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Application News

No.L465

High Performance Liquid Chromatography

Investigation of Synthetic Compounds in Drug Discovery by Nexera-i and LCMS-2020

Operational efficiency is an important issue to researchers involved in the organic synthesis stage of drug discovery typically conducted at pharmaceutical companies and universities.
Specifically, large numbers of drug candidates are synthesized daily in the drug discovery chemistry operations conducted throughout the pharmaceutical industry, and the synthesis and purity confirmation of these substances are primarily conducted by LC/MS. Typically, the LC/MS is treated as a shared instrument in an open-access environment, so rather than optimizing the analytical conditions for the various individual compounds, each type of compound is analyzed using a fixed set of analytical conditions. Further, the analyst conducting an analysis is often unaware of the type of compound that was analyzed by the previous analyst who used that instrument.
Reliable analysis in such an environment fundamentally requires an LC system that ensures low carryover performance. The new Nexera-i integrated Ultra High Performance Liquid Chromatograph effectively suppresses carryover using specially treated liquid-contact surfaces, such as the needle seal and sampling needle, thereby providing excellent quantitative performance with high accuracy in a wide variety of analyses. Furthermore, the Nexera-i can be connected with the high-scan-speed LCMS-2020. The built-in UV/VIS detector or PDA detector along with connection to an LCMS permit very detailed qualitative and quantitative analysis.
Here, we introduce an example of analysis of eight pharmaceutical substances in a workflow that is typically used for pharmaceutical synthesis confirmation analysis.

Investigation of Synthetic Compounds in Open Access Environment

A workflow in which multiple analysts in an open access environment can quickly verify the synthesis of a variety of compounds using the same method is perceived as one of the solutions that can lead to greater efficiency in the research and development process. This Application News describes an example in which measurement was conducted for a range of compounds with properties spanning acidic to basic, and high to low polarity, all using the same analytical conditions (Table 1).
Each of the various compounds was dissolved in dimethylsulfoxide (DMSO), and 0.1 µL was injected after diluting with methanol solution containing 5 % DMSO (Final concentration 20 mmol/L each). MS analysis was conducted using scan mode (*m/z* = 165 – 385) and positive / negative mode. The composition analysis results for the eight pharmaceutical compounds are shown below (Fig. 1.1 – 1.4). Also, assuming an actual workflow, we injected a blank solution (methanol) prior to analyzing the next sample. From these results, it is clear that even using high-sensitivity LC/MS analysis, low-carryover performance was maintained regardless of the polarity of the compound or its acidity / alkalinity. The excellent low-carryover performance of this system permits stable analysis without the influence of a preceding analysis on the subsequent analysis.

