

Application News

Preparative Purification Liquid Chromatograph – Nexera™ Prep

Seamless Purification for Drug Discovery with Screening, Preparative, and Purity check

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User Benefits

- ◆ Automated seamless purification can be performed, which includes screening, preparative, and purity checks.
- ◆ Open access software provides simple operation without complex settings.
- ◆ Nexera Prep achieves a compact footprint superior to a typical preparative LC system by LCMS-2050.

Introduction

In a drug discovery laboratory, the synthesis, screening and purification of target compounds are performed. These steps take significant time thus, a total workflow improvement is required. This article introduces the novel automation in Drug Discovery workflow for target screening, preparative, and purity check with Nexera Prep, which is integrated LC/MS analytical & preparative switching system.

Drug Discovery workflow

In drug discovery, target compound screening, purification, and purity check is performed as conventional workflow. Each task requires manual operations that include sample setting, up-scaling to prep LC, fractionation and purity check. Nexera Prep “LH-40” can change analysis and preparative mode and it achieves fully automated workflow for whole preparative tasks. (Fig.1 and Fig.2)

Nexera Prep with LCMS-2050

The LCMS-2050 single quadrupole mass spectrometer combines the user-friendliness of an LC detector with the excellent performance of MS to provide a complete package of easy-to-use high-level performance and compactness. The small footprint of the LCMS-2050 creates the flexibility to adapt to different needs. As with other LC detectors, it can be integrated into any Shimadzu LC architecture, whether it is a high throughput analytical system or a preparative LC with fraction collection. (Fig. 3)



Fig. 3 Nexera Prep with LCMS-2050

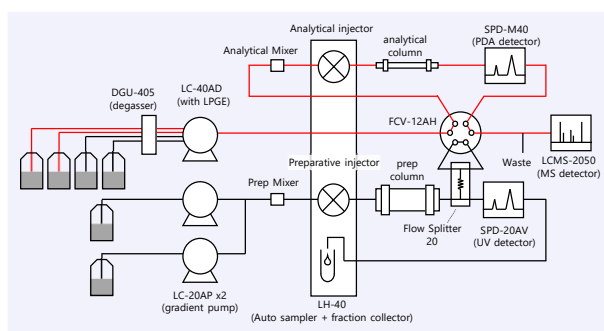


Fig. 1 Flow diagram of Nexera Prep during screening and purity check

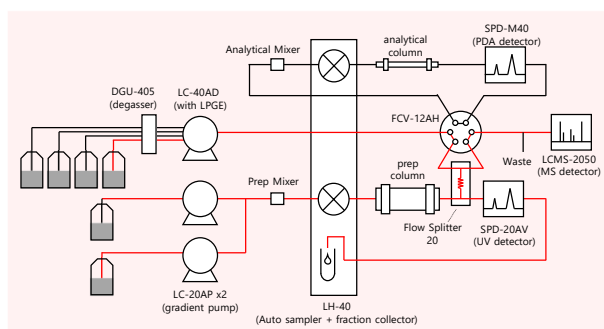


Fig. 2 Flow diagram of Nexera Prep during preparative

Seamless purification by Open Solution™

Open Solution creates a scale-up method using ASAPrep™ algorithm (Automated Scale-up from Analytical to Preparative). This algorithm automatically creates the “focused gradient” which is dedicated gradient profile for preparative scale utilizing information from screening results. (Application note: AD-0261) Open Solution can manage Nexera Prep's analytical & preparative mode. Users can achieve a seamless purification workflow from LC/MS screening, preparative LC/MS, and purity check with one system. (Fig. 4)

Nexera Prep × Open Solution

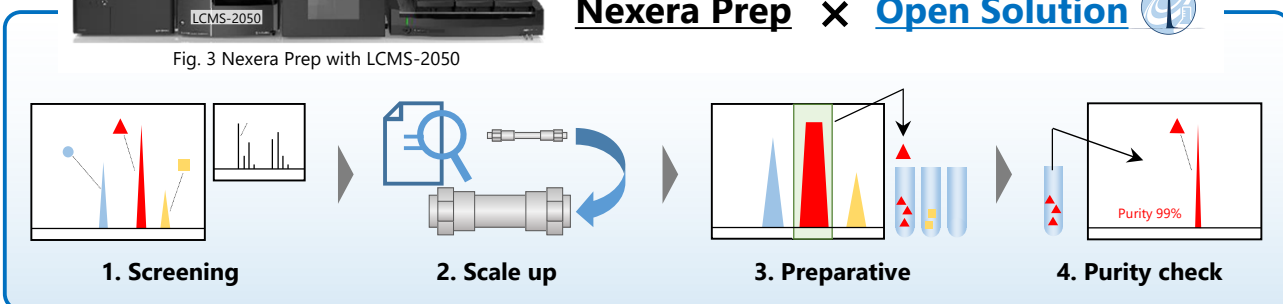
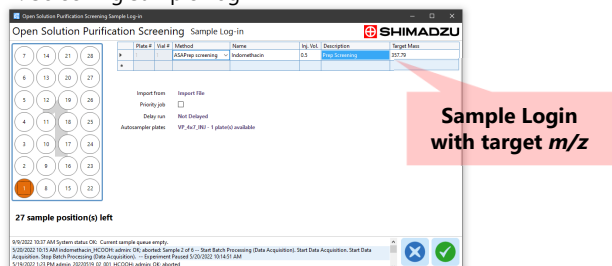


