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Application News

No.L456

High Performance Liquid Chromatography

Ion Analysis in Drugs (Part 3) Determination of Counterions (Cations) by Ion Chromatography

In Application News No.L387, we introduced examples of impurity ion analysis and counterion analysis in pharmaceuticals using ion chromatography. Typically, a variety of counterions are used to selecting the optimum salts in the development stage of a pharmaceutical product because the physicochemical and pharmacokinetic properties associated with the active pharmaceutical ingredients (API) will vary depending on differences in counterions. Furthermore, as inorganic substances such as catalysts and ions used during synthetic process may affect such properties as solubility and stability, it is very important to conduct analysis of ionic contaminants. High-sensitivity analysis of these ionic contaminants, even when present at trace levels in pharmaceutical products, can be conducted using ion chromatography. Further, by adding an organic solvent to the eluent, the principle component can be eluted more quickly, thereby shortening the analysis time.
Here, we introduce examples of analysis of sodium, potassium, magnesium and calcium as the principal counter cations found in pharmaceuticals.

Analysis of Trace Amounts of Cations

We conducted low-concentration analysis of a standard solution of sodium, potassium, magnesium and calcium. Table 1 shows the area reproducibility and retention time (n = 6), and Table 2 shows the analytical conditions used. The results of analysis of the cation standard solution are shown Fig. 1.

Table 1 Repeatability

	Conc (mg/L)	R.T. %RSD	Area %RSD
Sodium	2.5	0.02	0.07
Potassium	2.5	0.02	0.07
Magnesium	2.5	0.01	0.27
Calcium	2.5	0.02	0.28

Table 2 Analytical Conditions

Column	: Shim-pack IC-C4 (150 mm L. × 4.6 mm I.D.)
Mobile Phase	: A : 3.0 mmol/L Oxalic acid B : Acetonitrile A : B = 95 : 5 (v/v)
Flowrate	: 1.0 mL/min
Column Temp.	: 40 °C
Injection Volume	: 20 µL
Detection	: Conductivity (Non-suppressor mode)

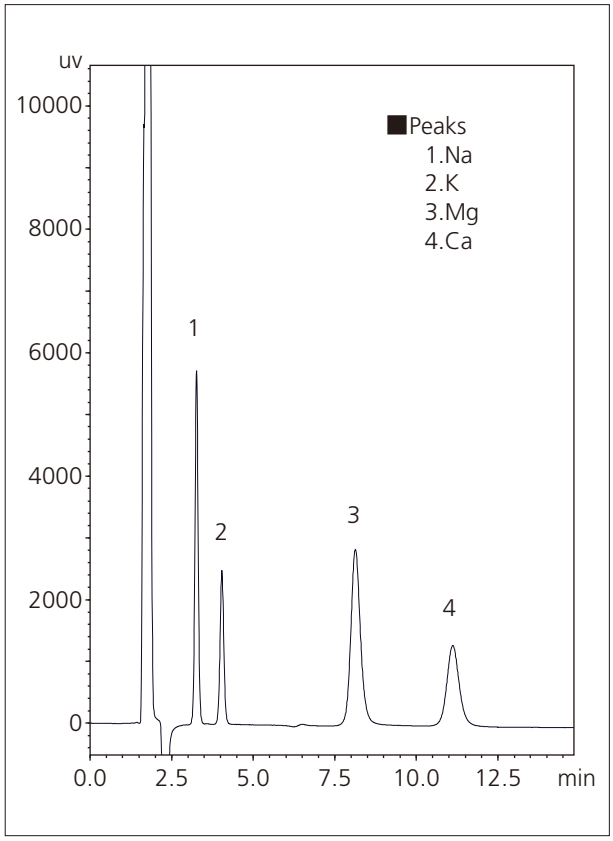

Fig. 1 Chromatogram of a Four-Cation Standard Mixture

Linearity of Calibration Curves

Each counter cation was used for four standard mixtures in the concentration range from 1.25 to 10 mg/L. Then measurements were done using an electrocoductivity detector to create calibration curves, which are shown in Fig. 2.

