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Application News

USP-Compliant Analysis and Robustness Evaluation of Pramipexole by i-Series

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User Benefits

- LC-2050C, with delay volume compatibility kit, is compatible with the delay volume of LC-2010, facilitating smooth method transfer.
- Design space generated by LabSolutions MD allows robustness evaluation of a test method without relying on the user's experience in chromatography.

■ Introduction

Pramipexole is a drug used to treat Parkinson's disease and other disorders. The United States Pharmacopeia (USP) specifies analytical conditions for this drug. "i-Series LC-2050C" integrated high-performance liquid chromatograph is equipped with delay volume compatibility with LC-2010, our former integrated HPLC, by using the optional delay volume compatibility kit. This compatibility ensures a smooth method transfer from LC-2010. In this paper, a case study is presented, analyzing Pramipexole hydrochloride, a compound listed in the USP, utilizing LC-2050C with the delay volume compatibility kit. The scientific basis (specificity and robustness) of the test method for the instrument change from LC-2010 to LC-2050C was evaluated using LabSolutions MD which is a dedicated software for supporting method development. Specifically, the effect on system suitability test, such as resolution and symmetry factor, was assessed by intentionally varying the flow rate and column oven temperature specified by the USP within a small range.

■ Analytical Conditions

The analytical conditions (system suitability test) for Pramipexole hydrochloride are presented in Table 1. Additionally, the analysis result using LC-2050C with the delay volume compatibility kit is shown in Fig. 1, while the analysis result using LC-2010 is illustrated in Fig. 2. These results indicate that LC-2050C and LC-2010 are delay volume compatible. Table 2 summarizes the results of the system suitability test for Pramipexole hydrochloride. Consequently, it was confirmed that both LC-2050C and LC-2010 systems met the system suitability criteria for the resolution and symmetry factor.

Table 1 Analytical Conditions (System suitability test)

System	: LC-2050C with compatibility kit
Sample	: Pramipexole Dihydrochloride (1.5 mg/mL) and Compound A (0.8 mg/mL)
Mobile phase	: A) 67 mmol/L (potassium) phosphate buffer containing 21 mmol/L 1-octanesulfonic acid sodium salt (pH 3.0) : B) Mobile Phase A/Acetonitrile = 50 : 50
Column	: Shim-pack Scepter™ C18-120 (150 mm × 4.6 mm I.D., 5 µm)*1
Injection Vol.	: 5 µL
Time program	: B Conc. 40%(0 min)→80%(15min) →40%(15.1-20min)
Column Temp.	: 40 ℃
Flow rate	: 1.5 mL/min
Detection (PDA)	: 264 nm

*1 P/N: 227-31020-05

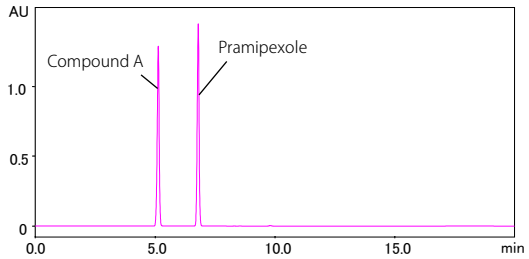

Fig. 1 Chromatogram by LC-2050C (with delay volume compatibility kit)

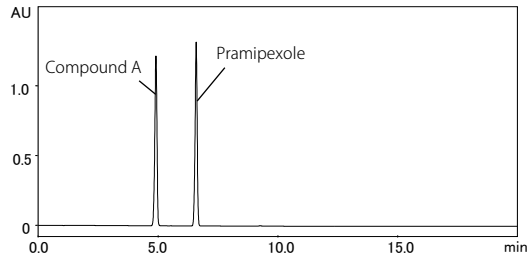

Fig. 2 Chromatogram by LC-2010

Table 2 Results of System Suitability Test

System suitability item	Criteria	Result (LC-2050C)	Result (LC-2010)
Resolution (Pramipexole and compound A)	≧6.0	10.7	9.9
Symmetry factor (Pramipexole)	≦2.0	0.94	0.93

■ Robustness Evaluation by LabSolutions MD

Robustness evaluations are crucial for understanding the effects of parameter changes on measurement results and confirming the reliability of the test method. LabSolutions MD supports robust method development based on Analytical Quality by Design (AQbD) approach. The robustness of Pramipexole hydrochloride under USP specifications was assessed by varying the flow rate by ±0.1 mL/min (at three levels : 1.4, 1.5, and 1.6 mL/min) and the column oven temperature by ±1 ˚C (at three levels : 39, 40, and 41 ˚C), resulting in nine different combinations (refer to Fig. 3). Plots illustrating the resolution between Pramipexole and compound A as well as the symmetry factor of Pramipexole at each flow rate and oven temperature level are provided in Fig. 4 and Fig. 6, respectively. In addition, design spaces of resolution and symmetry factor across the entire range of variation, with flow rate on the vertical axis and oven temperature on the horizontal axis, are displayed in Fig. 5 and Fig. 7.

