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Short Communication

Simultaneous ion chromatographic determination of chloride and calcium contained in Ringer's injection using a chelating agent as eluent

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ABSTRACT

A single-column ion chromatographic system with conductivity detector is described for the simultaneous determination of chloride and calcium contained in Ringer's injection. The separation was achieved by using a polymethacrylate-based anion-exchange column and 0.8 m*M* ethylenediaminetetraacetic acid (pH 5.5) as eluent. Good results were obtained by both the calibration plot approach and the single-point calibration approach. For chloride and calcium, the average recoveries of the two methods were 100.5% and 100.1%, respectively.

INTRODUCTION

Ringer's injection is a sterile solution of sodium chloride, potassium chloride and calcium chloride in water for injection. The chloride and calcium components are usually determined by the argentimetric method and chelatometric titration, respectively [1,2].

Ion chromatography, introduced by Small *et al.* [3], has become one of the most important methods for the rapid separation and highly sensitive measurement of analyte ions [4]. However, with a conventional ion chromatographic system, anions and cations cannot be separated simultaneously on the same column. Because a metal cation can form a chelate anion immediately on contact with a chelating agent such as ethylenediaminetetraacetic acid (EDTA) [5–10], the eluent containing the chelating agent was investigated for the separation of several anions and metal cations on a single anion-exchange column.

In this work, chloride and calcium could be separated in 25 min by ion chromatography with EDTA as eluent. The calibration plot approach and the single-point calibration approach could be used to determine chloride and calcium contained in Ringer's injection. The two methods are not only accurate and sensitive, but also simple and rapid.

EXPERIMENTAL

Reagents and solutions

All reagents were of analytical-reagent grade. Standard and sample solutions were prepared from a stock solution (chloride 467.7 μg ml^{-1}, calcium 8.213 μg ml^{-1}), which was obtained by dissolution of corresponding sodium chloride and calcium chloride, and Ringer's injection, respectively. The

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eluent was prepared by dissolving 0.8 mmol of EDTA in 1 l of deionized water followed by adjustment of the pH to 5.5 with sodium hydroxide solution. Before use the eluent was filtered through a 0.45 μm membrane filter.

Apparatus and procedure

Ion chromatographic studies were performed on a Waters ILC-1 ion/liquid chromatograph (Millipore, Milford, MA, USA), which consists of a Model 590 programmable solvent-delivery module, an ILCI six-channel injection valve equipped with a 100-μl sample loop, a Model 430 conductivity detector and a Model 740 data module.

A 75 × 4.6 mm I.D. stainless steel IC-Pak A HR column with a 6-μm polymethacrylate-based quaternary ammonium packing (Millipore) was employed for the separation. The flow rate of the eluent was kept at 0.7 ml min^{-1}. The sensitivity of conductivity detector was set at 2.5 μS full-scale. Each injection was 100 μl.

In order to determine the content of a sample by the calibration plot approach, the regression equation of the calibration graph of peak height *versus* concentration of test ion must first be set up. From this equation, the amount of test ion in a sample solution could then be obtained easily from its peak height. For the single-point calibration approach, a standard solution should be analysed before a sample solution. The calculation of the concentration of test ion in the sample solution is then based on the concentration of the standard and the ratio of the peak heights of the sample and standard.

RESULTS AND DISCUSSION

Eluent and solvent

The EDTA ion has a high affinity for the anion exchanger, leading to a high eluting power for the separation of anions. As a chelating agent, EDTA can chelate with alkaline earth metal ions to form metal chelate anions, which can be separated together with other test anions on the anion-exchange column. In addition, EDTA is less mobile than inorganic anions and therefore has a lower equivalent conductance. EDTA has been found to be a generally applicable eluent for the simultaneous ion chromatographic separation of anions and alkaline earth metal ions on a single anion-exchange column with conductivity detection.

