SO_4 + K_2Cr_2O_7$; 3: MCP; $K_2Cr_2O_7$: 5.46×10^{-3} mol l^{-1}; H_2SO_4: 0.7 mol l^{-1}; $Na_2C_2O_4$: 0.624 mol l^{-1}; MCP: 103.68 μg ml^{-1}. (b) TCH: 1: $Na_2C_2O_4$; 2: $H_2SO_4 + K_2Cr_2O_7$; 3: TCH; $K_2Cr_2O_7$: 4.55×10^{-3} mol l^{-1}; H_2SO_4: 0.65 mol l^{-1}; $Na_2C_2O_4$: 0.373 mol l^{-1}; TCH: 150.0 μg ml^{-1}.

parameters have significant influence on sensitivity of the system. The sensitivity for the determination of metoclopramide can be improved by using the stopped-flow model, but the situation was not true for the determination of tetracaine hydrochloride. Thus, the influence of the stopped-flow model only for the determination of metoclopramide was investigated. Under the above given conditions, the lifetime of the intermediate compound for the oxidization of was 173 s; residence time of the reaction zones in the SIA system was 24 s. The time from stopped-flow to the maximum absorbance of the intermediate is 149 s. It is shown that 100 s was the best time of the stopped-flow from the balance of the sensitivity and the sample frequency (see Fig. 4). In addition, the effect of the stopped-flow position (propelling volumes) was investigated in the range of 0–540 μl. It is observed that ΔA increased at first, reached the maximum at 390 μl, then decreased quickly with increasing propelling volumes. Considering the stability of the system, 380 μl of the propelling volume was selected as the best stopped-flow position.

3.1.6. Calibration curve, detection limit and stability

The stopped-flow and continuous-flow sequential injection modes for the determination of metoclopramide were studied. The results are presented in Table 2, which indicates that the continuous-flow model has the wider linear range and the higher sampling frequency, whereas the stopped-flow model has the higher sensitivity. Thus, different sequential injection models could be selected for different samples. Moreover, the quantity of metoclopramide was directly determined within the range of 13–130 μg ml^{-1}.

3.1.7. Interference of the foreign species

The effect of the common ions and the additives in pharmaceuticals were investigated in the determination of 50.0 μg ml^{-1} of metoclopramide and tetracaine hydrochloride by the continuous flow model. When the permitted relative deviation from ΔA is less than ±5%, the permissible ratio of co-existing substance are found to be as follows: K^+, Na^+, Cl^-, NH_4^+ (2000); SO_4^{2-}, NO_3^- (1700); ethanol, PO_4^{3-}, CO_3^{2-} and Ca^{2+} (1000); fructose and glucose (750); Zn^{2+} (550); starch, Cu^{2+} (450); glycin, Mg^{2+} (350); Al^{3+}(150); Fe^{3+} (100); citric acid and tartaric acid (50); urea (15) and ascorbic acid (5). It is clear that the interference of the foreign species is very small except for ascorbic acid. This is advantageous to the determination of metoclopramide and tetracaine hydrochloride in pharmaceuticals.

3.1.8. Samples analysis

The proposed method was applied to the determination of metoclopramide and tetracaine hydrochloride in pharmaceuticals by using the optimized experimental conditions. Several tablets containing metoclopramide were accurately

Table 2
The compare of two different sequential injection models

Parameters	MCP		TCH
	Continuous-flow	Stopped-flow	Continuous-flow
Linear range (μg ml^{-1})	13–130	3–42	25–300
Calibration equation, C (μg ml^{-1})	$\Delta A = -0.02598 + 0.00532C$	$\Delta A = 0.04459 + 0.01866C$	$\Delta A = 0.02467 + 0.00215C$
Correlation coefficient	0.9998	0.9988	0.9988
Detection limit[a] (μg ml^{-1})	9.4	1.0	18.0
R.S.D. (MCP, TCH)	2.67 (30.0)	2.44 (8.325)	2.07 (50.0)
Percentage (μg ml^{-1}) ($n = 11$)	2.32 (100.0)	2.78 (33.30)	1.98 (250.0)
Sampling frequency (h^{-1})	40	18	40

[a] The three-time standard deviation of the reagent blank/slope, $n = 11$.

Table 3
The results for the determination of MCP and TCH in the pharmaceuticals ($n = 5$)

Samples	This method[a]	Pharmacopoeia method	t[b]
MCP tablets 1 (mg tablet^{-1})	5.14 ± 0.07	5.06 ± 0.06	2.56
MCP tablets 2 (mg tablet^{-1})	5.26 ± 0.14	5.10 ± 0.12	2.45
MCP injection 1 (mg ml^{-1})	10.23 ± 0.02	10.25 ± 0.05	1.86
MCP injection 2 (mg ml^{-1})	10.35 ± 0.08	10.43 ± 0.07	2.18
TCH powder 1 (%)	99.24 ± 0.12	99.13 ± 0.15	2.05
TCH powder 2 (%)	99.29 ± 0.11	99.18 ± 0.17	2.16

[a] Mean ± standard deviation of five determinations.
[b] Theoretical value = 2.78, $n = 5$ with 95% confidence limits.

weighed, fine grinded and powdered. A given amount of this powder equivalent to about 12.0 mg of metoclopramide was dissolved in 0.1 mol l^{-1} sulfuric acid solution, transferred into 100 ml volumetric flasks, and diluted to the mark with water. The resulting solution was then filtered and the first portion of the filtrate rejected. Several injections of metoclopramide were diluted by 0.1 mol l^{-1} sulfuric acid and calibrated the volume. For tetracaine hydrochloride, the powders were accurately weighed, dissolved and diluted to the mark with water. The sample solutions were well mixed and determined by the continuous-flow model after appropriate dilution to adjust the concentration to meet the requirement of the adopted experimental conditions. In order to examine these results, the standard method was also used for determinations by closely following the procedure described in the pharmacopoeia [26]. In the standard methods, the dead-stop titration or the titration by perchloric acid was commonly used for the determination of pharmaceuticals, which have secondary amine or primary amine groups. The new method proposed in this work show higher selectivity than that of the standard method due to the use of the specific transient intermediate. For example, our results have shown that a lot of pharmaceuticals which have similar chemical structure, such as bupivacaine hydrochloride, lidocaine hydrochloride, sulfadiazine, sulfadimoxine, etc. could not produce any of the intermediates by potassium dichromate in sulfuric acid medium containing sodium oxalate. The results obtained by the two different methods are shown in Table 3. It is evident from the calculated t-test values that our results are in good agreement with those determined by the pharmacopoeia method. This confirms the validity of the method proposed in this work.

4. Conclusions

In this work, a new sequential injection spectrophotometric method was proposed for the determination of metoclopramide and tetracaine hydrochloride by using the transient intermediate under the non-equilibrium condition. Two different sequential injection models were investigated. This method is a suitable approach for automating monitor of metoclopramide and tetracaine hydrochloride in the pharmaceutical preparations. Compared with the common methods, the new method is simple and rapid, and has higher selectivity due to the use of the transient intermediate. The wider linear range makes this method suitable for sample analysis of different targets. In addition, it should be mentioned that this new method permits a significant saving of the reagents, only 130 and 280 μl of reagents for each determination of metoclopramide and tetracaine hydrochloride were needed, greatly minimizing the environmental pollution.

Acknowledgements

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