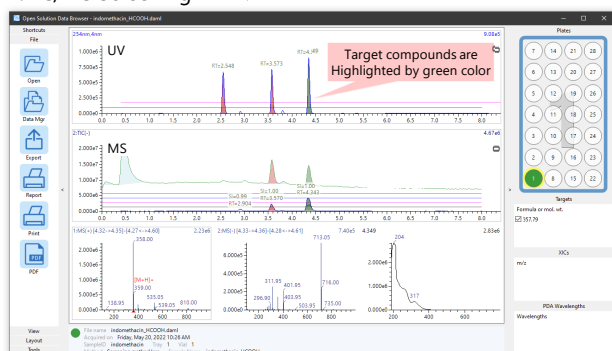
Fig. 4 Seamless purification by Nexera Prep and Open Solution

Purification of crude Drug compound

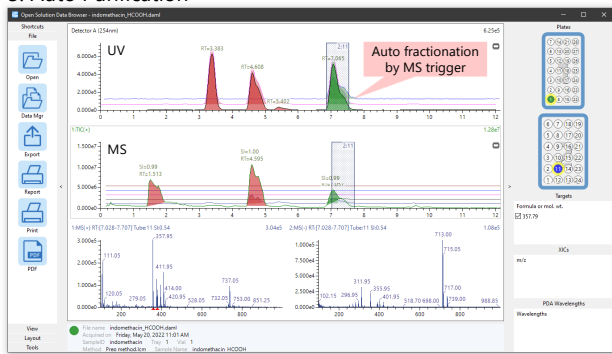
1. Screening Sample Login



2. LC/MS Screening



3. Auto Purification



4. Purity Check

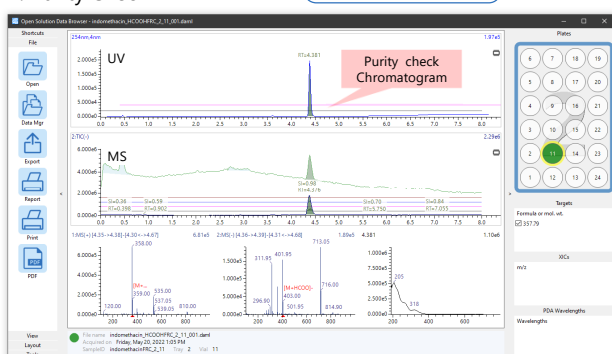


Fig. 5 Operation windows of Open Solution

We performed screening, purification, and purity check against Indomethacin which is a well-known drug compound. Table 1 shows the analytical conditions for the screening and purity check, and Table 2 shows the analytical conditions for the preparative step. The software operation windows are shown in Fig. 5 and obtained chromatograms are shown in Fig. 6.

Table 1 Analysis conditions for screening and purity check step

Column	: Shim-pack™ GISS C18 *1 (50 mm × 3 mm I.D., 1.9 μm)
Mobile phase	: A) 0.1 % formic acid in water (LPGE-A) B) 0.1 % formic acid in acetonitrile (LPGE-B)
Flow rate	: 1.5 mL/min
Time program	: B conc. 10 % (0 min) – 90 % (6-8 min)
Column temp.	: 40 °C
Injection volume	: 0.5 μL (screening: 20 mg/mL in DMSO)
Vial	: 4 mL vial kit *2
Detection	: 254 nm (SPD-M20A)
Pos./Neg., Scan m/z	: 100-1000 (LCMS-2050)
	*1 P/N: 227-30049-01 *2 P/N: : 221-34269-91

Table 2 Analysis conditions for preparative step

Column	: Shim-pack GISS C18 *3 (100 mm × 20 mm I.D., 5 μm)
Mobile phase	: A) 0.1 % formic acid in water B) 0.1 % formic acid in acetonitrile
Flow rate	: 20 mL/min
Make-up	: 1.5 mL/min (methanol, LPGE-D)
Time program	: B conc. XX*4 % (0 min) – XX+20 % (8-12 min)
Column temp.	: Ambient
Injection volume	: 200 μL (20 mg/mL in DMSO)
Vial	: 4 mL vial kit *2
Detection	: 254 nm (SPD-20AV)
Pos./Neg., Scan m/z	: 100-1000 (LCMS-2050)

*3 P/N: 227-30066-02

*4 The value of XX means Initial B conc. obtained by ASAPrep algorithm.

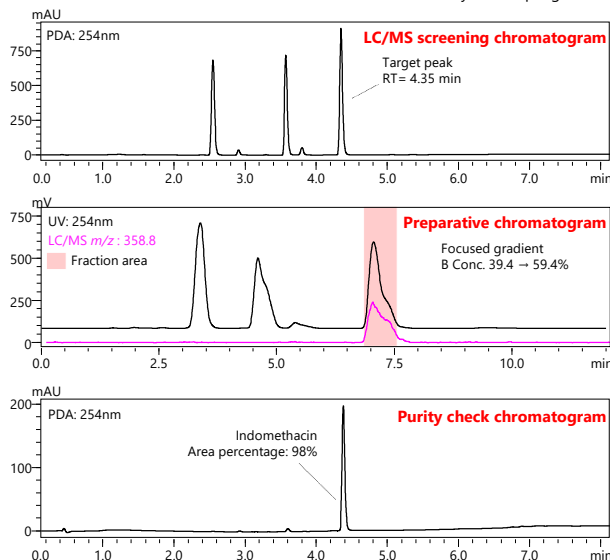


Fig. 6 Chromatograms of screening, preparative, and purity check analysis

Conclusion

This article describes seamless workflow for drug discovery from screening to preparative, and purity check by one system. Nexera Prep with LCMS-2050 and Open Solution software provide easy and labor-saving operations by fully automated purification workflow.

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