The active species of EDTA as the eluent is its anions, which are directly dependent on the pH and concentration of the eluent [5]. During the experiments on the ion chromatographic determination of chloride and calcium contained in Ringer's injection, when the pH of the eluent (0.8 m*M* EDTA) was adjusted to 5.5 with sodium hydroxide solution, good separation and satisfactory results were obtained. A typical chromatogram is shown in Fig. 1.

The solvent used for the test solutions can have a considerable effect on chromatographic separations. The eluent was selected as the solvent instead of water for the preparation of test solutions in order to improve the peak shape and increase the resolution of peaks between solvent and chloride.

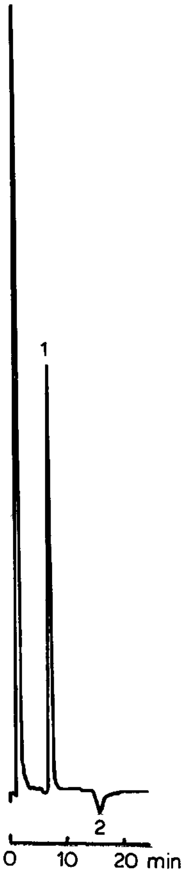

Fig. 1. Ion chromatogram of (1) chloride and (2) calcium in a sample solution prepared by diluting 0.15 ml of Ringer's injection to 100.0 ml. For chromatographic conditions, see Experimental.

TABLE I

COMPARISON OF RESULTS OBTAINED BY THE PROPOSED CHROMATOGRAPHIC METHODS AND THE US PHARMACOPEIA METHOD [2]

Method	Chloride		Calcium	
	Concentration (μg ml^{-1})	R.S.D. (%) (n = 3)	Concentration (μg ml^{-1})	R.S.D. (%) (n = 3)
Calibration plot	5791	0.38	85.08	2.4
Single-point calibration	5554	0.77	87.11	1.7
US Pharmacopeia method	5669	0.04	88.92	0.3

Linearity and detection limit

Volumes of stock solutions of 0.50, 1.00, 1.50, 2.00, 2.50 ml were diluted to 50.0 ml to prepare a series of working standard solutions. Each working standard solution was analysed five times consecutively. The linear relationship between the concentration of each component (c, μg ml^{-1}) and its peak height [h, μV; average of five measurements, relative standard deviation (R.S.D.) < 3.2%] could be described by the regression equation of the calibration graph:

$$h = 3064c + 2658\ (r = 0.9998;\ n = 5)\ \text{(chloride)}$$

$$h = 5674c + 275.4\ (r = 0.9902;\ n = 5)\ \text{(calcium)}$$

The results indicated that the calibration graphs were linear over the ranges 5.0–25 μg ml^{-1} of chloride and 0.08–0.40 μg ml^{-1} of calcium and the detection limits were 0.2 μg ml^{-1} of chloride and 0.04 μg ml^{-1} of calium under the recommended conditions.

Recovery

The recovery of added ions was studied [11]. A 0.10-ml volume of Ringer's injection, used as a fixed amount of the pre-analysed sample, was taken and standard ions were added at four different levels as 0, 0.50, 1.00 and 1.50 ml of the stock solutions, then each solution was diluted to 50.0 ml. With the calibration plot approach the recovery of the added standard was 99.11% for chloride and 98.05% for calcium, and with the single-point calibration approach 101.9% for chloride and 102.2% for calcium.

Assay

In addition to the two proposed methods, the US Pharmacopeia volumetric method [2] was used to determine the amounts of chloride and calcium in Ringer's injection for comparison. The results obtained by the three methods (Table I) are in good agreement. Although the precision of the US Pharmacopeia method is better than that of the proposed chromatographic methods, the latter methods are simple, rapid and sensitive.

CONCLUSIONS

As the standard and sample solutions were analysed consecutively in the approximately the same chromatographic environment, the experimental conditions of the single-point calibration approach need not be controlled very strictly. Compared with the calibration plot approach, the single-point calibration approach is more practical for the simultaneous determination of chloride and calcium contained in Ringer's injection by ion chromatography.

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