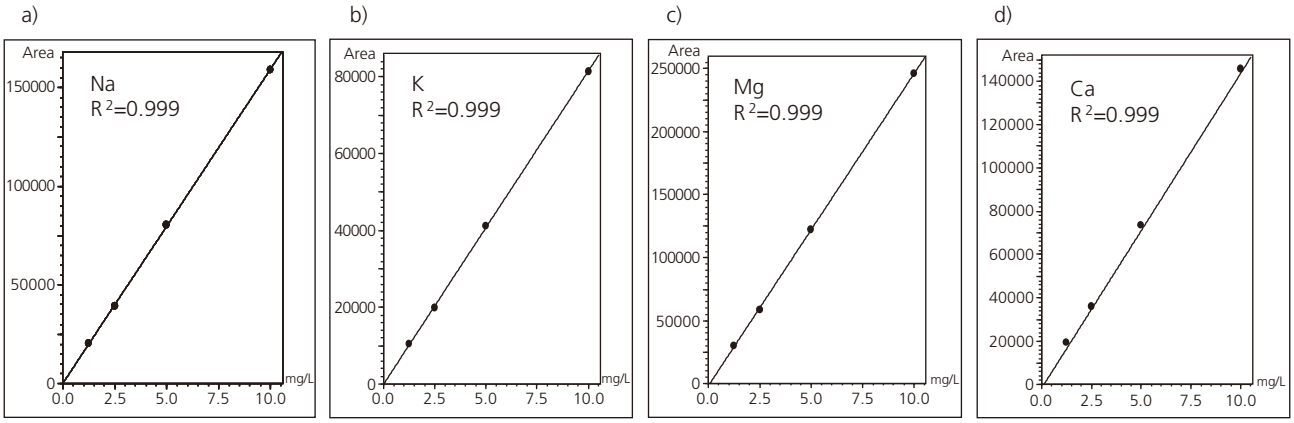

Fig. 2 Linearity of Calibration Curves
a) Sodium, b) Potassium, c) Magnesium, d) Calcium

Analysis of Counterions

Fig. 3 shows the results of analysis of a standard solution of diclofenac sodium (44.7 mg/L : 0.1 mmol/L) containing sodium salt, and Fig. 4 shows the results of analysis of a standard solution of benzyl penicillin (37.2 mg/L : 0.1 mmol/L) containing potassium salt. The analytical conditions are shown in Table 2. The quantitative values obtained for the counterions were 2.4 mg/L for sodium (0.1 mmol/L), and 3.9 mg/L (0.1 mmol/L) for potassium.

The mole ratios of the principal components and counterions were diclofenac : sodium = 1:1.1, and benzylpenicillin : potassium = 1:1.
In addition, the area repeatability obtained in repeat analysis (n=6) of each of the standard solutions was 0.02 % for sodium in diclofenac, and 0.09 % for potassium in benzylpenicillin, indicating excellent repeatability in both analyses.

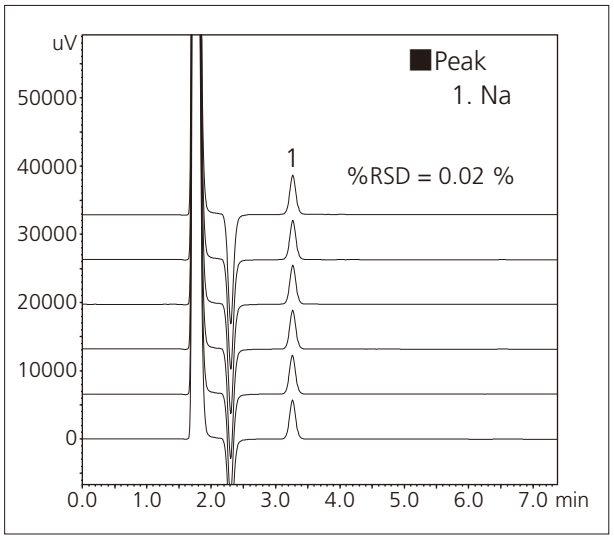

Fig. 3 Chromatogram of Diclofenac Sodium

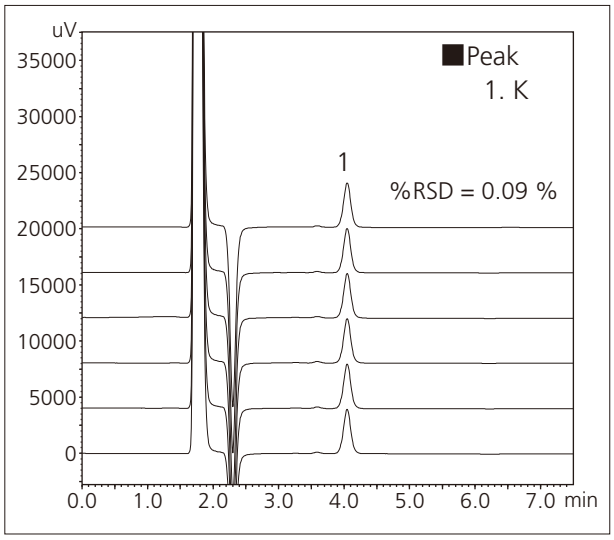

Fig. 4 Chromatogram of Benzylpenicillin Potassium

First Edition: May. 2014

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