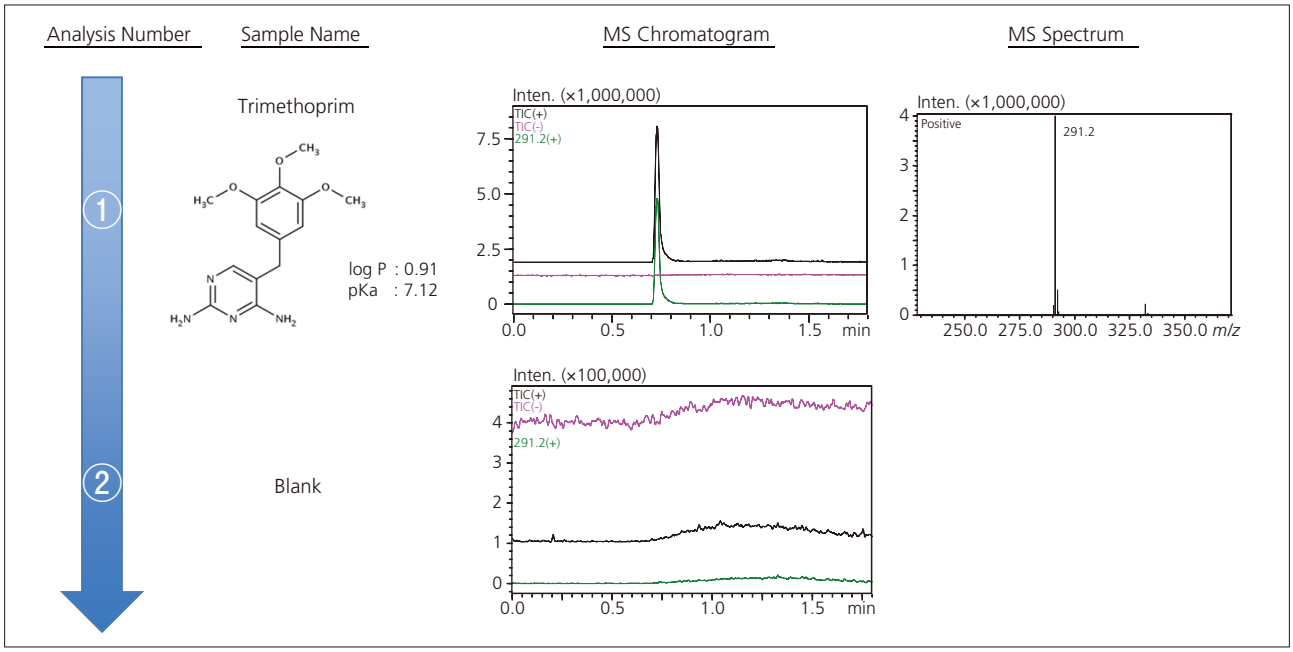

Fig. 1.1 Chromatograms and Spectra of Eight Pharmaceutical Compounds and Blank Solutions

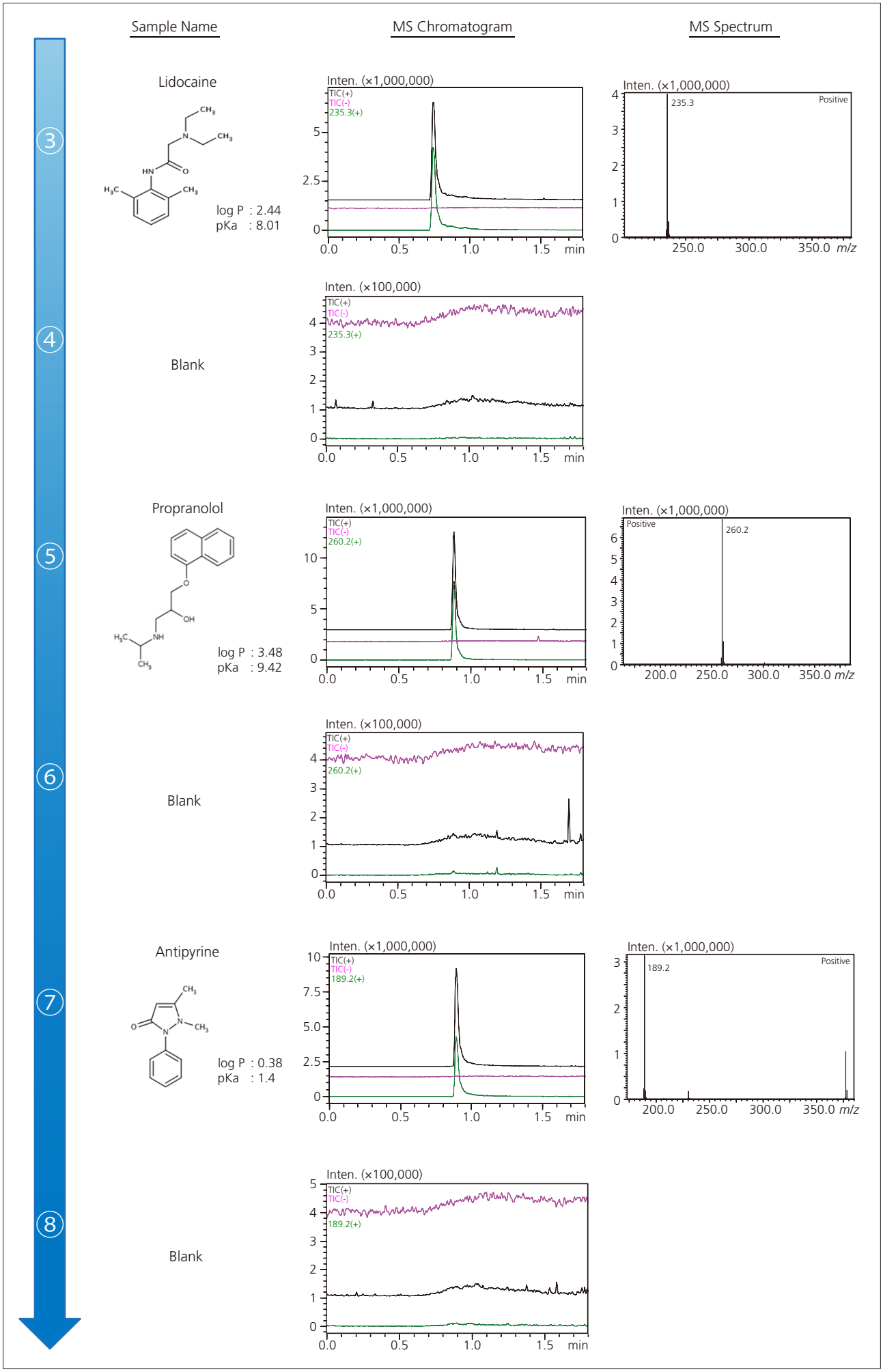

Fig. 1.2 Chromatograms and Spectra of Eight Pharmaceutical Compounds and Blank Solutions

