SHIMADZU
Excellence in Science

High Performance Liquid Chromatograph
Software for Efficient Method Development

Application News

Achieving Solvent Reduction and Lower Running Costs with Nexera™ X4

Shinichi Fujisaki

User Benefits

- Using narrow-bore columns enables a substantial reduction in solvent consumption.
- Nexera X4 features a low-dispersion design with minimized internal volume, enabling sharp peak shapes even when using narrow-bore columns.
- Using LabSolutions™ MD enables a more efficient workflow for developing and optimizing separation conditions.

■ Introduction

In recent years, there has been growing interest in sustainability within analytical laboratories. In liquid chromatography, the large volumes of organic solvents used as mobile phases present challenges from both environmental and cost perspectives. One approach to reducing solvent consumption is to downscale analyses by using small-diameter columns. Such solvent-saving strategies not only contribute substantially to lowering running costs, but also reduce the amount of waste solvent, enabling more environmentally conscious laboratory operations. However, analytical downscaling requires effective suppression of band broadening within flow channels and highly accurate low-volume injections. Nexera X4 (Fig. 1) delivers exceptional instrument performance that meets these demands and provides stable analytical results even when small-diameter columns are used. This article presents a case study in which analysis was downscaled and solvent consumption was significantly reduced by combining Nexera X4 with a 1-mm-ID column (Shim-pack™ NovaCore C18-HB). In addition, the optimization of separation conditions was streamlined by using LabSolutions MD, a dedicated software for supporting method development.

Fig. 1 Nexera™ X4

■ Analytical Conditions and Target Compounds

The analytical conditions and target compounds are summarized in Table 1. In this study, a mixed standard containing eight small-molecule pharmaceuticals was used as a model sample. Separation conditions for this sample were optimized using a 1-mm-ID column.

Table 1 Analytical Conditions and Target Compounds

System : Nexera X4	
Sample : (A) Antipyrine, (B) Benzoic acid, (C) Salicylic acid, (D) Hydrocortisone, (E) Furosemide, (F) Naproxen, (G) Probenecid, (H) Diclofenac	
Mobile phase	
Pump A : 0.1% formic acid in water	
Pump B : Acetonitrile	
Column : Shim-pack NovaCore C18-HB*1 (50 mm × 1.0 mm I.D., 1.7 µm)	
Analytical conditions	
B Conc.	: 5%(0 min)→70%(X *2 min)→5%(X~X+5 min)
Column Temp.	: 30, 40, 50 ˚C
Flow rate	: 0.1 mL/min
Mixer	: Micro mixer
Sample loop Vol.	: 15 µL
Injection Vol.	: 0.3 µL
Detection	: 254 nm (SPD-M40 X4, STD cell)

*1 : P/N 227-32901-01
*2 : X (Gradient time)= 2, 3, 4

■ Enhancing the Efficiency of Separation Optimization with LabSolutions MD

Fig. 2 shows the chromatogram obtained under the analytical conditions listed in Table 1 (gradient time: 2 min, column oven temperature: 40 ˚C). Compounds (C) and (D) co-eluted (red circle in Fig. 2), indicating that optimization of the separation is required. LabSolutions MD enables anyone to perform rapid and error-free exploration of separation conditions by automatically generating analysis schedules under comprehensive combinations of parameters (steps (1)–(4) in Fig. 3). For example, when varying the gradient time (red box in Fig. 3), an entered center value of 3 min is adjusted by one step above and below the center at 1-min increments, resulting in automatically generated schedules of 2, 3, and 4 min. In this study, nine analytical schedules (Fig. 4) were automatically generated by varying the gradient time (2, 3, 4 min; three patterns) and column oven temperature (30, 40, 50 ˚C; three patterns), enabling comprehensive evaluation of the separation.

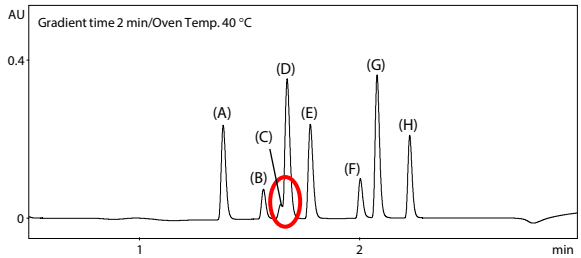


Fig. 2 Chromatogram Obtained Using the 1-mm-ID Column
(Before separation optimization)
(Peak labels correspond to those in Table 1)

