Ultra High Performance Liquid Chromatograph

Application News

Maximizing Operational Productivity through Ultra-Fast Analysis with Nexera™ X4

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User Benefits

◆ The low internal volume design of Nexera X4 significantly improves solvent delivery responsiveness and shortens re-equilibration time in gradient elution, enabling high-throughput analysis.

◆ The independently actuated plungers and the pressure feedback mechanism incorporated into the solvent delivery pump ensure excellent reproducibility of both retention times and peak areas.

■ Introduction

In multi-sample analyses in pharmaceutical development, improving throughput per analysis directly translates to enhanced productivity. Nexera X4 (Fig. 1) is a next-generation ultra-high-performance liquid chromatograph (UHPLC) that inherits the technologies cultivated in Shimadzu's Nexera series and delivers best-in-class analytical performance. Its low-internal-volume design significantly improves solvent delivery responsiveness, enabling ultra-fast analysis. In addition, the solvent delivery pump equipped with independently actuated plungers and a pressure feedback mechanism greatly reduces pulsation and provides highly stable and reproducible solvent delivery even under ultra-high-pressure conditions. All high-pressure sample flow paths employ end-surface-sealed connections that minimize carryover and peak broadening originating from voids (dead volume) in the fittings. Tool-free fittings (Fig. 2) are used throughout these flow paths to enhance usability. In this article, data are presented demonstrating how the superior solvent delivery responsiveness of Nexera X4 reduces cycle times compared with existing UHPLC systems and enables high-throughput analysis.

Fig. 1   Nexera™ X4

Fig. 2   Tool-Free Fittings

■ Analytical Conditions and Target Compounds

The analytical conditions and target compounds are summarized in Table 1. In this study, a mixed standard sample containing nine low-molecular-weight pharmaceuticals was used as a model. Ultra-fast analysis with a 3-minute cycle time (gradient elution) was applied to this sample.

Table 1 Analytical Conditions and Target Compounds

System : Nexera X4	
Sample : (1) Quinidine, (2) Antipyrine, (3) Benzoic acid, (4) Salicylic acid, (5) Hydrocortisone, (6) Furosemide, (7) Naproxen, (8) Probenecid, (9) Diclofenac	
Mobile phase	
Pump A : 0.1% formic acid in water	
Pump B : Acetonitrile	
Column : Shim-pack Scepter™ C18-120 [*1] (50 mm × 2.1 mm I.D., 1.9 μm)	
Analytical conditions	
B Conc.	：5%(0 min)→95%(1.4~1.8 min)→5%(1.8~3 min)
Column Temp.	：45 °C
Flow rate	：1.2 mL/min
Mixer	：Micro mixer
Sample loop Vol.	：15 μL
Injection Vol.	：1 μL
Detection	：254 nm (SPD-M40 X4, STD cell）

*1 P/N : 227-31012-03

■ Excellent Reproducibility in Ultra-Fast Analysis

Fig. 3 shows the chromatograms obtained from six repeated analyses, overlaid and with baseline shifts indicated. The retention times of all compounds were consistent, and all chromatograms showed perfect overlap. Table 2 summarizes the reproducibility (%RSD) of retention times and peak areas for each compound across the six injections. Good reproducibility was confirmed for all compounds. The high solvent delivery performance of Nexera X4—including rapid response and stable flow—enables cycle time reduction while maintaining excellent reproducibility.
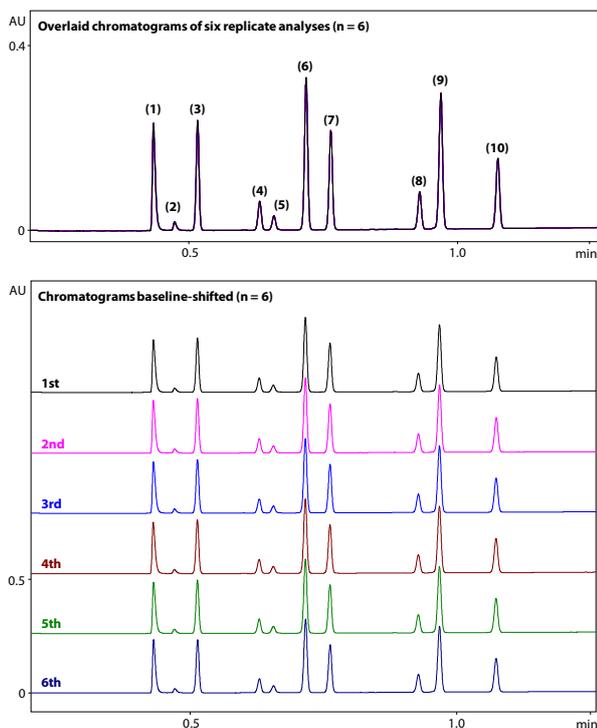
Fig. 3   Chromatograms from Repeated Analyses (n = 6)
Overlaid (Upper), Baseline-Shifted (Lower)

Table 2   Reproducibility (%RSD) of Each Sample over Six Repeated Analyses

Sample	Retention time	Peak area
(1) Quinidine	0.06	0.33
(2) Impurity of quinidine	0.07	0.35
(3) Antipyrine	0.03	0.37
(4) Benzoic acid	0.04	0.33
(5) Salicylic acid	0.03	0.40
(6) Hydrocortisone	0.03	0.30
(7) Furosemide	0.02	0.34
(8) Naproxen	0.01	0.34
(9) Probenecid	0.01	0.36
(10) Diclofenac	0.02	0.36

■ Conclusion

Examples of high-throughput analysis achieved by reducing analytical cycle times are presented. Nexera X4 delivers significantly improved solvent delivery responsiveness through low internal volume design, as well as high solvent delivery stability via independently actuated plungers and a pressure feedback mechanism. This enables excellent reproducibility even in ultra-fast gradient analyses with a 3-minute cycle time. By utilizing Nexera X4 for multi-sample analyses, cycle times per analysis can be shortened, contributing to maximized productivity in analytical operations.

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