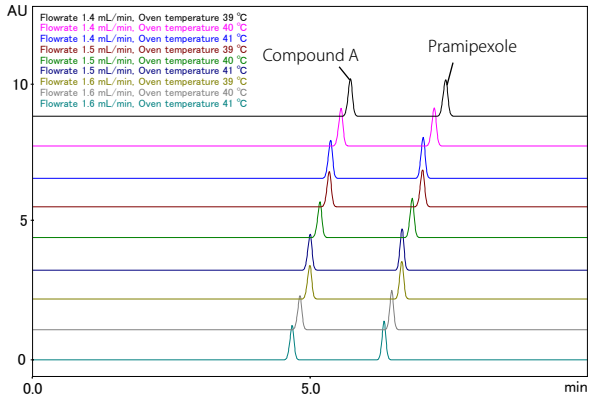

Fig. 3 Chromatograms at Each Level of Flow Rate and Oven Temperature

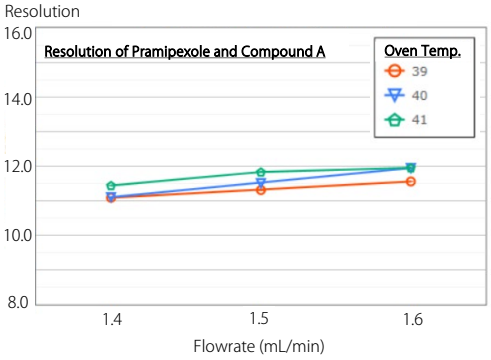

Fig. 4 Plots of Resolution

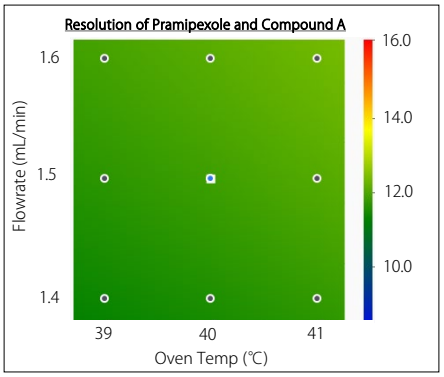

Fig. 5 Design Space of Resolution

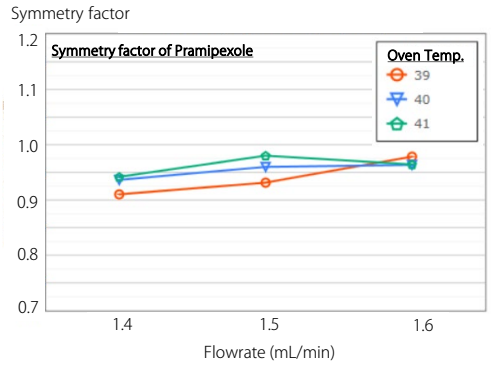

Fig. 6 Plots of Symmetry Factor

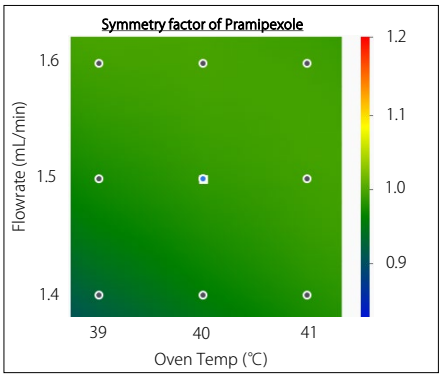

Fig. 7 Design Space of Symmetry Factor

At their respective levels of flow rate and column oven temperature, the resolutions between Pramipexole and compound A varied between 11 and 12 (refer to Fig. 4). This outcome is represented as a design space (refer to Fig. 5). In Fig. 5, the green area (resolution : 11-12) covers the entire variation range, indicating minimal variation in resolution and meeting the criterion (≥6.0) for resolution in the system suitability test. The symmetry factor of Pramipexole varied between 0.9 and 1.0 at their respective levels of flow rate and column oven temperature (refer to Fig. 6). In the design space of the symmetry factor (Fig. 7), the green area (symmetry factor : 0.9-1.0) extends across the entire region, indicating minimal variation in the symmetry factor and meeting the criterion (≤2.0) for the symmetry factor in the system suitability test. Therefore, utilizing the design space can verify the robustness when parameters are varied, without relying on user's experience on chromatography.

■ Conclusion

Through USP-compliant analysis of Pramipexole, it has been demonstrated that LC-2050C (utilizing delay volume compatibility kit) and LC-2010 are delay volume compatible, thereby facilitating smooth method transfer. Moreover, method validation is commonly necessary during test method alterations. The design space function of LabSolutions MD effectively assesses analytical performance parameters such as specificity (resolution) and robustness, enabling reliable method management without depending on user experience.

＜References＞

1) US Pharmacopeia 43-NF38, 2022
"Pramipexole Dihydrochloride"

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