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Application News

No.L466

High Performance Liquid Chromatography

Analysis of Impurities in New-generation Antidepressants by Prominence-i

Pharmaceutical companies in Japan are under notification by the Ministry of Health, Labour and Welfare to carefully consider the administration of the new-generation antidepressant drugs that have been on the market since 1999 in Japan to patients under the age of 18[1]. Further, to ensure the properties and suitability of these drugs, they are listed in the United States Pharmacopoeia (USP) and European Pharmacopoeia (EP).
The new Prominence-i integrated high-performance liquid chromatograph features separation compatibility with the systems of other companies. Further, use of the delay volume-compatible system kit option provides separation compatibility with the previous LC-2010 model, thereby permitting the smooth transfer of methods from the currently used instrument.
Here, using the new Prominence-i integrated high-performance liquid chromatograph, we introduce an example of analysis of compounds related to the abovementioned new-generation antidepressants.

Analysis of Impurities of Duloxetine Hydrochloride

Antidepressant drugs are psychotropic drugs that affect neurotransmitters such as noradrenaline and serotonin that are present in the brain. Among these are seven types referred to as new-generation antidepressants, and one of these, duloxetine hydrochloride, is used as a serotonin–norepinephrine reuptake inhibitor (SNRI).
We conducted measurement of duloxetine hydrochloride (0.2 mg/mL) for system suitability using the analytical conditions of Table 1, as specified in the USP[2]. Fig. 1 shows the chromatogram acquired using the Prominence-i in the upper, single chromatogram trace, and the expanded views of the chromatograms acquired using (a) another company's LC system above, and that acquired using the (b) Prominence-i below, in the lower, dual chromatogram trace. Similarly, Fig. 2 shows the chromatogram acquired using the Prominence-i in the upper, single chromatogram trace, while in the lower, dual chromatogram trace, expanded views of the chromatogram obtained using the (a) LC-2010 in the upper of the two traces, and that acquired using the (b) Prominence-i with the delay volume-compatible system kit option in the lower trace. From Fig. 1 and 2, it is clear that the Prominence-i displays separation that is compatible with the other company's LC system and the LC-2010 system.
In addition, from the results of system suitability testing (Fig. 1 (b) Prominence-i) using the system suitability solution of duloxetine hydrochloride, it is clear that system suitability was satisfied for all items, as shown in Table 2.

Table 1 Analytical Conditions

Column	: ZORBAX SB-C8 (150 mm L. × 4.6 mm I.D., 3.5 µm)
Flowrate	: 1.0 mL/min
Mobile Phase	: Acetonitrile / 2-Propanol / 25 mmol/L Phosphate Solution (pH 2.5) Containing 50 mmol/L 1-Hexanesulfonic Acid Sodium Salt (13 / 17 / 70)
Column Temp.	: 40 °C
Injection Volume	: 10 µL
Detection	: UV 230 nm

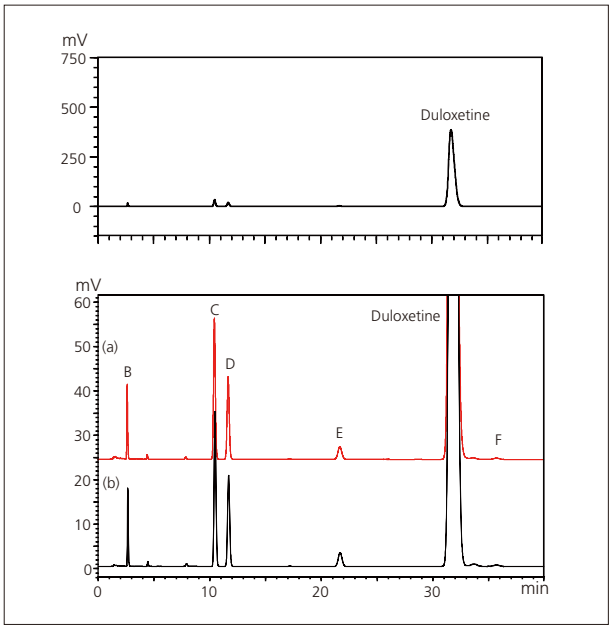

Fig. 1 Chromatograms of Duloxetine Hydrochloride
Upper: Prominence-i
Lower: Expanded Chromatograms by
(a) another Company's LC System, (b) Prominence-i