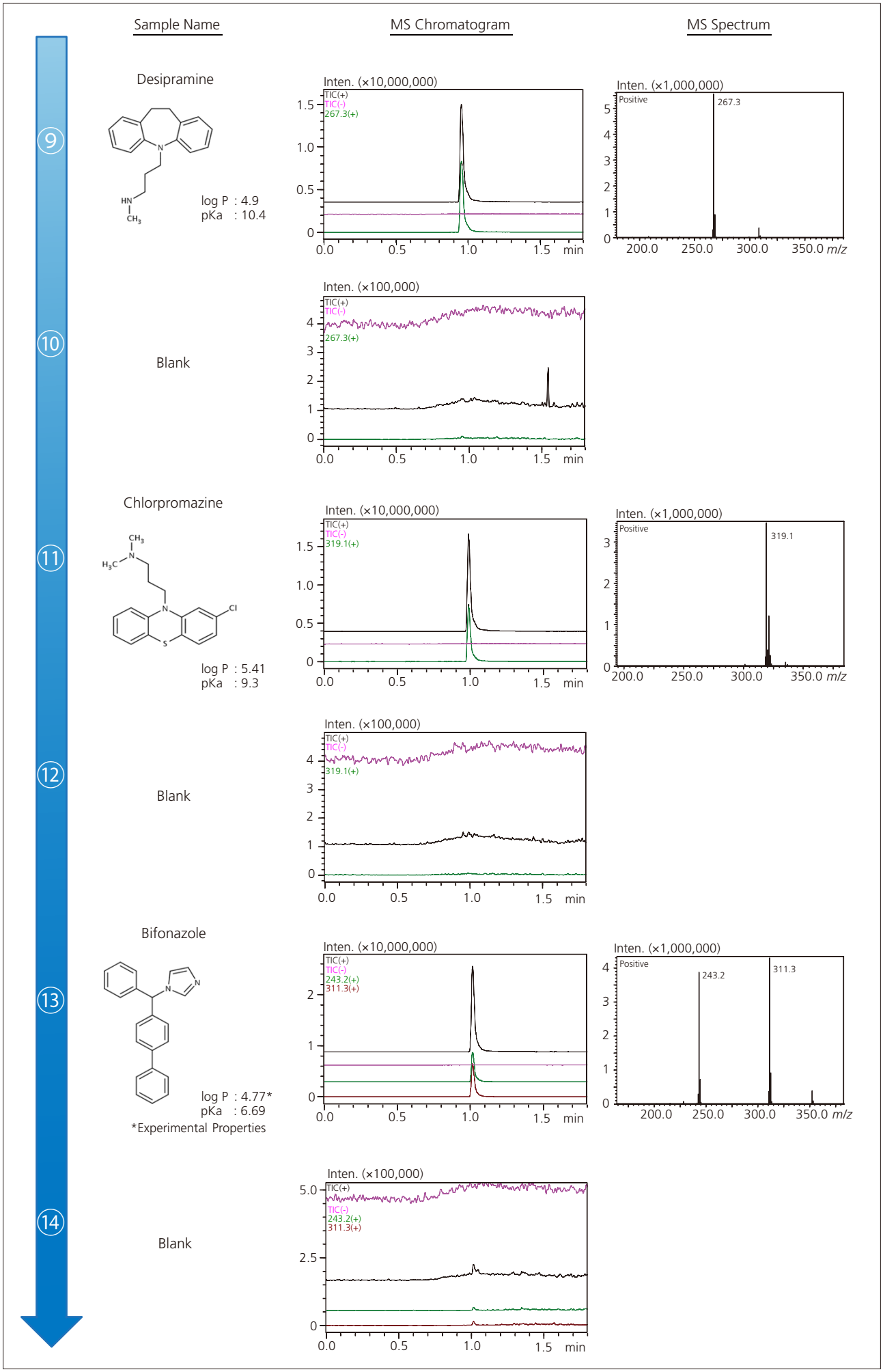

Fig. 1.3 Chromatograms and Spectra of Eight Pharmaceutical Compounds and Blank Solutions

