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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

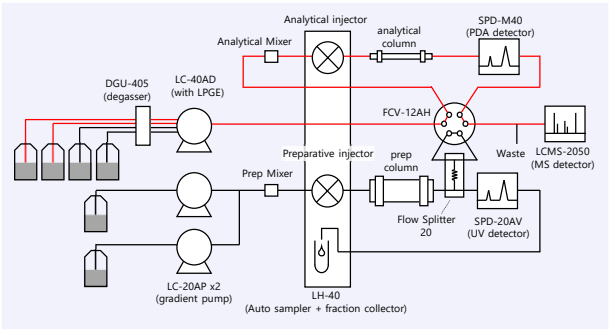


Fig. 1 Flow diagram of Nexera Prep during screening and purity check

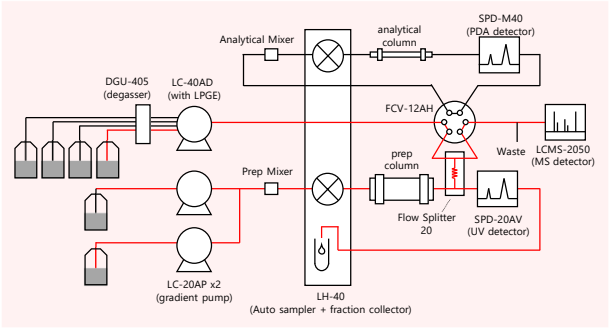


Fig. 2 Flow diagram of Nexera Prep during preparative

■ 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)

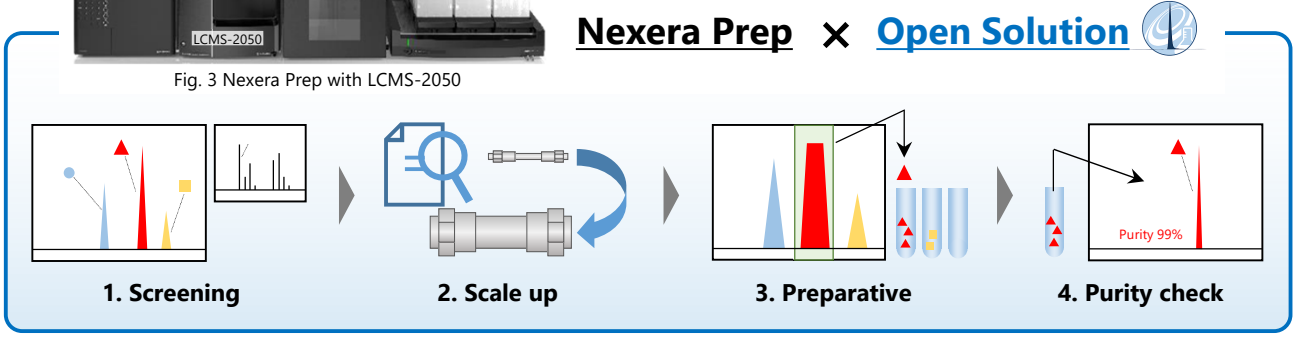
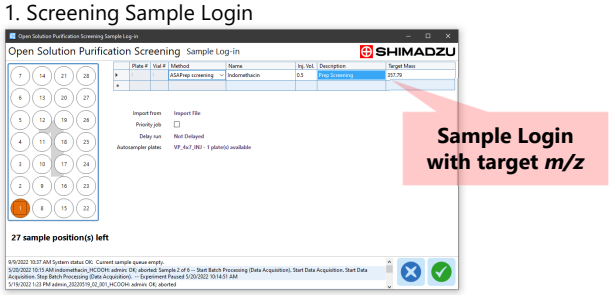


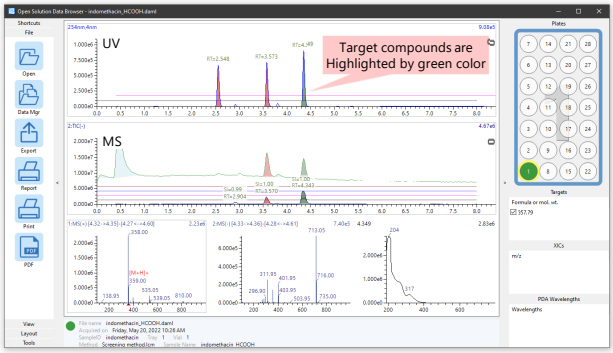
Fig. 4 Seamless purification by Nexera Prep and Open Solution

■ Purification of crude Drug compound

1. Screening Sample Login



2. LC/MS Screening



ASAPrep
Scale up algorithm

3. Auto Purification

Re-inject function

4. Purity Check

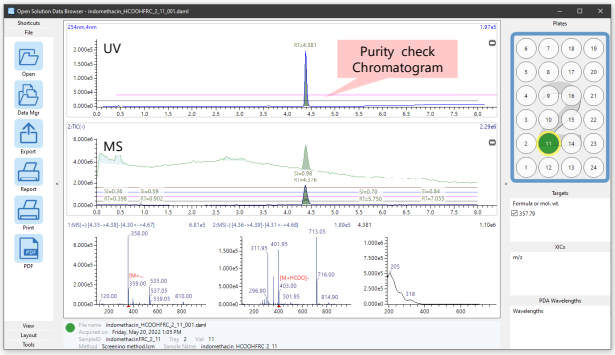


Fig. 5 Operation windows of Open Solution

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 ℃
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.

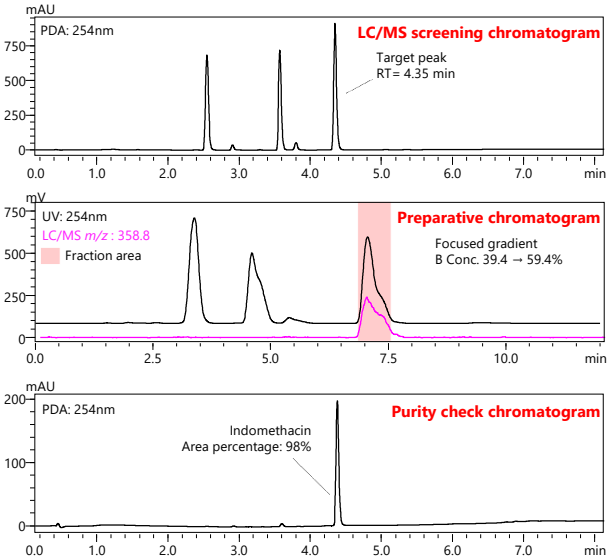


Fig. 6 Chromatograms of screening, preparative, and purity check analysis

■ 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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