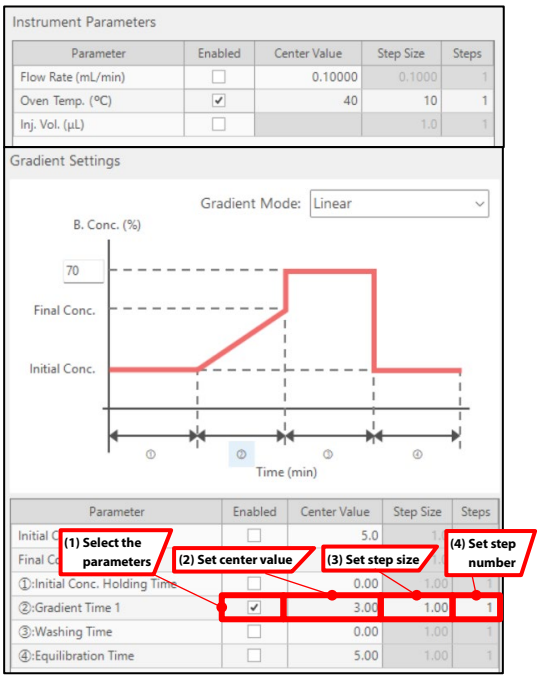


Fig. 3 Analysis Schedule Creation Screen

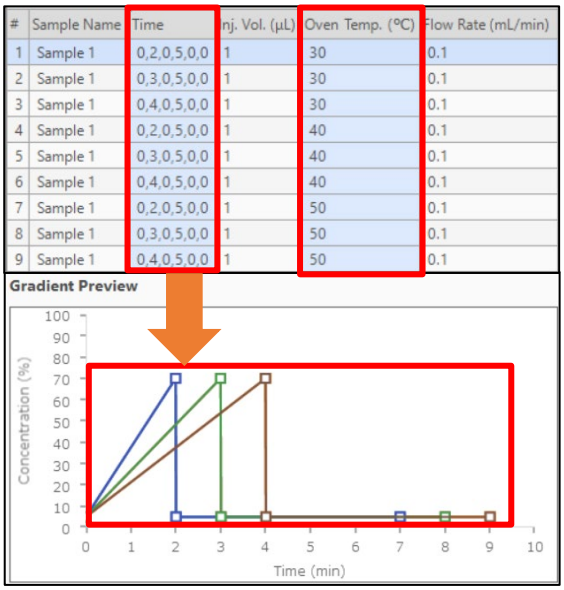


Fig. 4 Automatic Generation of Analysis Schedule

Fig. 5 shows the chromatograms obtained by comprehensively varying the gradient time and column oven temperature. A longer gradient time tended to improve the separation between peaks, while higher column oven temperatures resulted in earlier elution of the compounds and a shorter overall analysis time. Considering both the resolution between compounds and the need to minimize analysis time, the condition of a 3-min gradient and a column oven temperature of 50 ˚C ((8) in Fig. 5) was selected as the optimal separation condition. Fig. 6 shows the chromatogram obtained under the optimal conditions.

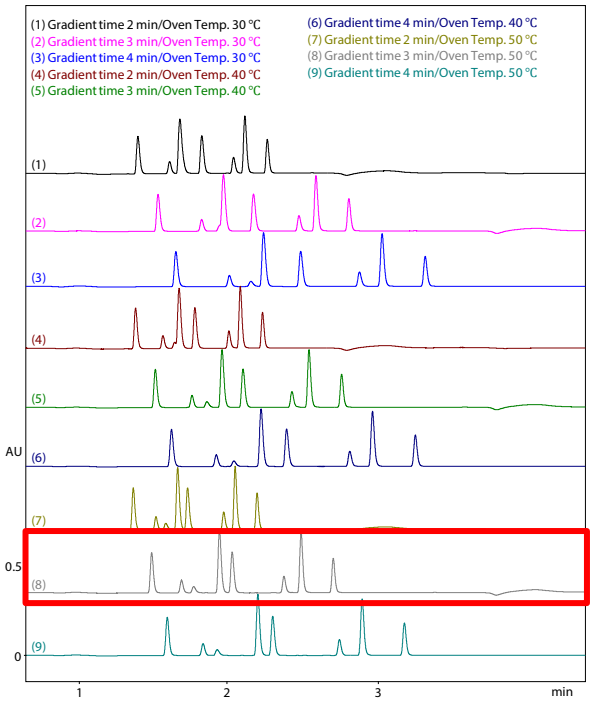


Fig. 5 Chromatograms Obtained by Varying the Gradient Time and Column Oven Temperature

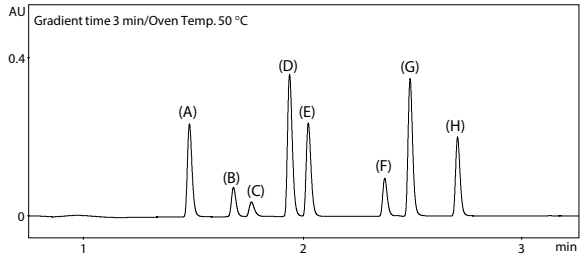


Fig. 6 Chromatogram Under the Optimal Separation Conditions: (8) in Fig. 5 (Peak labels correspond to those in Table 1)

■ Reduction of Solvent Consumption Using a 1-mm Column

Fig. 7 compares solvent consumption for column inner diameters of 1.0, 2.1, and 3.0 mm. Switching from a 3-mm column to a 1-mm column reduces solvent consumption by approximately 9-fold, while switching from a 2.1-mm column to a 1-mm column achieves a reduction of about 4.5-fold. These reductions not only help lower running costs but also contribute to reducing environmental impact by decreasing the volume of waste solvent.