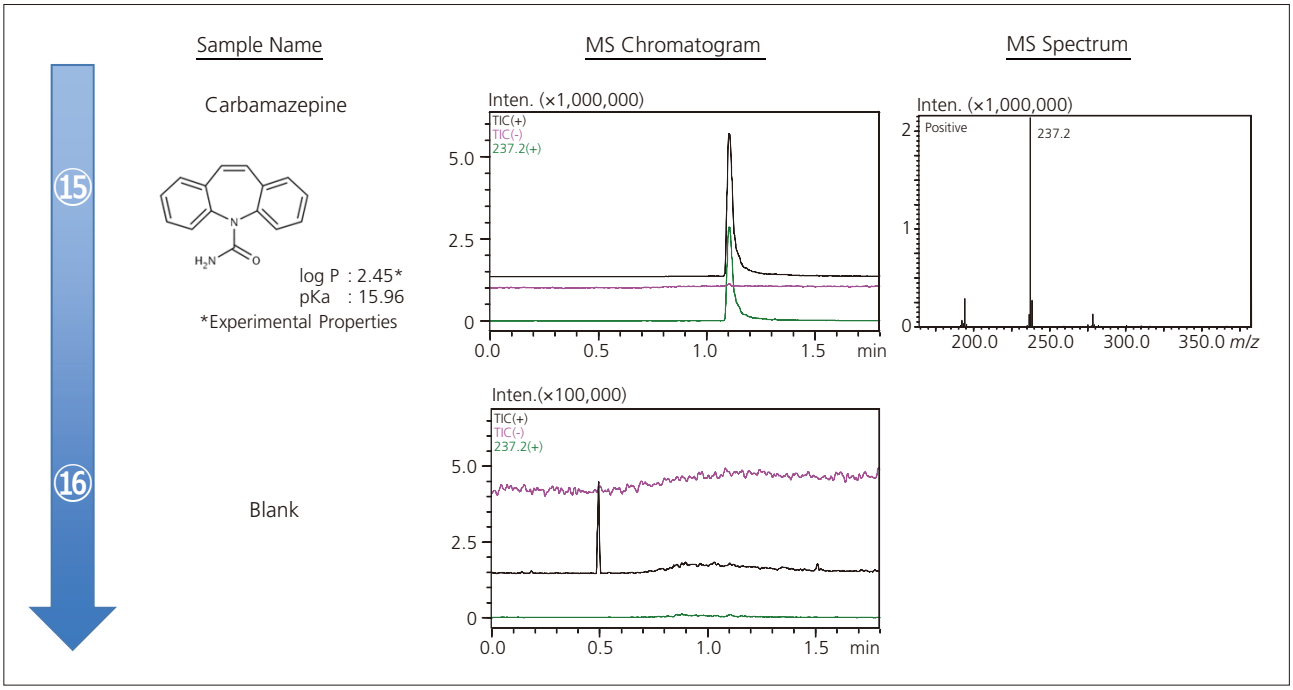

Fig. 1.4 Chromatograms and Spectra of Eight Pharmaceutical Compounds and Blank Solutions

Table 1 Analytical Conditions

[LC]		[MS]	
Column	: Shim-pack XR-ODS Ⅱ (50 mm L. × 2.0 mm I.D., 2.2 µm)	Detection(MS)	: LCMS-2020
Mobile Phase	: A) 0.1 % Formic Acid in Water B) 0.1 % Formic Acid in Acetonitrile	Probe Voltage	: +4.5 kV (ESI-Positive Mode) -3.5 kV (ESI-Negative Mode)
Time Program	: B. Conc. 5 % (0 min) → 95 % (1 - 1.5 min) → 5 % (1.51 - 3 min)	Nebulizing Gas Flow	: 1.5 mL/min
		Drying Gas Flow	: 15.0 L/min
Flowrate	: 1.0 mL/min	DL Temp.	: 250 °C
Column Temp.	: 40 °C	Block Heater Temp.	: 400 °C
Injection Volume	: 0.1 µL	DL, Q-array Voltages	: Default Values
Rinse Solution	: 0.2 % Formic Acid in Methanol	Event Time	: 0.03 sec
Rinse Mode	: Before and After	Scan Range	: *m/z*: 165-385

An Autosampler that Supports Open Access Environment

The direct access mechanism of the Nexera-i permits individual access to separate sample racks, making it possible to load samples in a rack other than the one in which sample injection operations are being conducted for the current analysis (Fig. 2). This, in effect, permits an analyst to load samples for analysis without interrupting an ongoing analysis of another analyst, making it suitable for use as a joint-use instrument. The result is that instrument utilization efficiency is enhanced, thereby permitting a more efficient research and development process.

Furthermore, synthetic products developed in a laboratory setting are almost always produced in small quantities. This is a scenario in which the Nexera-i autosampler excels, as it supports very small-volume injections, thereby permitting analysis of limited-volume samples.

Fig. 2 Direct Access for Each Sample Rack

[References]
Drug Bank (http://www.drugbank.ca) April 2014

First Edition: Aug. 2014

Shimadzu Corporation
www.shimadzu.com/an/

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