Application Brief: 140

Fast Determination of Inorganic Counterions in a Pharmaceutical Drug Using High-Pressure Capillary Ion Chromatography

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Key Words

- Capillary IC
- High Pressure IC
- HPIC
- Dionex ICS-5000
- Dionex IonSwift MAX-100
- Type 2 Diabetes

Introduction

One of the most important applications of ion chromatography (IC) is the determination of counterions in active pharmaceutical ingredients (APIs) and in drug products in pharmaceutical industry.[1] Approximately 50% of drugs on the market are developed in salt forms.[2,3] Certain physicochemical and biopharmaceutical properties of APIs can be improved 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. IC can also be used in quality control to verify identity, strength, and purity of ionic APIs.

This application brief describes the determination of counter anion chloride in a drug for type 2 diabetes treatment with the Thermo Scientific Dionex ICS-5000 Capillary HPIC system, which can operate at backpressures up to 5000 psi. This capability facilitates higher sample throughput by simply increasing the flow rate. As shown in Figure 1, the analysis of a counterion can be achieved in less than 8 min at 24 µL/min compared to 15 min at a 12 µL/min flow rate using a Thermo Scientific Dionex IonSwift MAX-100 capillary column and suppressed conductivity detection. The Dionex IonSwift™ MAX-100 column uses monolith technology and is designed for the separation of small molecules and inorganic anions using a hydroxide gradient delivered by an eluent generator. At a 24 µL/min flow rate, about 4500 psi backpressure is generated.

Scaling down from standard bore to capillary scale brings many benefits to IC users. One of the most important values is that the system can be left always on and ready for analysis because of its low consumption of eluent (15 mL of source water a day at 10 µL/min flow rate). The amount of waste generated is significantly decreased and the Thermo Scientific Dionex Eluent Generation Cartridge producing the eluent lasts 18 months under typical conditions in continuous operation mode, which translates into reduced overall cost of ownership.

Column:	Dionex IonSwift MAX-100, MAX-100G, 0.25 mm	Inj. Volume:	0.4 µL
Eluent:	Thermo Scientific Dionex EGC-KOH (Capillary)	Temperature:	35 °C
Gradient:	A) 0.1 mM KOH (0.1 min), 0.1–2 mM (0.1 to 2 min), 2–15 mM (2 to 8 min), 15–35 mM (8 to 12 min), 35 mM (12 to 20 min)	Detection:	Suppressed Conductivity Thermo Scientific Dionex ACES 300
	B) 0.1 mM KOH (0.05 min), 0.1–2 mM (0.05 to 1 min), 2–15 mM (1 to 4 min), 15–35 mM (4 to 6 min), 35 mM (6 to 7.5 min)	Sample:	3.66 mg/mL of 100 mg tablet in water
		Sample Prep:	Filtered, treated with Thermo Scientific Dionex OnGuard RP cartridge, diluted 1:10
Flow Rate:	A) 12 µL/min	Peaks:	1. Chloride 16.6 mg/L, 0.453 mg/tablet
	B) 24 µL/min		2. Carbonate —

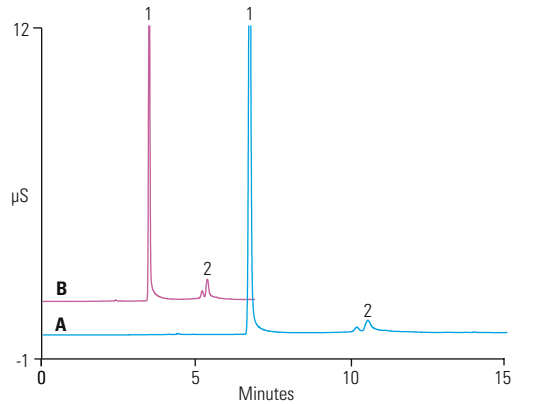

Figure 1. Capillary IC determination of the counterion in a drug used to treat type 2 diabetes.

Conditions

A Dionex ICS-5000 Capillary HPIC system, Thermo Scientific Dionex AS-AP Autosampler, and Thermo Scientific Dionex Chromeleon Chromatography Data System software were used in this experiment. All experimental parameters are listed in Figure 1.

Sample Information and Preparation

Extract the counterion analyte by dissolving the diabetes treatment tablet in water at elevated temperature. After filtration, dilute the sample solution tenfold prior to analysis.

References

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