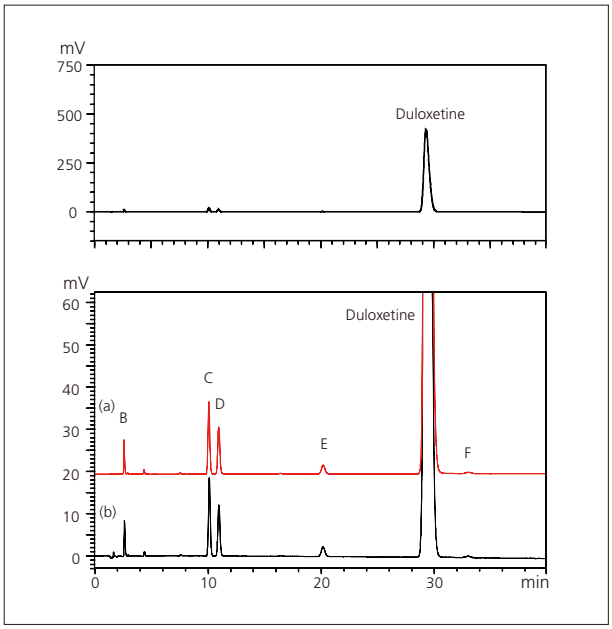

Fig. 2 Chromatograms of Duloxetine Hydrochloride
Upper: Prominence-i (with delay volume-compatible system kit)
Lower: Expanded Chromatograms by (a) LC-2010,
(b) Prominence-i (with delay volume-compatible system kit)

Table 2 Results of USP System Suitability Test Using Duloxetine (Fig. 1 (b) Prominence-i)

System Suitability Requirements	Criteria	Observed	Result
Resolution Between Duloxetine and Duloxetine Related Compound F	≥ 1.5	4.2	PASS
Symmetry Factor for Duloxetine	≤ 1.5	1.3	PASS
Peak area %RSD for Duloxetine	≤ 1.0	0.17	PASS

Analysis of Impurities of Escitalopram Oxalate

Escitalopram oxalate is used as a selective serotonin reuptake inhibitor (SSRI). We conducted measurement of a standard solution of escitalopram oxalate (0.5 mg/mL) using the analytical conditions shown in Table 3, as specified in the USP[3]. Fig. 3 shows the chromatogram acquired using the Prominence-i in the upper, single chromatogram trace, and the expanded views of the chromatograms acquired using (a) another company's LC system above, and that acquired using the (b) Prominence-i below, in the lower, dual chromatogram trace.

Similarly, Fig. 4 shows the chromatogram acquired using the Prominence-i in the upper, single chromatogram trace, while in the lower, dual chromatogram trace, expanded views of the chromatogram obtained using the (a) LC-2010 in the upper of the two traces, and that acquired using the (b) Prominence-i with the delay volume-compatible system kit option. From Fig. 3 and 4, it is clear that the Prominence-i has separation compatibility with the other company's LC system and LC-2010 system.

In addition, from the results of system suitability testing (Fig. 4 (b) Prominence-i (using the delay volume-compatible system kit option)) using the system suitability solution of Escitalopram oxalate, it is clear that the system suitability was satisfied for all items, as shown in Table 4.