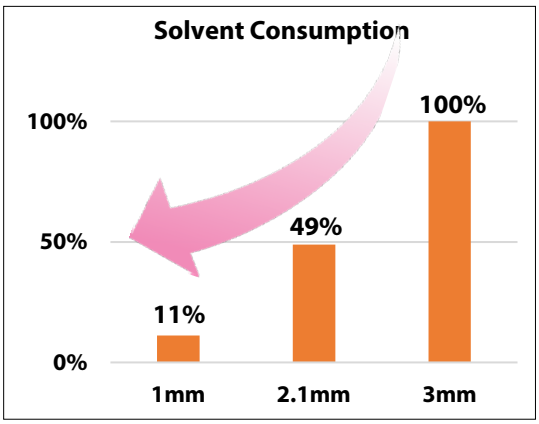


Fig. 7 Comparison of Column Inner Diameter and Solvent Consumption
(Linear velocity kept constant across column IDs)
(Using the 3 mm column's solvent consumption as 100% for comparison)

■ Maximizing the Performance of 1-mm-ID Columns with Nexera X4

When using 1-mm-ID columns, minimizing extra-column dispersion caused by system flow channel is essential for maximizing the inherent performance of the column. Fig. 8 compares chromatograms obtained with Nexera X4 and a typical UHPLC system using a 1-mm-ID column. While Nexera X4 provides sharp peak shapes, the typical UHPLC system shows broader peaks due to the influence of extra-column dispersion. With its low-dispersion design and minimized internal volume, Nexera X4 enables full performance of small-diameter columns.

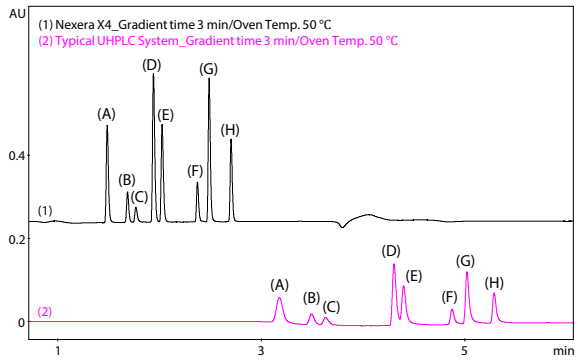


Fig. 8 Comparison of Chromatograms Under the Optimal Conditions
(1) Nexera X4, (2) Typical UHPLC System
(Peak labels correspond to those in Table 1)

■ Conclusion

This article introduced an approach for reducing solvent consumption by using small-diameter columns. Reducing solvent usage not only lowers running costs but also contributes to reducing environmental impact by decreasing the amount of waste solvent. Although suppressing dispersion within the flow path is essential when scaling down an analysis, Nexera X4 maximizes the performance of small-diameter columns through its low-dispersion design. Furthermore, when combined with the method-development support software LabSolutions MD, it also streamlines the exploration of optimal separation conditions.

01-01174-EN First Edition: Jun. 2026

SHIMADZU
Shimadzu Corporation
www.shimadzu.com/an/

Please fill out the survey

Related Products Some products may be updated to newer models.

Nexera X4 Ultra High-Performance Liquid Chrom…

Ultra High-Performance Liquid Chromatograph

Related Solutions

Pharmaceutical and Biopharmaceutical

Small Molecule Pharmaceutical

Price Inquiry

Product Inquiry

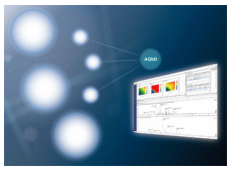
Technical Service / Support Inquiry

Other Inquiry

› Please fill out the survey

Related Products Some products may be updated to newer models.

› Nexera X4 Ultra High-Performance Liquid Chrom…
Ultra High-Performance Liquid Chromatograph



› Method Development System
Automatic Optimization of Gradient Conditions with…

› Shim-pack NovaCore
Organic Silica Hybrid Core-Shell Column

Related Solutions

› Pharmaceutical and Biopharmaceutical

› Small Molecule Pharmaceutical

› Price Inquiry

› Product Inquiry

› Technical Service / Support Inquiry

› Other Inquiry