

Determination of Inorganic Counterions in Pharmaceutical Drugs Using Capillary IC

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Introduction

One of the most important applications of ion chromatography (IC) is to determine counterions in active pharmaceutical ingredients (API) and drug products in the pharmaceutical industry.^{1,2} Approximately 50% of all drugs on the market are developed in salt forms.^{3,4} Certain suboptimal physicochemical and biopharmaceutical properties of APIs can be overcome by pairing a basic or acidic drug molecule with a counterion to create a salt version of the drug with high solubility, stable crystalline form, and good bioavailability. Ion chromatography with suppressed conductivity detection plays an important role in the salt selection process to establish correct molecular mass of the entity in early stages of drug development. Ion chromatography can also be used in quality control to verify identity, strength, and purity of ionic APIs.

This study describes the determination of inorganic anions and cations in two different drugs using the capillary Thermo Scientific™ Dionex™ ICS-5000 system. Scaling down from standard bore to capillary scale brings many benefits to IC users. Capillary Reagent-Free™ IC (RFIC™) systems deliver fast results by reducing eluent preparation, system startup, and equilibration times. Perhaps most importantly, the system can be left on (i.e., running), always ready for analysis because of its low consumption of eluent (15 mL a day). Having the system always on and ready significantly streamlines the IC workflow. An always on system maintains stability and requires less frequent calibrations. The amount of waste generated is significantly decreased and the Thermo™ Scientific™ Dionex EGC Eluent Generator cartridge producing the eluent lasts 18 months under continuous operation mode, which translates into reduced overall cost of ownership.

Figure 1 shows the analysis of chloride in a drug used to treat type 2 diabetes using the Thermo Scientific™ Dionex™ IonPac™ AS19 capillary column designed for diverse sample matrices. This column is ideally suited for use with the RFIC system. The analysis time for this counteranion is less than 5 min.

Column: Dionex IonPac AS19, Capillary, 0.4 × 250 mm
 Eluent Source: Dionex EGC-KOH (Capillary)
 Eluent: 40 mM KOH
 Flow Rate: 10 µL/min
 Inj. Volume: 0.4 µL
 Column Temp.: 30 °C
 Detection: Suppressed conductivity,
 Thermo Scientific™ Dionex™ ACES™ 300
 Anion Capillary Electrolytic Suppressor
 Sample: 100 mg strength tablet
 Sample Prep.: Thermo Scientific™ Dionex™ OnGuard™ RP cartridge,
 filtered, 1:10 dilution

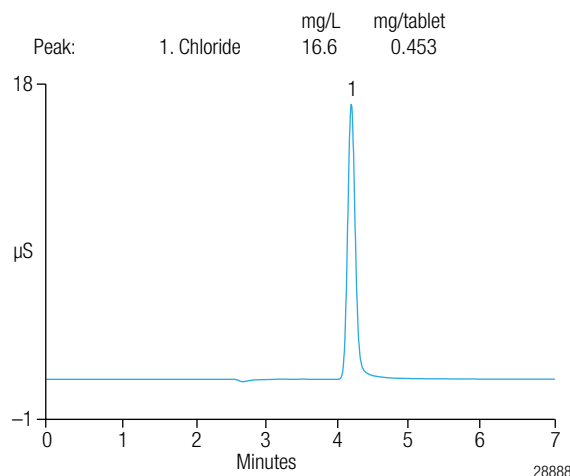


Figure 1. Determination of a counteranion in a drug used to treat type 2 diabetes.

Column: Dionex IonPac CS12A, Capillary, 0.4 × 250 mm
 Eluent Source: Dionex EGC-MSA (Capillary)
 Gradient: 20 mM MSA
 Flow Rate: 10 μ L/min
 Inj. Volume: 0.4 μ L
 Column Temp.: 30 °C
 Detection: Suppressed conductivity,
 Thermo Scientific™ Dionex™
 CCEs™ 300
 Cation Capillary Electrolytic Suppressor
 Sample: 10 mg strength tablet
 Sample Prep.: Dionex OnGuard RP cartridge,
 filtered, 1:10 dilution

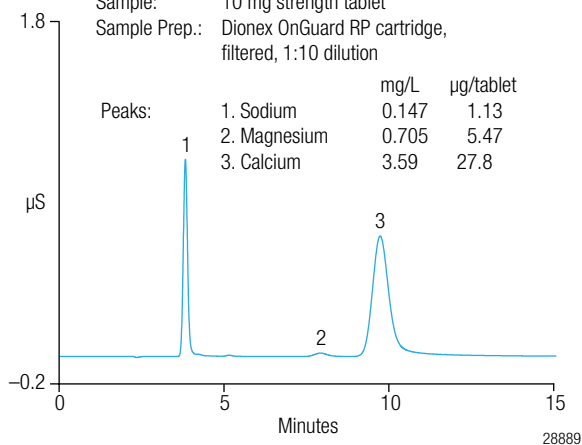


Figure 2. Determination of a counteranion in a drug used to control cholesterol.

Analysis of the counteranion calcium in a drug used to control cholesterol is illustrated in Figure 2. Using the Dionex IonPac CS12A column, calcium is well separated from sodium and magnesium present in the excipients.

Equipment and Conditions

The Dionex Capillary ICS-5000 system, Thermo Scientific™ Dionex™ AS-AP Autosampler, and Thermo Scientific™ Dionex™ Chromeleon™ Chromatography Data System software are used in this experiment. All experimental parameters are listed in the figures above.

Sample Preparation

Extract the counterion analyte by dissolving the tablet in water after 50 °C. Treat the sample using the Dionex OnGuard RP cartridge, then filter through a 0.4 μ m syringe filter, and dilute the sample solution 10-fold prior to analysis.

References

- Dionex Corporation (now part of Thermo Scientific). *Quantification of Anions in Pharmaceuticals*. Application Note 116, LPN 0924, 2007, Sunnyvale, CA.
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- Berge, S.M.; Bighley, L.M.; Monkhouse, D.C. *Pharmaceutical Salts*. *J. Pharm. Sci.* 1977, 66 (1), 1–19.

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