Table 3 Analytical Conditions

Column	: Shim-pack VP-ODS (250 mm L. × 4.6 mm I.D., 5 µm)
Flowrate	: 1.0 mL/min *2.0 mL/min (45 - 60 min)
Mobile Phase	: A) Acetonitrile / 25 mmol/L Phosphate (Potassium) Buffer (pH 3.0) (1/9) B) Acetonitrile / 25 mmol/L Phosphate (Potassium) Buffer (pH 3.0) (13/7)
Time Program	: B. Conc. 5 % (0 min) → 35 % (35 min) → 100 % (45 - 60 min) → 5 % (60.1 - 68 min)
Column Temp.	: 45 °C
Injection Volume	: 20 µL
Detection	: UV 237 nm

Table 4 Results of USP System Suitability Test Using Escitalopram (Fig. 4 (b) Prominence-i (with Delay Volume-Compatible System Kit))

System Suitability Requirements	Criteria	Observed	Result
Symmetry Factor for Escitalopram	0.8-3	2.9	PASS
Peak Area %RSD for Escitalopram	≤ 2.0	0.067	PASS

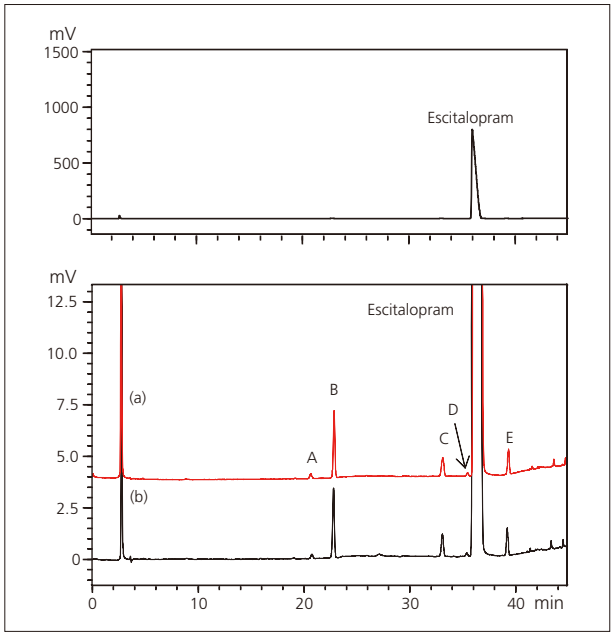

Fig. 3 Chromatograms of Escitalopram Oxalate
Upper: Prominence-i
Lower: Expanded Chromatograms by
(a) another Company's LC System, (b) Prominence-i

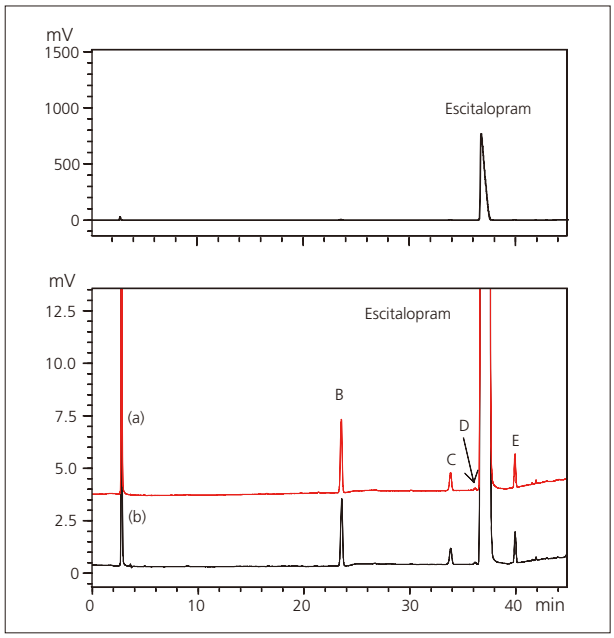

Fig. 4 Chromatograms of Escitalopram Oxalate
Upper: Prominence-i (with delay volume-compatible system kit)
Lower: Expanded Chromatograms by (a) LC-2010,
(b) Prominence-i (with delay volume-compatible system kit)

[References]
1) Revision to "Cautions in Usage," Notification No. 329001 by Department of Food Safety, Pharmaceutical and Food Safety Bureau, Japanese Ministry of Health, Labour and Welfare (March 29, 2013)
2) Second Supplement to U.S. Pharmacopeia 35-NF 30, 2012
- Official Monographs "Duloxetine Hydrochloride"
3) U.S. Pharmacopeia 35-NF 30, 2012
- General Chapters <621>
- Official Monographs "Escitalopram Oxalate"

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